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CONTENTS

SHORT COMMUNICATION

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ORIGINAL ARTICLE

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IMPACT OF EARLY EXERCISE-BASED CARDIAC REHABILITATION ON HOSTILITY, ITS BEHAVIORAL COMPONENTS AND DISEASE PERCEPTION IN PATIENTS AFTER MYOCARDIAL INFARCTION

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ABSTRACT

Aim: Hostility and its behavioral components, anger and aggression are psychosocial risk factors for coronary heart disease. The purpose of the study was to evaluate the effectiveness of physical training on the level of negative emotions, the cognitive aspect of adaptation to disease and physical capacity in patients after MI who participated in cardiac rehabilitation.

Materials and Methods: We enrolled 60 post-MI men and women in the study. They underwent an 8-week training program. Before and after completion of trainings patients underwent exercise test and a psychological examination.The Buss-Perry Aggression Questionnaire and the Brief Illness Perception Questionnaire were performed with results analysis in the entire group and in subgroups of men, women, patients under 60 years of age (younger) and over 60 years of age (older).

Results: After rehabilitation a significant reduction in the general level of negative emotions was found in younger: 67.8±4.6 *vs* 63.9±3.7 points ($p< 0.01$). Similarly, a significant reduction in the sense of the impact of the disease on life was found only in younger 6.96±0.5 *vs* 5.48±0.5 points ($p<0.01$). There was a significant improvement in overall adaptation to the disease in women from 40.6±2.2 to 35.7±1.9 points ($p < 0.05$).Moreover,patients with higher levels of negative emotions had more difficulty adapting to the disease $r=0.361$, $p<0.01$. Physical capacity increased significantly in all groups.

Conclusions: Participating in cardiac rehabilitation improved physical capacity, beneficially contributed to a decrease in negative emotions and had a positive effect on disease adaptation but only in younger post -MI patients.

KEY WORDS: hostility, disease perception, cardiac rehabilitatin, negative emotions

INTRODUCTION

Traditional risk factors include dyslipidemia, smoking, hypertension, diabetes, obesity, age, sex, low physical activity and psychosocial factors. Age and sex are unmodifiable factors, others are subject to modification [1-3]. Psychosocial factors include low socioeconomic status, lack of social support, stress at work and in family life, depression, hostility, and anger [4, 5]. Mental health is an important component of the well-being of patients with or at risk of CVD. It is advisable to consider mental health status when assessing and managing patients with CHD [4]. Hostility is a personality trait characterized by a negative attitude toward others, a high level of anger, and a tendency to engage in aggressive social relationships. The current review suggests that anger and hostility are associated with the outcomes of coronary heart disease (CHD) both in healthy and in the CHD population [4, 6-7]. Based on a meta-analysis by Chida et al.,anger and hostility were found to be associated with a 20% increased risk of CHD incidents in healthy individuals and a 24% increase in those with CHD already diagnosed [8]. Hostility is believed to be related to stress reactivity, excessive sympathetic arousal, reduced heart rate variability, inflammation, and platelet aggregation [9-12]. It is not clear whether and how these personality traits can be modified by interventions.There is growing evidence that mental health may be causally linked to biological processes and behaviors that contribute to and cause cardiovascular disease [4]. Previous studies have concluded that prevention and treatment of CHD should focus, among other factors, on psychological management of anger and hostility [7, 8]. However, in practice, access to professional psychological interventions is limited. The impact of exercise-based cardiac rehabilitation, without professional psychological intervention, on the level of these negative emotions has been less studied.Moreover, participation in cardiac rehabilitation helps patients change their beliefs by offering them a different perspective on how to approach the disease. Illness perceptions are the cognitive representations or beliefs that patients have about their illness. These perceptions have been found to be important determinants of behaviour and have been associated with adherence to treatment, rehabilitation, and recovery [13].

AIM

The purpose of the study was to evaluate the effectiveness of exercise training on the level of negative emotions (hostility, anger, aggression), the cognitive aspect of adaptation to disease, and physical capacity in patients after MI who participated in outpatient cardiac rehabilitation (CR).

MATERIALS AND METHODS

We enrolled 60 consecutive post-MI men and women referred to the ambulatory part of the Department of Coronary Artery Disease and Cardiac Rehabilitation. Inclusion criteria were: previous MI within 2 months, clinical stability for at least 2 weeks prior to enrollment in the study, optimal medical treatment. Exclusion criteria were: unstable angina, congestive heart failure, uncontrolled hypertension, valvular heart disease. After exclusion, 60 patients were enrolled in the study protocol. The analysis of the results was carried out in the entire group and in subgroups of men, women, patients under 60 years of age (younger) and over 60 years of age (older).Before and after completing the TP, patients underwent a symptom-limited exercise test on a cycloergometer (EST) and a psychological examination based on the Buss-Perry Aggression Questionnaire(BPAQ) and the Brief Illness Perception Questionnaire (Brief IPQ) [14, 15].After initial investigation, the patients underwent an 8-week TP, started on average 40 days after MI.

The study protocol was approved by the Institutional Ethics Committee on Human Research and each participant gave his/her consent in writing.

All patients underwent EST performed on a cycloergometer with a workload increased every 3 min by 50 Watts (W) using a computerized system Case 8000 Marquette Electronics. ECG was continuously monitored before, during and for 10 min after the test. The following parameters were analyzed: maximum workload (W), duration (min), blood pressure (BP, mmHg), HR (bpm) at rest and at maximum effort.

The Buss-Perry Aggression Questionnaire (BPAQ) consisted of 29 items. Using a five-point scale, respondents indicated to what extent each item fits or does not fit. Based on BPAQ , the level of anger (range 7-35), physical aggression (range 9-45), hostility (range 8-40), verbal aggression (range 5-25) and the general level of negative emotions based on the sum of scores (range 29-145) were evaluated before and after CR.

The Brief Illness Perception Questionnaire (Brief IPQ) consisted of 8 questions on various aspects of cognitive and emotional adjustment to illness and comprehensibility of the illness. Answering those items requires marking the appropriate number of points from 0 to 10 on the scale. Based on the results obtained, the following areas were evaluated: disease consequences, timeline (duration of the disease), personal control, treatment control, identity (the feeling of being burdened with symptoms), concern (worrying about the disease), understanding the disease and emotional response. On scales 1, 2, 5, 6, 8 a lower result in the second measurement means an improvement in the patient's condition, while on scales 3, 4, 7 a higher score means better adaptation to the disease. Furthermore, we have evaluated general adjustment to the disease based on the sum of scores related to all aspects of perception of the disease. Reducing the sum of points is an expression of an improvement in the perception of the disease.

The patients were qualified for TP on the basis of their EST results. The limit of training HR was calculated as the sum of resting HR and 60-80% of HR reserve, i.e. the difference between maximal and resting HR. All of them underwent 24 interval trainings on a cycloergometer 3 times a week. Each training session lasted 40 min and included a 2-minute warm-up, six 4-minute exercise bouts separated by 2-minute rests in between with gradually increasing workload until HR limit achieved during EST was reached. During each session, ECG, HR, and BP were measured at baseline, at the end of each interval, and at recovery.

STATISTICAL ANALYSIS

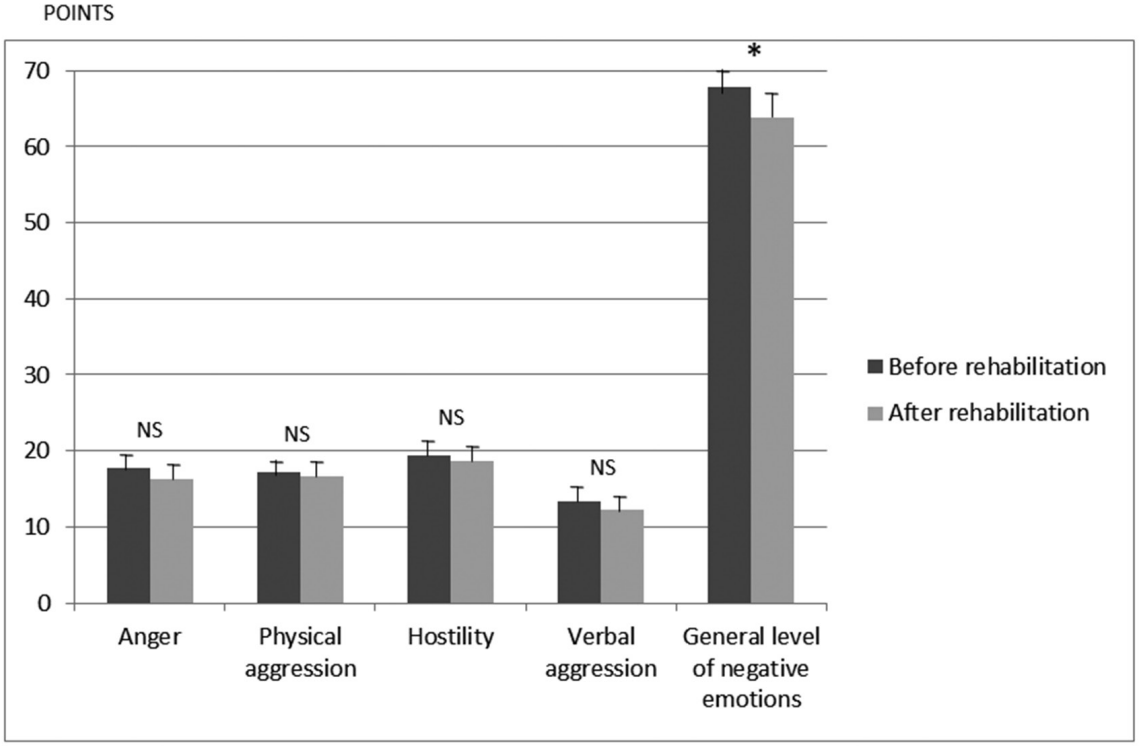
Statistical analysis was performed with the SAS statistical package (version 9.4; Cary NC, USA). The compatibility of the continuous variable distribution with the normal distribution was verified with the Shapiro-Wilk test. The results of continuous variables were presented as mean ± SD in the case of normal distributions or median and quarter range (IQR) in the case of skewed distributions. To compare the parameters of continuous type Student's t-test or nonparametric Wilcoxon and Mann-Whitney tests were used. The strength of the linear relationships between the variables was analyzed using the Spearman correlation coefficients. The results of the nominal variables were presented as an absolute number and %, and the proportion difference was verified by the chi^2 test or Fisher's exact test. $P<0.05$ were considered statistically significant.

RESULTS

We analyzed 60 consecutive post-MI patients referred for early CR. In the studied group, 26 (43%) of the patients were classified as younger (<60 years of age, mean age 50.5±1.2) and 34 (57%) were older (≥60 years of age, mean age 64.7±0.7). The clinical characteristics of the patients studied are listed in Table 1. Most of them had hypertension and hypercholesterolemia. There were no differences between men and women in terms of age, coronary risk factors, clinical status, and concomitant medications. Only female patients waited significantly longer for CR than our male patients.

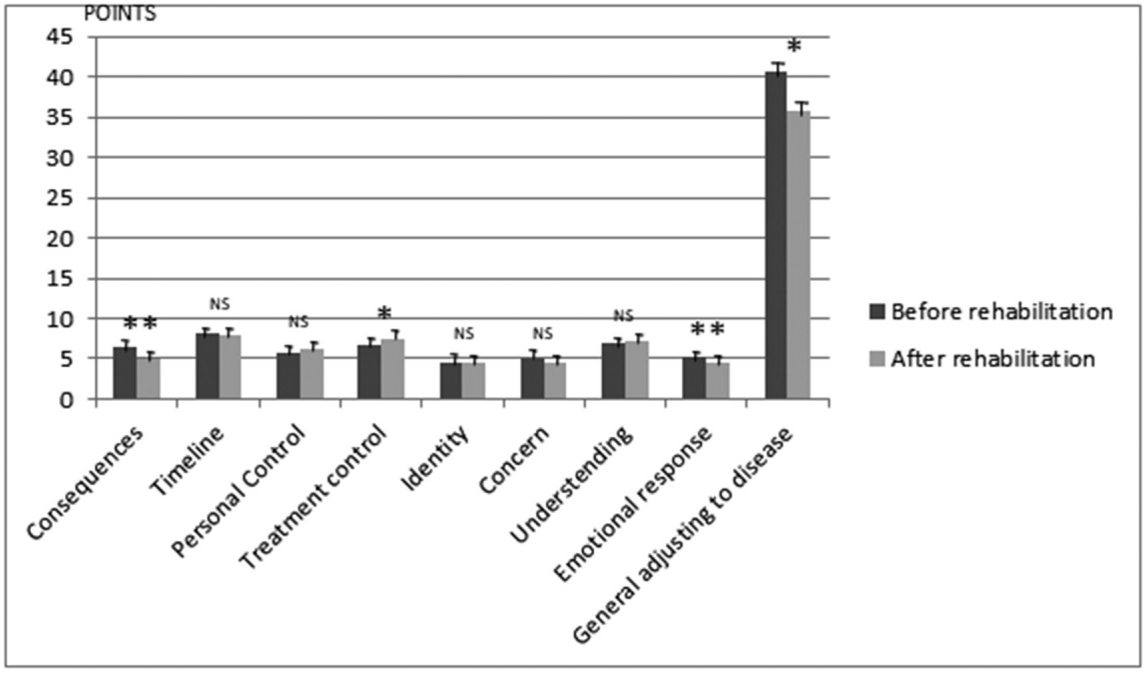
The examined group had a moderate level of negative emotions of 67.15±2.4 points. The subgroups of men, women, and elderly patients also had a moderate level of aggression, adequate 65.73±3.9, 68.52±2.8, 66.62±2.3 points. After CR only a significant reduction in the general level of negative emotions was found in the younger group (Fig. 1). There were no changes in the level of aggression and its components, both in the entire study group and in other subgroups.

After CR, the dimension of perceived consequences of the disease on life decreased significantly in the entire study group from 6.49±0.4 to 5.51±0.3 points ($p<0.01$). In the subgroup of women, there was a significant improvement in overall



*All values are mean ±SD.*P <0.05 vs. baseline.*

Fig. 1. Changes in the level of negative emotions in patients under 60 years of age due to exercise-based rehabilitation.



*All values are mean ±SD.*P < 0.05,**P < 0.01 vs. baseline.*

Fig. 2. Changes in disease adjustment in women due to exercise-based rehabilitation.

adjustment to the disease and the impact of treatment on the disease, as well as a significant reduction in the perceived impact of the disease on life (illness consequences) and the emotional response (Fig. 2). In the subgroup of men, no significant changes in perception of the disease and adaptation to the disease and treatment were observed. A significant reduction in the sense of the impact of the disease on life was found only in younger patients after CR from 6.96±0.5 to 5.48±0.5 points ($p<0.01$). In the elderly group, no differences were found in adaptation to the disease.In the entire group, a positive correlation was found between disease perception and the level of aggression and its components. Patients with higher levels of negative emotions had more difficulty adapting to the disease (Table 2).

Table 1. Clinical characteristics of the study groups

	All groups (n=60)	Men (n=30)	Women(n=30)	p-value
Age [yr]	58.3± 8.4	57.5 ± 9.2	59.0 ± 7.5	NS
Younger<60 yr old, n(%)	26(43.3)	14 (53.8)	12(46.2)	NS
Elderly≥60 yr old n (%)	34 (56.7)	16 (47.1)	18 (52.9)	NS
History of MI, n (%)	30 (100)	30 (100)	30 (100)	NS
Hypertension, n (%)	48 (80.0)	26 (86.7)	22 (73.3)	NS
Type 2 DM, n (%)	16 (26.6)	9 (30.0)	7 (23.3)	NS
Hypercholesterolemia, n (%)	49 (81.7)	23 (76.7)	26 (86.6)	NS
Time to CR, days	40.7 ± 27.8	42.9 ± 27.5	48.0 ± 29.0	p < 0.05
LVEF [%]	54.3 ± 8.6	54.6 ± 8.3	54.0 ± 8.8	NS
Smoking	27(45.0)	11(36.7)	16(53.3)	NS
B-blockers, n (%)	59 (98.3)	30 (100)	29 (96.7)	NS
ACE-I, n (%)	47 (78.3)	26 (86.7)	21 (70.0)	NS
Statins, n (%)	58 (96.7)	29 (96.7)	29 (96.7)	NS
Clopidogrel, n (%)	23 (37.0)	12 (40.0)	11 (36.6)	NS
Ticagrelol, n (%)	35 (58.3)	17 (56.7)	18 (60.0)	NS
Aspirin, n (%)	59 (98.3)	29 (96.7)	30 (100)	NS

ACE-I - angiotensin converting enzyme inhibitors; CR - cardiac rehabilitation; DM - diabetes mellitus; LVEF - left ventricular ejection fraction;

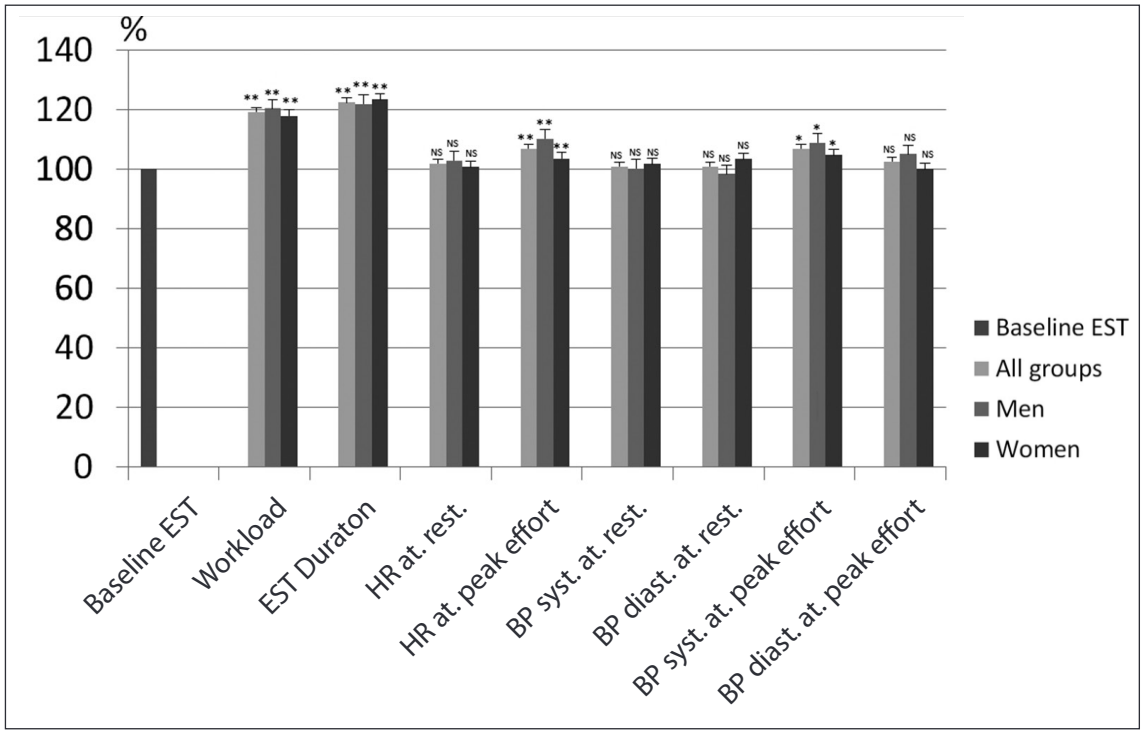
Table 2. The correlation between adaptation to the disease and the level of aggression hostility and anger

	Correlation coefficient r	Anger	Physical aggression	Hostility	Verbal aggression	General level of negative emotions
			P-value			
Illness consequence	r	0.189	0.345	0.234	0.039	0.249
	P	NS	<0.01	NS	NS	<0.05
Identity	r	0.270	0.240	0.053	0.297	0.257
	P	<0 .05	NS	NS	<0.05	<0.05
Emotional response	r	0.395	0.235	0.230	0.278	0.384
	P	< 0.01	NS	NS	< 0.05	<0 .01
General adjustment to the disease	r	0.316	0.363	0.180	0.140	0.361
	P	< 0.05	< 0.01	NS	NS	<0.01

Physical capacity improved significantly after TP in the entire study group and separately in men and women. In the entire group, an increase in the duration of EST was 22% and the workload 19%, while in men they were 22 % and 20%, and in women 23% and 18%, respectively (Fig. 3).

DISCUSSION

The benefits of comprehensive cardiac rehabilitation and supervised exercise training for patients with coronary heart disease have been well documented [16]. Apart from improving physical capacity, the effects of CR include improvement of mental competence [17]. The preponderance of evidence suggests that interventions to improve mental health may have beneficial effects on cardiovascular health [4]. The main finding of this study is that exercise training even without professional psychological intervention contributed to a decrease in negative emotions in younger patients after MI under 60 years of age and had a positive effect on adaptation to the disease in younger men and in women, regardless of age. Younger people, both women and men, are more susceptible and have greater possibilities to release emotions under the influence of physical activity. Older people have better emotional control, a higher sense of responsibility in social relationships, but they are less spontaneous, characterized by rather mental stiffness that is related to aging of the organism [18, 19].To our knowledge, our study was the first to evaluate the influence of exercise training alone without psychological intervention on negative emotions in patients after MI. In the available literature, researchers achieved a reduction in the level of negative emotions in patients undergoing CR but only under the influence of psychological interventions. Menarquez et al. achieved a reduction in the level of anxiety, depresion, and anger in



P <0.05,P < 0.01 vs. baseline EST. EST – exercise stress test; HR – heart rate; BP – blood pressure; diast. – diastolic; syst. – systolic.*

Fig. 3. Percentage changes in the results of the exercise stress test in all studied groups and separately in men and women before and after cardiac rehabilitation.

a group of 33 patients after MI and an episode of unstable coronary heart disease [20]. In the study of Hazelton et al. 380 people (67.9% men and 32.1% women) underwent comprehensive CR, including psychological intervention. They obtained a reduction in anger level in the men's group [21].In our study, participation in exercise-based rehabilitation without psychological support also had a positive effect on adaptation to the disease in women and younger people after MI. Marogna et al. obtained similar results in a group of 67 patients after CR, but with psychological intervention [22]. In our study, we also found a positive correlation between disease perception and the level of aggression and its components after CR in post-MI patients. Patients with a higher level of negative emotions had more difficulty adapting to the illness. People with a tendency toward aggression may adapt to the disease consequences worse because they perceive the illness as weakness. They feel more burdened with the disease symptoms, they look for the culprits of the current situation, and target their aggression towards the environment. However, negative emotions can also be significant motivators for specific behaviors, e.g. putting more effort to showing yourself in a better light during competition or social challenges. Therefore, an increased level of aggression can act as a stimulator for taking actions, e.g., physical activity. For example, in the study by Kim et al., anger positively influenced the effectiveness of a healthy lifestyle, including exercises, in a group of 208 hypertensive women over 65 years of age [23]. In our study, we also found that an 8-week TP not only positively influenced the manifestation of negative emotions, but also led to a significant improvement in physical capacity in all trained patients and separately in men and women. The positive effects of TP on physical capacity have been well documented in the literature [16, 24]. In summary, we found that exercise-based CR even without professional psychological intervention decreased the level of negative emotions in people under 60 years of age and had a positive effect on adaptation to the disease in women regardless of age and younger men after MI. Furthermore, exercise training as the basic element of CR resulted in an improvement in physical capacity, which is a parameter of a good prognosis in patients with CHD [25].

LIMITATIONS

An acknowledged limitation of this study is the lack of a non exercised control group. However, at present, it is considered unethical to suggest that post-MI patients avoid physical activity. Moreover, the small number of patients limits the generalizability of our results.

CONCLUSIONS

1. Participation in the physical training program improved physical capacity and contributed beneficially to a decrease in negative emotions but only in younger patients under 60 years of age after MI.

2. Younger people after MI were more prone to lowering the level of negative emotions under the influence of exercise training.
3. Participation in exercise-based rehabilitation even without professional psychological intervention had a positive effect on disease adaptation in younger men under 60 years of age and in women regardless of age.
4. Patients after myocardial infarction with a higher level of negative emotions had more difficulty adapting to the disease.

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CONFLICT OF INTEREST
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ORIGINAL ARTICLE

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MORPHOLOGICAL CHARACTERISTICS OF REPARATIVE OSTEOGENESIS IN THE RATS LOWER JAW UNDER THE CONDITIONS OF USING ELECTRICAL STIMULATION

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ABSTRACT

Aim: The purpose of the study was to identify the morphological features of reparative osteogenesis in the rats lower jaw under the conditions of using electrical stimulation.

Materials and Methods: An experiment was conducted on 24 mature male rats of the WAG population. Two groups were formed. Group 1 included 12 rats that were modeled with a perforated defect of the lower jaw body. Group 2 included 12 animals that were modeled with a perforated defect similar to group 1. In animals, a microdevice for electrical action was implanted subcutaneously in the neck area on the side of the simulated bone defect (a temporary Videx AG 4 battery; a constant sinusoidal electric current of an unchanging nature 1 milliampere, frequency 30 W). The negative electrode connected to the negative pole of the battery was in contact with the bone defect. The battery and electrode were insulated with plastic heat shrink material. Morphological and statistical methods were used.

Results: The positive effect of electrical stimulation on reparative osteogenesis was due to a decrease in the severity of hemodynamic disorders, activation of angiogenesis in granulation tissue, which was one of the components of the regenerate that filled the bone defect, matured and turned into connective tissue; stimulation of the proliferative potential of fibroblastic cells and cells with osteoblastic activity in granulation tissue; increasing the proliferative potential of osteoblastic elements of bone tissue bordering the cavity; stimulation of macrophage cells and processes of cleansing the bone cavity from fragments of a blood clot and alteratively changed tissues; formation of clusters of adipocytes in the loci of connective and granulation tissue of the regenerate; the process of metaplasia of connective tissue into bone tissue; an increase of the foci of hematopoiesis in the intertrabecular spaces of lamellar bone tissue.

Conclusions: A comprehensive clinical and experimental study conducted by the authors proved that electrical stimulation activates the reparative osteogenesis in the lower jaw, which occurs through direct osteogenesis and does not finish on the 28th day of the experiment.

KEY WORDS: electrical stimulation, rats, morphology, reparative osteogenesis, lower jaw

INTRODUCTION

Trauma is the most common cause of maxillofacial injuries. The epidemiology of maxillofacial fractures varies according to geographical areas and socio-economic factors [1]. Maxillofacial fractures have a multi-factorial etiology (road traffic accidents, accidental falls, assaults, industrial mishaps, sports injuries, firearm injuries etc.) [2]. Mandibular fractures are the most common fractures of facial skeleton. Fractures of the mandible account for 36% to 59% of all maxillofacial fractures [3, 4].

Treatment of patients with mandibular fractures is a pressing issue of medical and social importance. The main goal of treatment for this category of patients is restoration of the anatomical integrity of the lower jaw. Known surgical methods of treatment do not allow for complete high-quality reposition, fixation of bone fragments, and entail the development of posttraumatic and postoperative complications [5, 6]. Recent facts indicate the need, together with the treatment, to use methods of stimulating reparative osteogenesis, which would lead to rapid and high-quality restoration of the bone tissue of the lower jaw. Today, biological and physical methods for stimulating reparative osteogenesis are known [7]. One of the physical and promising methods may be the use of electrical stimulation.

AIM

The purpose of the study was to identify the morphological features of reparative osteogenesis in the rats lower jaw under the conditions of using electrical stimulation.

MATERIALS AND METHODS

An experiment was conducted on 24 mature male rats of the WAG population. Two groups were formed.

Group 1 included 12 rats that were modeled with a perforated defect of the lower jaw body. Anesthetized rats underwent a 1.0-1.2 cm long incision of the skin, subcutaneous tissue, and superficial fascia in the left submandibular area. A fragment of the outer surface of the branch and body of the lower jaw was skeletonized. With a ball-shaped drill and a straight tip with a diameter of 3.0 mm, a transcortical perforated defect of the body of the lower jaw was formed in the form of a channel, departing from the lower edge of the jaw upwards by 2 mm. The wound was sutured in layers with vicryl.

Group 2 included 12 animals that were modeled with a perforated defect similar to group 1. In animals, a microdevice for electrical action was implanted subcutaneously in the neck area on the side of the simulated bone defect (a temporary Videx AG 4 battery; a constant sinusoidal electric current of an unchanging nature 1 milliampere, frequency 30 W). The negative electrode connected to the negative pole of the battery was in contact with the bone defect. The battery and electrode were insulated with plastic heat shrink material.

In groups 1 and 2 the animals were removed from the experiment on 3, 7, 14 and 28 days (3 animals for each experimental period).

The study material was a fragment of the body of the lower jaw from the zone of the perforated defect modeling. The material was fixed in a 10% solution of neutral formalin (pH 7.4) for 24-48 hours, decalcified, carried out according to the generally accepted method and embedded in paraffin. From paraffin blocks, serial sections with a thickness of 4-5 μm were made, which were stained with hematoxylin and eosin, picrofuchsin according to van Gieson.

Examination of the microslides was carried out using a laboratory microscope ZEISS Primostar 3 (Carl Zeiss, Germany) with a built-in color digital camera. Morphometry was carried out using the Labscope program, during which the specific volumes of the fibrous, cellular and vascular components of granulation tissue were calculated at different experimental periods.

The indicators in the groups were processed statistically using the Statistica 10.0 program. Mean values of indicators in groups were compared using the non-parametric Mann-Whitney U-test. Differences were considered significant at $p<0.05$.

RESULTS

During survey microscopy on the 3rd day of the experiment, a bone defect was discovered in the lower jaw of rats of groups 1 and 2, passing through the entire thickness of the jaw. The defect cavity in both groups was filled with a blood clot; fragments of the epithelial layer, muscle, connective and bone tissues with dystrophic and necrotic changes, diffuse infiltration of neutrophilic leukocytes, macrophages, lymphocytes and histiocytes.

In group 2, compared to group 1, in the bone defect cavity there were significantly fewer blood clot fragments and alteratively changed tissues, and in the latter, diffuse cellular infiltration was characterized by a lower content of neutrophilic leukocytes and a larger number of the cells of macrophage line. Small loci of granulation tissue were also found in the bone defect cavity. The latter in group 1 was visualized at the edges of the bone defect, and in group 2 – at the edges and central part.

In groups 1 and 2, the granulation tissue was characterized by the presence of fibrous (specific volume in group 1 – (23.5±0.55)%, in group 2 – (34.3±0.94)%), vascular (specific volume in group 1 – (11.7±0.60)%, in group 2 – (21.5±0.67)%) and cellular (specific volume in group 1 – (64.8±0, 76)%, in group 2 – (44.2±1.31)%) components, among which the latter prevailed, which is a characteristic feature of immature granulation tissue (Fig. 1a, 1b).

In both groups, the fibrous component of the granulation tissue was characterized by the presence of thin branched connective tissue fibers. The cellular component was represented by neutrophilic leukocytes, macrophages, lymphocytes, histiocytes, fibroblastic differon cells. The latter in group 2 compared to group 1 was characterized by a lower content of neutrophilic leukocytes and a greater number of macrophages and cells of the fibroblastic series (Fig. 1a, 1b).

The vascular component was represented by vessels of different shapes and sizes, and in group 2 compared to group 1 the diameter of the vessels was significantly smaller. In group 1, granulation tissue was characterized by severe hemodynamic disturbances, manifested by dilation and congestion of blood vessels, edematous changes in the vascular walls, perivascular edema, formation of thrombi in the cavity of some vessels, small focal hemorrhages (Fig. 1a).

A comparative intergroup analysis of the obtained morphometric parameters showed a more pronounced degree of maturity of granulation tissue in group 2 compared to group 1, as evidenced by a larger ($p<0.05$) value of the specific volume of fibrous and vascular components, a smaller ($p<0.05$) value of the specific volume of cellular component.

In the bone cavity on the 7th day compared to the previous period in group 1 and especially in group 2 a more pronounced decrease in blood clot elements and alteratively changed tissues, an increase in the volume of granulation tissue, and the appearance of connective and osteogenic fibroreticular tissues were revealed (Fig. 2). On the 7th day compared to the 3rd day the granulation tissue became more mature, as evidenced by an increase ($p<0.05$) of the specific volumes of fibrous (in group 1 – (35.3±0.81)%, in group 2 – (45.8±0.49)%) and vascular (in group 1 – (20.8±0.44)%, in group 2 – (39.0±0.71)%) components, a decrease ($p<0.05$) of the specific volume of cellular component (in group 1 – (43.9±0.81)%, in group 2 – (15.2±0.8)%).

Also, compared to the previous term, on the 7th day, in some of the fields of vision, the granulation tissue turned into connective tissue. In group 1, hemodynamic disturbances in the granulation and connective tissues similar to the 3rd day were found (Fig. 3). In group 2, compared to group 1, the

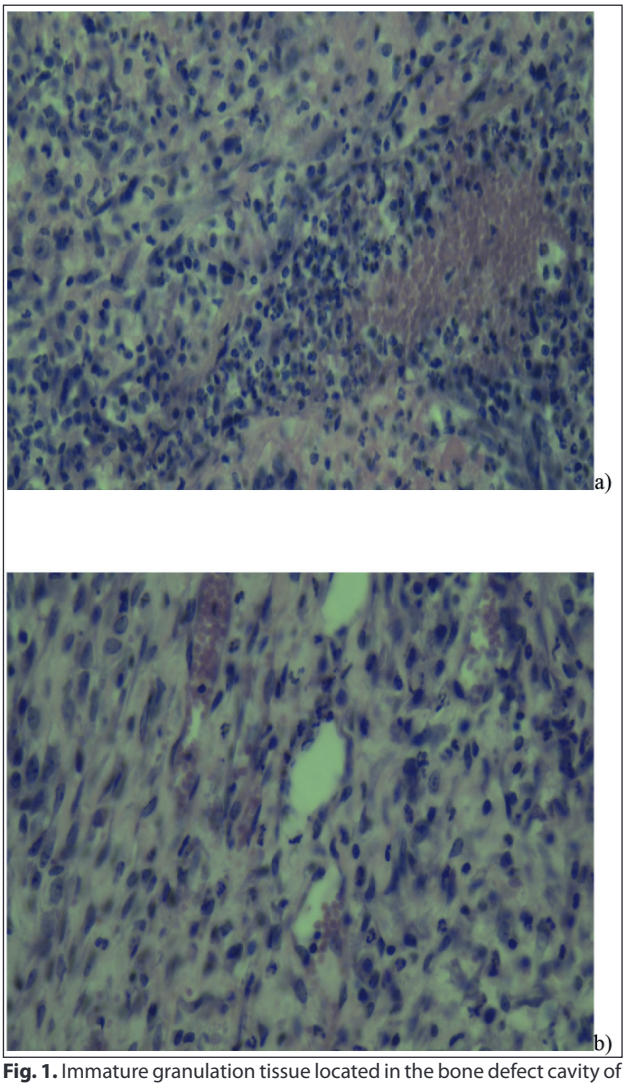

Fig. 1. Immature granulation tissue located in the bone defect cavity of the lower jaw of a rat from group 1 (a) and group 2 (b). Hemodynamic disturbances in granulation tissue in group 1 (a). Hematoxylin and eosin staining, × a) 400, × b) 400.

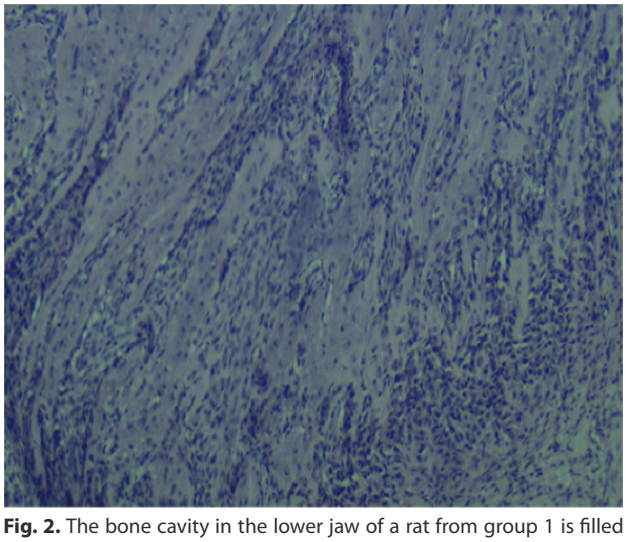

Fig. 2. The bone cavity in the lower jaw of a rat from group 1 is filled with regenerate, represented by granulation, connective and osteogenic fibroreticular tissues. Hematoxylin and eosin staining, ×400.

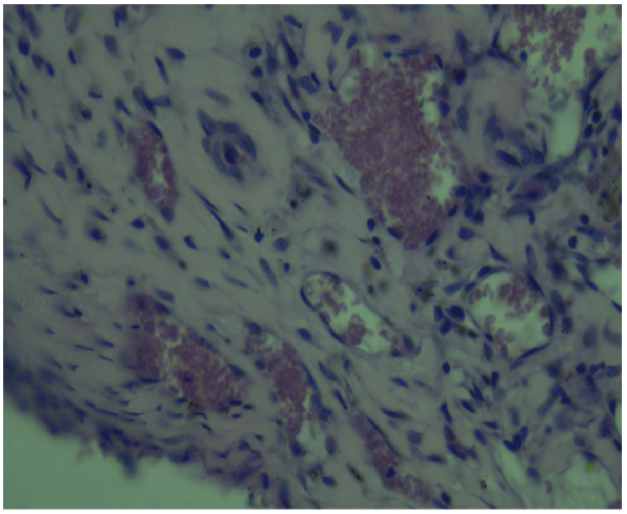

Fig. 3. Hemodynamic disturbances in granulation tissue located in the bone defect cavity of the lower jaw of a rat from group 1. Cells with pronounced osteoblastic activity are mainly around the blood vessels. Hematoxylin and eosin staining, ×400.

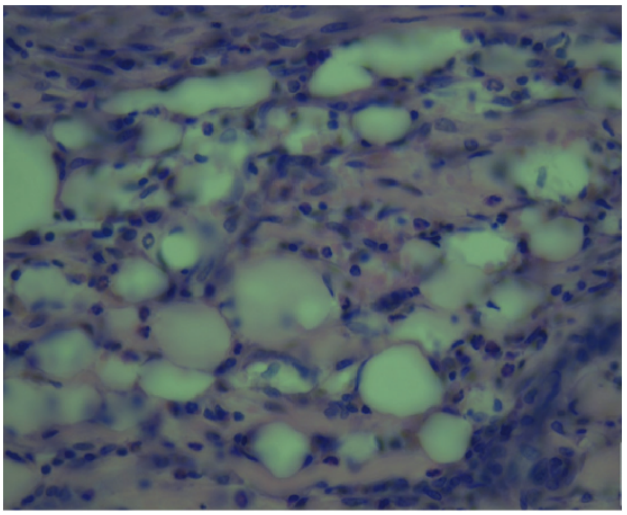

Fig. 4. Groups of adipocytes in the regenerate filling the bone cavity of the lower jaw of a rat from group 2. Hematoxylin and eosin staining, ×400.

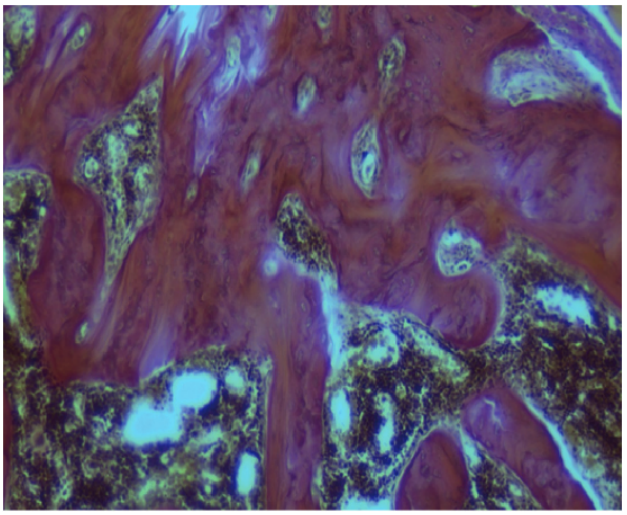

Fig. 5. Lamellar bone tissue from the regenerate area in a rat from group 2. Staining with picrofuchsin according to van Gieson, × 400.

specific volumes of fibrous and vascular components had a significantly ($p<0.05$) greater value, the specific volume of cellular component was significantly ($p<0.05$) smaller, which indicated a greater degree of granulation tissue maturity in group 2.

The appearance of osteogenic fibroreticular tissue in the regenerate in both groups, from our point of view, was due to the activation of the proliferative potential of osteoblastic elements of the bone tissue bordering the cavity; the appearance in granulation and connective tissues of cells with pronounced osteoblastic activity, mainly around the vessels (Fig. 3). The latter microscopic findings were more pronounced in group 2 compared to group 1. In group 2, groups of adipocytes of different sizes and round-oval shapes were found in the bone cavity between the connective tissue fibers, in the areas of granulation tissue (Fig. 4).

On the 14th day, the regenerate filling the bone cavity in the lower jaw of rats of both groups was represented by granulation, connective, osteogenic fibroreticular and lamellar bone tissues. In these animals compared to 7th day in group 1 the volume of granulation, connective and osteogenic fibroreticular tissue increased, but in group 2 the volume of granulation and connective tissue decreased and the volume of osteogenic fibroreticular tissue increased. In group 2 on the 14th day compared to the 7th day the number of adipocytes in the granulation and connective tissues localization increased. On the 14th day in group 2 compared to group 1 the volume of granulation and connective tissues was smaller, while the volume of osteogenic fibroreticular and lamellar bone tissues was larger, which indicated more intensive and qualitative healing processes.

More intensive bone defect healing processes in group 2 compared to group 1 were also evidenced by the results of the morphometric study of granulation tissue. Thus, in group 2 compared to group 1, the specific volumes of fibrous (in group 1 – (64.3±1.00)%, in group 2 – (79.7±0.76)%) and vascular (in group 1 – (5.7±0.45)%, in group 2 – (13.9±0.31)%) components had a significantly ($p<0.05$) greater value, but the specific volume of cellular component (in group 1 – (30.0±0.94)%, in group 2 – (6.4±0.81)%) had a significantly ($p<0.05$) smaller value.

In group 2, in the lamellar bone tissue, the intertrabecular spaces were filled with connective tissue, with the presence of foci of hematopoiesis in some of them. Areas of connective tissue metaplasia into bone tissue were also noted in group 2.

On the 28th day, the bone cavity in both groups was filled with connective, osteogenic fibroreticular and lamellar bone tissues. In group 2, compared to group 1, the healing processes of the bone defect occurred more intensively, which was evidenced by a smaller volume of connective and osteogenic fibroreticular tissues, a larger volume of lamellar bone tissue (Fig. 5). In group 2, compared to the 14th day, adipocyte clusters were visualized in the connective tissue locations, the number of which was significantly smaller. Foci of hematopoiesis were found in the intertrabecular spaces of lamellar bone tissue, the number of which was significantly greater in group 2 compared to group 1. The bone beams in the lamellar bone tissue did not have an orderly spatial orientation in both groups. Consequently, on the 28th day of the experiment in rats of both groups, reparative osteogenesis in the lower jaw continued, but this process occurred more intensively in group 2, as evidenced by the fact that the majority of the regenerate volume was lamellar bone tissue.

DISCUSSION

The bone tissue of the lower jaw is characterized by good regenerative properties, due to which its damage can be restored. Regeneration of bone tissue, as is known, is a staged process that occurs rather slowly [8]. Data from molecular biology, biochemistry, morphology and genetics made it possible to distinguish the following stages of reparative osteogenesis: alterative-resorptive; degenerative-inflammatory and proliferative; synthetic; remodeling and finishing [9, 10].

The search of methods for stimulating reparative osteogenesis is an urgent issue today and a priority for scientific research. Data from the literature and the results of a complex experimental and morphological study conducted by the authors prove the effectiveness of the method of electrical stimulation of reparative osteogenesis in the lower jaw. The latter occurs through direct osteogenesis, but the regeneration process, as is known, can occur through indirect osteogenesis [11]. The positive effect of electrical stimulation revealed by the authors is due to several mechanisms.

The results of the authors' morphometric study of the granulation tissue, which was one of the components of the regenerate that filled the bone defect, revealed significantly higher values of the specific volume of blood vessels during electrical stimulation compared to the control group. This fact indicates that the applied method stimulates angiogenesis. Blood vessels, as is known, transport oxygen, nutrients, soluble factors, numerous cells, etc. [12]. Survey microscopy and morphometry showed that neovascularization stimulated the maturation of granulation tissue and its further transformation into connective tissue, and activated the proliferative potential of fibroblastic cells and cells with osteoblastic activity.

Neovascularization is important in the processes of reparative osteogenesis. Bone tissue renewal can be outlined as a complicated mechanism centered on the interaction between osteogenic and angiogenic events capable of leading to bone formation and tissue renovation [12]. In the conditions of insufficient angiogenesis and hypoxia, the intensity of the reparative osteogenesis processes decreases [13]. Some studies have shown that under hypoxic conditions, the regeneration process occurs through indirect osteogenesis [14].

Electrical stimulation acted as a factor activating macrophage cells, which contributed to a more intensive cleansing of the bone cavity from blood clot fragments and alteratively changed tissues, which also had a positive effect on the processes of reparative osteogenesis.

An interesting fact was the presence of groups of adipocytes

of different sizes and shapes in the loci of connective and granulation tissues in the regenerate, which filled the bone cavity in the lower jaw of rats in cases of electrical stimulation. The presence of these cells suggests their participation in the processes of reparative osteogenesis.

Some studies have shown that adipocytes play an important role in the reparative osteogenesis of maxillofacial defects. The effectiveness of the use of mesenchymal stem cells obtained from adipose tissue in the treatment of bone tissue defects has been proven. These cells are characterized by an active ability to directly differentiate into mature osteoblasts; produce chemokines which useful for facilitating the homing of endogenous stem cells to the site of the bone defect [15]. In the study conducted by the authors, under the conditions of electrical stimulation, adipose tissue was transformed into bone tissue in the regenerate that filled the bone cavity.

The use of electrical stimulation for reparative osteogenesis activation has been studied for many years in both in vitro and in vivo models using numerous approaches ranging from different configurations, electrode parameters, and electrical current sources [16-18]. Numerous clinical and experimental studies have proven the effectiveness of electrical stimulation due to the effect on the migration, proliferation, differentiation, adhesion, and function of bone-forming cells; activation the transformation of stem cells into osteogenic cells [18-20]; involvement in the locus of bone tissue damage the cells necessary for healing (neutrophils, macrophages, fibroblastic cells, etc.); activation chondrogenesis in cases of regeneration through indirect osteogenesis [18]; activation nervous regulation, thereby activating microcirculation.

The effect of electrical stimulation on cell apoptosis remains unclear and controversial. Some studies report stimulation of cell apoptosis, while other studies describe a reduced effect or its absence [18].

Previous studies conducted by the authors showed a positive effect of combined use of hydroxyapatite-containing osteotropic material ("Biomin GT") and electrical stimulation in the treatment of bone tissue defects of the lower jaw in rats [21].

CONCLUSIONS

A comprehensive clinical and experimental study conducted by the authors proved that electrical stimulation activates the reparative osteogenesis in the lower jaw, which occurs through direct osteogenesis and does not finish on the 28th day of the experiment.

The positive effect of electrical stimulation is due to a decrease in the severity of hemodynamic disorders, activation of angiogenesis in granulation tissue, which is one of the components of the regenerate that fills the bone defect, matures and turns into connective tissue; stimulation of the proliferative potential of fibroblastic cells and cells with osteoblastic activity in granulation tissue; increasing the proliferative potential of osteoblastic elements of bone tissue bordering the cavity; stimulation of macrophage cells and processes of cleansing the bone cavity from fragments of a blood clot and alteratively changed tissues; formation of clusters of adipocytes in the loci of connective and granulation tissue of the regenerate; the process of metaplasia of connective tissue into bone tissue; an increase of the foci of hematopoiesis in the intertrabecular spaces of lamellar bone tissue.

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A MEDICAL AND SOCIOLOGICAL STUDY AMONG DOCTORS ON THE MOTIVATIONAL COMPONENT OF ENSURING THE QUALITY OF MEDICAL CARE IN HEALTH CARE FACILITIES

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ABSTRACT

Aim: To analyze the impact of medical reform on the motivational component of improving the quality of medical care in health care facilities in Sumy based on the results of amedical and sociological study of doctors.

Materials and Methods: The study involved 154 doctors working in inpatient and outpatient departments of health care facilities in Sumy. Sumy in June-August 2023. The studyused a systematic approach, bibliosemantic, comparative and statistical analysis, and logical generalization. The data were processed and statistically analyzed using Google Forms and Microsoft Excel 2010 for Windows.

Results: The study showed that 49 respondents (31.8%) are satisfied with the material and technical support at the workplace and working conditions. Almost all doctors (138 people(89.6%)) said that the actual amount of their salary does not correspond (partially or fully) to the workload at the workplace. Only 4.5% of them said that they receive extra payments for thequality of healthcare services, 21.4% of them said that they receive extra payments periodically,and 74.1% said that they do not receive extra payments at all. Despite the high level of workloadand dissatisfaction with salaries, the majority of respondents (109 people (70.2%)) would not agree to change their profession to another one, even if the salary was higher. According to doctors, the most important incentives for improving the quality of healthcare services are: moral satisfaction from work and well-coordinated teamwork (76.6% of answers), financial incentives (74.7% of answers), opportunities for professional and career growth (48.7% of answers), respect from patients and society (46.8% of answers), and management recognition (13.6% of answers).

Conclusions: The study has shown that today, in the context of health care system reform,there is practically no effective motivational component to improve the quality of health care in health care facilities in Sumy: 40.9% of people gave negative answers, 42.2% of people indicated only its partial existence. Regardless of the length of service, for all respondents, oneof the most important motivational incentives is not only material but also moral factors and public recognition.

KEY WORDS: quality of medical care, motivational component of quality improvement,health care facility, health care reform, health care workers

INTRODUCTION

The level of job satisfaction and motivation of health care workers (HCWs) are crucial factors for both health care facilities (HCFs) and the entire health care system (HCS) of each country [1]. In addition, maintaining high levels of job satisfaction amongst EPs through motivation patterns has a potential direct impact on the quality of healthcare received by the population, as well as on patient adherence to timely examinations and treatment [2, 3].

The World Health Organization (WHO), through the Global Strategy for Human Resources for Health, clearly emphasizes the importance of directing the efforts of organizers in the HCF to improve the working conditions of the HCPs, creating a remuneration system in the HCF, opportunities for their continuous career and professional growth, free access to medical education programs based on the principles of evidence to optimize the use of limited resources, in particular in emergencies, and increase motivation to improve the HCPs' performance [4, 5]. In addition, an effective strategic plan to improve physician job satisfaction will help prevent the loss of qualified professionals in the health care system [6]. Thus, the aim of our study was to assess the level of physicians' job satisfaction and the impact of the national SPS reform on the implementation of a system of motivation to improve the QOL in the HCF in Sumy. Sumy.

AIM

To analyze the impact of medical reform on the motivational component of improving the quality of medical care in health care facilities in Sumy based on the results of a medical and sociological study among doctors.

MATERIALS AND METHODS

The study involved doctors working in inpatient and outpatient departments of health care facilities in Sumy. Sumy, during June-August 2023. A total of 154 respondents were

involved, including 84 women (54.5%) and 70 men (45.5%). The survey questionnaires were reviewed and approved by the Academic Council of the Educationaland Research Medical Institute of Sumy State University. The study used a systematic approach, bibliosemantic, comparative and statistical analysis, and logical generalization. The data were processed and statistically analyzed using Google Forms and Microsoft Excel 2010 for Windows.

RESULTS AND DISCUSSION

The doctors who participated in the survey were distributed by place of work: specialist doctors working in inpatient departments – 88 people (57.1%), specialist doctors working in outpatient departments – 53 people (34.4%), specialist doctors who combine work in both departments – 13 people (8.4%).

When dividing the respondents into professional groups, it was found that half of them (78 people (50.6%)) are therapeutic specialists, 56 people (36.4%) are surgical specialists, and

20 people (13.0%) indicated that they are specialists in other fields (anesthesiologist, radiologist, laboratory doctor, rehabilitation specialist).

When analyzing the data, it was found that 55 respondents (37.5%) have more than 15 years of experience in healthcare organizations, 48 respondents (31.2%) are young professionals with up to 5 years of experience, 35 respondents (22.7%) have been working in healthcare organizations for 6 to 10 years, and 16 respondents (10.4%) have 11 to 15 years of experience.

During the survey, 74 people (48.1%) indicated that they had no certification category, 39 people (25.3%) had the highest certification category, 25 people (16.2%) had the second certification category, and 16 people (10.4%) had the first certification category.

The majority of the surveyed doctors (95 people (61.7%)) indicated that they work for one rate, 49 people (31.8%) – for more than one rate, 10 people (6.5%) work for less than one rate.

Doctors who do not have a certification category are more likely to work at one rate (38 people (51.4%)); doctors with a higher certification category are also more likely to work at 1 rate (29 people (74.4%)) (Table 1).

The study showed that only 49 respondents (31.8%) are satisfied with the material and technical support at the workplace and working conditions, 92 (59.7%) respondents said they were rather dissatisfied with working conditions, and 13 respondents (8.5%) were completely dissatisfied with working conditions and material and technical support. It should be noted that doctors who do not have a certification category are less satisfied with working conditions than doctors with the first or higher certification category.

The survey has shown that 85 doctors (55.2%) receive a salary in the range of UAH 15,000 to 20,000, 25 doctors (16.2%) – from UAH 10,000 to 15,000, 18 doctors (11.7%) – from UAH 20,000 to 25,000, 14 doctors (9.1%) – more than UAH 25,000, 12 doctors (7.8%) – less than UAH 10,000. It is worth noting the correlation between the level of salary and the certification category of doctors from the surveyed group: 59.7% of respondents with no category and 44.1% of respondents with the second category have a salary level of up to UAH15,000.

Almost all doctors (138 people (89.6%)) indicated that the actual amount of their salary does not correspond (partially or fully) to the workload at the workplace, and only 19 doctors (12.3%) indicated that the amount of their salary corresponds to the actual workload at work.

The analysis of the answers to the question "What level of salary do you consider fair foryourself?" showed that the majority of doctors (88 people (57.2%)) consider a salary of UAH 40,000 or more to be fair for them, 66 doctors (42.8%) – within UAH 30,000-35,000.

There is a difference in doctors' responses to the assessment of fair salary according to the length of service in health care facilities: 74.1% of doctors with up to 5 years of work experience, 57.4% of doctors with 6-10 years of work experience, 51.3% of doctors with 11-15years of work experience, and 49.7% of doctors with more than 15 years of work experience consider a salary of UAH 40 000 or more to be fair. It can be argued that as the length of serviceof doctors in HCFs increases, their requirements for salary decrease and they are more likely tobe satisfied with the actual level of salary.

Analyzing doctors' answers about receiving additional payments (bonuses) for the qualityof their work, it can be

Table 1. Distribution of respondents' answers by certification category and actual employment at the workplace (in absolute values and relative values (%))

	No attestation category		II attestation category		I attestation category		Higher attestation category	
	absolute value	relative value (%)	absolute value	relative value (%)	absolute value	relative value (%)	absolute value	relative value (%)
More than one rate	31	41.9	6	24.0	5	31.4	7	17.4
One rate	38	51.4	18	72.0	10	62.3	29	74.4
Less than one rate	5	6.7	1	4.0	1	6.3	3	7.7
In total	74	100	25	100	16	100	49	100

stated that the system of financial incentives for doctors for quality healthcare in HCFs is unsatisfactory: only 4.5% of people said they receive additional paymentsall the time, 21.4% said they receive additional payments periodically. The overwhelming majority of doctors (74.1%) said they did not receive any additional payments at all. It should be noted that all respondents with less than 5 years of work experience do not receive any material incentives for the quality of their work. However, the proportion of doctors with morethan 15 years of work experience who receive a surcharge for quality of work is only 16.9%.

All respondents indicate a high level of workload at the workplace. Despite the high workload, the vast majority of doctors (102 people (66.2%)) spend less than 50% of their working time working with patients. They note that a significant portion of their working timeis spent working with documentation, in particular in electronic form. However, the respondents (121 people (78.6%)) are ready to work even more for the appropriate additional payment for their work, only 33 people (21.4%) indicated that they are not ready to work more. These findings once again confirm that despite the SPSS reform, the issues of optimizing the organization of healthcare work management and logistics at the level of healthcare facilities remain unresolved.

The results of the survey made it possible to determine the motivating factors for choosing the profession of a doctor (respondents had the opportunity to choose several answers). The answers received show that the most common motivating factor among respondents is the desireto benefit and help society (61.7% of answers); 48.7% of people chose to work as a doctor because of professional interest; 32.5% of people noted an important motivating factor was theopportunity for self-realization and creativity; 29.9% of people chose their profession for the opportunity to help their relatives and friends with treatment; for 28.6% of people, the motivating factors are social status, stable job, respect of society for the profession; for 23.4% of people, an important motivating factor is a sense of being needed by society; for 18.2% of people, it is getting material benefits (Fig. 1).

The majority of respondents (109 people (70.2%)) would not agree to change their profession to another one, even if it offered higher salary. 45 respondents (29.8%) would agreeto change their profession to a higher-paid one, including the majority of respondents with lessthan 10 years of experience in healthcare.

At the time of the survey, 72 people (46.8%) indicated that they had additional part-timework in their profession (39.0%) or outside their profession (7.8%). Among them are 6 doctors(8.3%) with up to 5 years of work experience, 22 doctors (30.6%) with 6-10 years of work experience, 27 doctors (37.5%) with 11-15 years of work experience, and 17 doctors (23.6%) who have been working in healthcare facilities for more than 15 years.

To the question "In your opinion, is there a health care quality management system in thehealth care facility you work for?" 29 respondents (18.8%) answered no, another 50 respondents(32.5%) answered "rather yes", which indicates partial implementation of the QMS in the healthcare facility; 75 respondents (48.7%) confirmed the existence of the QMS.

Despite the fact that almost half of the surveyed doctors indicated the existence of QIMSin the healthcare facilities where they work, only 26 people (16.9%) noted the existence of a system of motivation for QMS provision, 63 people (40.9%) said that there was no system of motivation for medical staff in the healthcare facility, 65 people (42.2%) indicated only partialexistence of such a system in the healthcare facility.

According to doctors, the most important incentives for improving QOL are (multiple answers were possible): moral satisfaction from work and well-coordinated teamwork (76.6% of answers), financial incentives (74.7% of answers), opportunities for professional and careergrowth (48.7% of answers), respect from patients and society (46.8% of answers), and management recognition (13.6% of answers).

It should be noted that with increasing length of service,

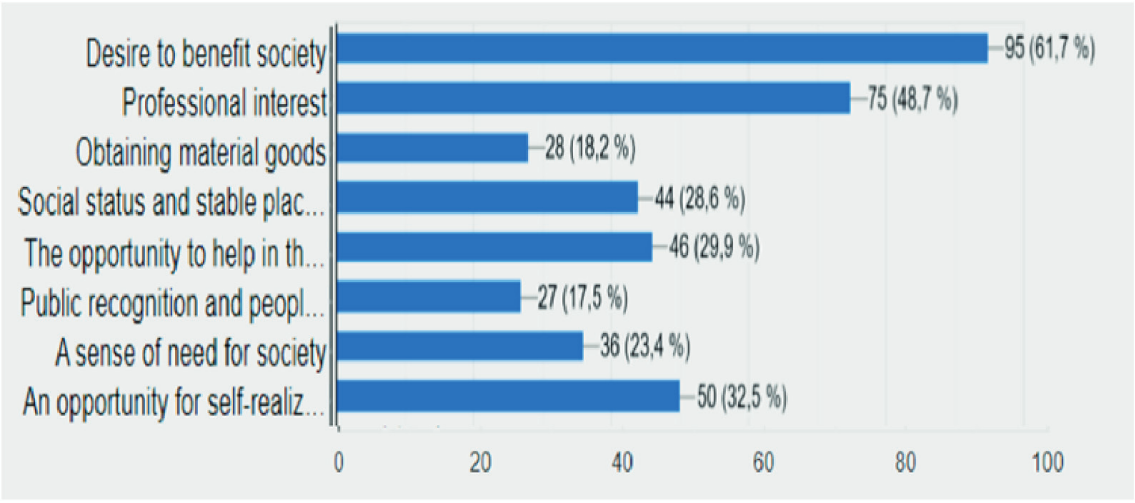

Fig. 1. Distribution of respondents' responses to motivational factors for choosing a doctor's profession (in absolute values and relative values (%)).

Table 2. Distribution of respondents' answers by groups of motivational incentives for improving QMS and length of service (relative value %)

	Incentives				
	Moral satisfaction	Financial incentives	Professional and career growth	Respect from patients and society	Management recognition
Work experience up to 5 years	48.4	48.7	55.0	26.6	16.3
Work experience of 6-10 years	37.7	94.8	33.1	55.9	6.5
Work experience of 11-15 years	61.0	60.4	21.4	22.1	4.6
More than 15 years of experience	52.0	74.7	18.1	73.4	1.3

the importance of management recognition for doctors is gradually leveled: length of service up to 5 years – 16.3% of answers,length of service 6-10 years – 6.5% of answers, length of service 11-15 years – 4.6%, length ofservice more than 15 years – 1.3% of answers. However, regardless of the length of service, oneof the most important motivational incentives for all respondents is moral satisfaction from work and well-coordinated teamwork, as well as recognition and respect from society (Table 2).

The study showed that almost all respondents (150 people (97.4%)) believe that an effective system of incentives for the provision of quality healthcare services in the healthcare facilities where they work should be introduced.

The data obtained during our study showed that despite the high level ofworkload, doctors are ready to work more and better if their salaries are increased. As of today,the motivational component of improving the QOL in HCFs in the city is not effective. Sumy is practically absent, but the respondents consider it necessary to implement it, as evidenced bytheir positive responses. It has been found that the most important motivational incentives for doctors are moral satisfaction from work and well-coordinated teamwork, recognition and respect of society.

CONCLUSIONS

It was found that 89.6% of the doctors in the study group consider their actual salary to be inconsistent with their workload. There is a correlation between the level of salary and the certification category of doctors in the study group. Salariesof less than UAH 15,000 are received by 59.7% of respondents without categoryand 44.1% of respondents with the second category.

The survey showed that the overwhelming majority of respondents (74.1% of answers) do not receive additional payments for the quality of medical care; 83.1% of respondents said that the healthcare facilities where they work do not have an effective system of motivating medical staff to work efficiently.

It was found that respondents are ready to work more and better for additional pay(78.6% of responses), despite the high level of workload. However, the issues of optimizing the organization of healthcare work management and logistics remainunresolved in HCFs.

It was found that, in addition to material incentives, moral factors are important motivational factors for improving the quality of medical care for respondents: moral satisfaction from work and well-coordinated teamwork (76.6% of responses), respect from others and society as a whole (46.8% of responses), andmanagement recognition (13.6% of responses).

The study showed that respondents (97.4% of answers) believe that an effective system of motivation for medical staff should be introduced in healthcare facilitiesto improve the quality of medical services.

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PARAMETERS OF CENTRAL AND INTRACARDIAC HAEMODYNAMICS IN WOMEN WITH THYROID HYPERPLASIA AND ACALCULOUS CHOLECYSTITIS

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ABSTRACT

Aim: The study aimed to investigate some parameters of functional status of central and intracardiac haemodynamics in women with thyroid hyperplasia and acalculous cholecystitis.

Materials and Methods: Functional changes of haemodynamic status in women with thyroid hyperplasia and acalculous cholecystitis were investigated. All data are obtained through general and special clinical methods, standard and special laboratory methods of examination, physiological, biochemical and statistical methods. Parameters of central and intracardiac haemodynamics have been recorded by the method of two-dimensional M-mode echocardiography in the echo chamber "Toshiba-140" (Japan) at the resting state.

Results: An increase in heart rate (by 45.6%) was observed in patients, which led to decreased duration of cardiac cycle and ejection time. Statistically significant ($p<0.05$, 11.7% on average) increase in total peripheral vascular resistance was indicated. Dynamics of changes of parameters of central and intracardiac haemodynamics indicates different parallel existing pathways of secondary disturbances in the part of cardiovascular system. A significant increase in peripheral vascular resistance associated with decreased elasticity (increased vascular rigidity) of the arteries is the element of concentric type of left ventricular hypertrophy. The increase in volume in the absence of vasospastic reactions and increasing venous tone is an element of eccentric hypertrophy.

Conclusions: It is possible to talk about the presence of systolic dysfunction in patients, which, however, is predominantly of functional character. The revealed specific changes in homeostatic haemodynamic characteristics in the women's body with thyroid hyperplasia and acalculous cholecystitis require the development of new, more effective and preferably drug-free (due to liver pathology and detoxification dysfunction) approaches to medical treatment of such patients.

KEY WORDS: thyroid hyperplasia, acalculous cholecystitis, hypothyroidism, cardiovascular system, cardiac haemodynamics

INTRODUCTION

Endemic environmental iodine deficiency, as well as the absence or insufficiency of this microelement's dietary intake, which leads to hypersecretion of pituitary thyroid stimulating hormone, resulting into hypertrophy and hyperplasia of thyroid secretory epithelium [1], is a serious biomedical problem for Ukraine [2]. Especially – for Transcarpathian region [2].

The analysis of scientific literature on the issue allows us to conclude that thyroid hyperplasia is currently widespread pathology, especially among women. Structural changes in the gland may result in various types of disorders of body's hormonal status. That is, the presence of hyperplasia is not yet an indicator of the certain type of developing disease [3–7]. This statement becomes even more actual when liver pathology is added to thyroid dysfunction. In particular, cholecystitis, because it is the most common not only among liver diseases, but also among other types of somatic pathology. Women suffer from cholecystitis more often than men, so the problem of determining specific features of the course of thyroid hyperplasia accompanied by cholecystitis should be given special attention [8–9].

Despite the prevalence of these pathologies and considerable number of works on their study, obtained information is still insufficient to give complete description and comprehensive explanation of the relationship and reciprocal effects between metabolic processes within thyroid gland and liver [10]. Such complexity of the matter is due to multifactorial impact of morphological structure and functional conditions of both glands on the overall hormonal status and functioning of most physiological systems of the body under the development of pathological processes [11-13].

The mechanisms of thyroid hormones' action on the cardiovascular system are multifactorial. The following are considered to be main ones: genomic effects and non-genomic direct actions on the myocardium. The latter includes influences on functional status of cardiomyocytes' plasma membrane, sarcoplasmic reticulum and mitochondria, and impact on the parameters of peripheral circulation [14–16].

Triiodothyronine and thyroxine actions on cardiomyocytes are implemented at the level of nuclei and extra-nuclear formations. Triiodothyronine has a direct effect on gene transcription level. It is indicated by changes in RNA amount and protein synthesis, showing direct nuclear-mediated effect on the heart [17–18]. Non-genomic, or non-nuclear, actions of thyroid hormones on the membrane include increased activity of sinoatrial pacemaker and enhanced transport of glucose, Na and Ca, based on the presence of Na-K-ATPases and Ca-ATPases within the inner side of cardyomyocytes' membrane and sarcoplasmic reticulum [17–20].

Due to these effects, patients with thyroid hyperplasia developing into hypothyroidism (in the areas with iodine deficiency) have decreased cardiac output, increased total peripheral vascular resistance in systemic circulation and increased diastolic blood pressure, which leads to a decrease in pulse pressure. Myocardial oxygen consumption also decreases. Disorders of lipid metabolism, which are inseparably related to metabolism of thyroid hormones, are also considered to be a direct cause of changes in functional status of cardiovascular system [17– 20].

Although hypothyroidism has been identified as a risk factor for atherosclerosis and other cardiovascular diseases as early as 1938 by C. Smyth and A. Arbor, for a long time, especially in national medicine, such its aspect was not given appropriate attention. It can be explained by the fact that the risk of myocardial infarction in the case of hypothyroidism is not as high as could be expected – because of partial compensation of its negative effects by reduced myocardial oxygen demand. However, it must be noted that such results of the studies were obtained and analyzed mainly in patients with already diagnosed hypothyroidism, and in most cases on the background of replacement therapy.

In the national medical literature, there is practically no analysis of thyroid function studies in cardiological patients, in particular those with myocardial infarction. Nevertheless, only such analysis can objectify the significance of hypothyroidism as a factor in development of atherosclerosis, its complications and other cardiovascular pathologies. According to B.C. Tanis et al., among patients with myocardial infarction and dyslipidemia, elevated TSH levels have been detected in 27% of women over 60 years of age and in 6.7% of men under 50 years of age [21–26].

There is no doubt about the role of hypothyroidism, including subclinical hypothyroidism, in the development of cardiovascular diseases after the publication of the Rotterdam Study results [27]. The risks increase not only because of dyslipidemia and hypertension, but also due to abnormalities in microcirculation and coagulation homeostasis. In such patients hypercoagulation, increased platelet activity, increased concentration of coagulation factor VII and homocysteine level are observed. According to E.A. Hak, H.A. Pols, T.J. Visser et al., quite often in such patients, especially in the case of arrhythmia, and without previous clinical observation for hypothyroidism, hormonal studies show low levels of thyroid hormones and elevated thyroid stimulating hormone levels [27]. In the myocardium, hypothyroidism causes serious edema within muscle fibers and interstitial tissue. These changes are diffuse by nature, but with prolonged course of hypothyroidism, local and then diffuse fibrosis develops. Objective examination reveals an increase in heart size and expansion of its walls, totally resulting in atrial and ventricular conduction violation [21–24].

AIM

The study aimed to investigate some parameters of functional status of central and intracardiac haemodynamics in women with thyroid hyperplasia and acalculous cholecystitis.

MATHERIALS AND METHODS

PATIENT CHARACTERISTICS AND RESEARCH METHODS

87 women aged 22-54 years with chronic acalculous cholecystitis as the main diagnosis, and with thyroid hyperplasia, were chosen for examination. The control group, randomized by age, consisted of 20 healthy women.

All data are obtained through general and special clinical methods, standard and special laboratory methods of examination, physiological, biochemical and statistical methods [28]. Parameters of central and intracardiac haemodynamics have been recorded by the method of two-dimensional M-mode echocardiography in the echo chamber "Toshiba-140" (Japan) at the resting state.

CRITERIA

When analyzing the data obtained, the values of studied haemodynamic parameters in healthy women from the control group have been determined by us during clinical examination. These values, considering as normal, were used for comparison purposes.

STATISTICAL ANALYSIS

Statistical analyses were performed using the methods of variation statistics. Such statistical values as arithmetic mean, its average error, correlation coefficient and Student's reliability criterion were calculated. Statistical analysis was performed using Microsoft Excel 2003 software. Differences were considered significant at $p<0.05$.

RESULTS

The characteristics of examined women are shown in Table 1.

During the study period, in all women having thyroid hyperplasia and acalculous cholecystitis certain features of central and intracardiac haemodynamics were found (Table 2).

According to the mechanism of thyroid hormones' action on cardiovascular system, in ill patients we have registered an increase in heart rate (by 45.6%), which leads to a decrease in duration of cardiac cycle and ejection time. Statistically significant ($p<0.05$) increase of total peripheral vascular resistance (by 11.7% on average) has been observed. It is probably due to the non-nuclear effects of thyroid hormones

Table 1. Age composition of the groups of examined women

Examined groups	Number of examined women	
	abs.	%
Control (n=20):		
22-30 years	4	20.0
31-40 years	10	50.0
41-54 years	6	30.0
With thyroid hyperplasia (n=87):		
22-30 years	18	21,0
31-40 years	43	49,0
41-54 years	26	30,0

Table 2. Parameters of haemodynamics in examined groups of women

Parameters of haemodynamics	Control group	Patients with thyroid hyperplasia
HR*, bpm	67.5±3.8	98.3±2.4**
Systolic AP, mm Hg	120±5	121±2
Diastolic AP, mm Hg	80±4	78±2
CO, L/m	5.00±0.30	4.92±0.22
Total peripheral vascular resistance, kPa×sec/m^2	14.5±0.5	16.2±0.8*
Duration of cardiac cycle, msec	950±21	893±30*
Ejection time, msec	305±9	283±5*
EDV, mL	97.5±2.4	125.1±3.0*
EDVI, mL/m^2	64.0±1.9	69.0±1.6*
ESV, mL	45.1±3.0	53.1±2.9*
ESVI, mL/m^2	23.5±2.2	28.9±1.2*
SV, mL	61.2±2.4	72.0±2.7*
SVI, mL/m^2	33.0±2.8	40.1±1.3*
Myocardial contractility index, kPa/sec	21.2±0.7	24.8±0.9*

**Abbreviations: HR – heart rate; AP – arterial pressure; CO – cardiac output; EDV – end-diastolic volume; ESV – end-systolic volume; EDVI – end-diastolic volume index; ESVI – end-systolic volume index; SV – stroke volume; SVI – stroke volume index.*

*** Statistically significant difference in comparison to values of haemodynamic parameters in control group, p<0,05.*

and their influences on lipid metabolism disorders. At the same time, an increase in stroke volume (by 17.6%) and its index (by 21.5%) prevailed, which was provided by a certain raise of myocardial contractility index (by 17.5%) to some extent under greater peripheral vascular resistance.

In relation to the values of end-diastolic and end-systolic volumes and their corresponding indices, it must be noted that the latter increased to a greater or lesser extent in patients with thyroid hyperplasia and acalculous cholecystitis: EDV – by 28.3%, ESV – by 17.7%, EDVI – by 7.8%, and ESVI – by 23.0%. Such dynamics of changes indicates the presence of systolic dysfunction in examined patients. When the usual blood volume flowing from pulmonary veins is added to increased end-systolic volume, diastolic volume in heart chambers also raises up. Finally, the values of diastolic pressure and end-diastolic volume are above physiological normal state, too.

Despite the fact that such an increase in preload through Frank-Starling mechanism leads to the raise of stroke volume, because of functional changes in contractility the end-systolic volume remains increased. Theoretically, this compensatory mechanism is aimed at maintaining the value of stroke volume in the case of dysfunction caused by decreased elasticity of cardiac muscle, which predominantly occurs due to non-nuclear effects of thyroid hormones in the studied pathology.

DISCUSSION

Thyroid hyperplasia, developing in either hyper- or hypothyroidism, is widespread and serious clinical pathology, especially when associated with liver and hepatobiliary dysfunctions, and particularly among women [8–9]. Scientific literature, especially national, is still lacking complete description and comprehensive explanation of functional interconnections between thyroid gland and liver and their common impact on overall hormonal status and functional conditions of physiological systems in the case of development of pathological process [11-13].

Our study revealed changes in parameters of central and intracardiac haemodynamics under the combination of hypothyroidism and cholecystitis. They are theoretically expected and based on both direct and indirect actions of thyroid hormones. In the first case such effects are implemented trough hormonal actions on cardiac muscle. In the second case – through affecting lipid metabolism in association with hepatobiliary disorder [14-26].

In general, the dynamics of changes in central and intracardiac haemodynamics indicates different, parallel existing pathways of secondary disorders in cardiovascular system. Thus, a significant increase in total peripheral vascular resistance, associated with a decrease in vascular elasticity, which at the same time means increased rigidity of blood vessels' walls, is the component of concentric type of left ventricular hypertrophy. Increased stroke volume under the absence of vasospastic reactions and raised venous tone represent the element of eccentric hypertrophy [14, 21-24].

It should be emphasized that observed changes in cardiovascular system in examined women with thyroid hyperplasia and acalculous cholecystitis are predominantly functional (increased heart rate, myocardial contractility, etc.). It is evidenced by the absence of significant changes in blood pressure, since with progression of pathological process, blood pressure stabilization at a high level takes place.

Based on the data obtained, it is also possible to talk about the presence of systolic dysfunction in patients, which, however, is predominantly functional.

CONCLUSIONS

The study confirmed that in women patients with thyroid hyperplasia and acalculous cholecystitis, changes in thyroid status and parameters of central and intracardiac haemodynamics in their pure form do not correspond to those typical for either thyroid hyperplasia of hypothyroid type, or acalsulous cholecystitis. Revealed changes have mixed and predominantly functional character.

The revealed specific changes in homeostatic haemodynamic characteristics in the women's body with thyroid hyperplasia and acalculous cholecystitis require the development of new, more effective and preferably drug-free (due to liver pathology and detoxification dysfunction) approaches to medical treatment of such patients.

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QUANTITATIVE MORPHOLOGICAL FEATURES OF THE STRUCTURAL REARRANGEMENT OF THE VENOUS BLOOD VESSELS OF THE PROSTATE GLAND IN POST-RESECTION PORTAL HYPERTENSION

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ABSTRACT

Aim: Using quantitative morphological methods to study the peculiarities of the structural reconstruction of the venous bad of the prostate at the conditions of post-resection portal hypertension**.**

Materials and Methods: Morphologically, the venous bed of the prostate of 15 intact white rats, 30 animals with post-resection portal hypertension, 17 rats with a combination of post-resection portal hypertension with hepatargia, enteral, cardiac, and renal insufficiency was studied. Rats were slaughtered one month after the start of the experiment by bloodletting under general thiopental anesthesia. Morphometry of the venous blood vessels of the prostate gland was performed on histological specimens, during which the diameter of the postcapillary venules, the diameter of the venules, the external diameter of the venous vessels, the internal diameter of the venous vessels, the thickness of the wall of the venous vessels was determined. Also it was studied the height of endothelial cells, diameter of their nuclei, nuclear-cytoplasmic ratio in these cells, relative volume of damaged endothelial cells, density of vessels of microcirculatory bed per 1 mm^2 of prostate tissue.

Results: It was found that resection of the left and right lobes of the liver leads to the development of postresection portal hypertension and pronounced remodeling of the vessels of the venous bed of the prostate gland, which was characterized by the expansion of the capillary venules of the prostate by 36.5%, with the occurrence of multiple organ failure by 38.5% ($p<0.001$), an increase in the lumen of veins, thinning of their wall, atrophy, dystrophy, and necrobiosis of endothelial cells, disruption of structural cellular homeostasis, endothelial dysfunction, hypoxia, dystrophic-necrotic changes in cells, stromal structures, infiltration, and sclerosis. Morphological changes in the structures of the prostate dominated when post-resection portal hypertension was combined with multiple organ failure.

Conclusions: Post-resection portal hypertension in laboratory sexually mature white male rats leads to pronounced remodeling of the venous bed of the prostate gland, which is characterized by the expansion of the lumen of the vessels, thinning of their walls, atrophic, dystrophic and necrobiotic changes in endothelial cells, a violation of structural cellular homeostasis in them, endothelial dysfunction, hypoxia, dystrophic-necrotic changes in cells, stromal structures, infiltration and sclerosis. Morphological changes in the structures of the prostate dominated when post-resection portal hypertension was combined with multiple organ failure.

KEY WORDS: prostate gland, venous bed, portal hypertension, quantitative morphology

INTRODUCTION

Today, liver resection is often used in of medical institutions surgical departments due to the tumors, metastasis, liver injuries, intrahepatic cholangiolithiasis, alveolar echinococcosis, and liver transplantation [1, 2]. Removal of significant volumes of the liver can lead to post-resection portal hypertension, in which a number of severe complications occur: bleeding from varicose veins of the esophagus and stomach, rectum, ascites, splenomegaly, secondary hypersplenism, parenchymal jaundice, portosystemic brain damage, multiple organ failure [2, 3]. With the development of post-resection hypertension in the portal system, the organs in which venous blood outflow is disturbed are the first to suffer, which leads to venous hemoptysis, hypoxia, and damage to the regulatory mechanisms of homeostasis. The development of portal hypertension after removal of significant volumes of the liver is an unfavorable sign for patients. When venous pressure increases, porto-portal and porto-caval anastomoses occur in the portal hepatic vein. The latter ensure the outflow of venous blood from the portal system into the basins of the lower and upper vena cava, where hemodynamics are disturbed, which can be complicated by the dysfunction of the organs of the large blood circulation [4, 5, 6].

Quantitative morphology is widely used by modern researchers to objectify structural changes in organs and body systems in various physiological and pathological conditions. In recent years, experimenters and clinicians are increasingly interested in the venous course of organs, which are part of the transport system of blood circulation and provide full-fledged venous drainage and tissue homeostasis necessary for life [7]. Without a comprehensive study of the venous system of organs, the pathogenesis of various diseases cannot be adequately explained. Insufficiency and violation of venous blood flow is one of the leading factors in the development of significant trophic disorders in organs and systems in portal hypertension [8]. It is important to indicate that the venous vessels of the prostate gland with increased venous pressure in the portal hepatic vein have not been fully studied.

AIM

Using quantitative morphological methods to study the peculiarities of the structural rearrangement of the venous bed of the prostate gland in conditions of post-resection portal hypertension.

MATERIALS AND METHODS

The work was performed on 62 laboratory sexually mature male rats, weighing 195 - 200 g, which were divided into three groups. The 1st control group included 15 intact animals, the 2nd – 30 rats with post-resection portal hypertension, the 3rd – 17 animals with post-resection portal hypertension, at which was developed multiple organ failure.

Post-resection portal hypertension was modeled by removing the left and right lateral lobes of the liver, which accounted for 58.1% of its volume. Animals were kept in standard vivarium conditions. Rats were euthanized by bloodletting under thiopental anesthesia 30 days after the start of the experiment. The cut pieces of the examined organ were fixed in Buen's solution, passed through ethyl alcohols of increasing concentration and placed in paraffin blocks. After deparaffinization, microtome sections with a thickness of 5-6 μm were stained with hematoxylin and eosin, according to van Gieson, Mallory, Masson, and toluidine blue [7].

Morphometry of the venous blood vessels of the prostate gland was performed on histological specimens, during which the diameter of the postcapillary venules, the diameter of the venules, the external diameter of the venous vessels, the internal diameter of the venous vessels, the thickness of the wall of the venous vessels was determined. Also it was studied the height of endothelial cells, diameter of their nuclei, nuclear-cytoplasmic ratio in these cells, relative volume of damaged endothelial cells, density of vessels of microcirculatory bed per 1 mm^2 of prostate tissue [9].

50 measurements were made in each histological specimen.

Morphometry was performed with the help of a light microscope «Olimpus BX-2» with a digital video camera and a package of application programs «Video Test 5.0» and «Video size 5.0».

Quantitative parameters were processed statistically. Processing of the results was carried out in the Department of Systemic Statistical Research of I. Horbachevsky Ternopil National Medical University, Ministry of Health of Ukraine in the Statsoft STATISTIKA software package (license No. BXXP303F737429FA-8). The difference between comparative values was determined by the Mann-Whitney and Student criteria [10].

All manipulations with experimental animals were carried out in compliance with generally accepted bioethical norms according to the international and national regulations: «European Convention for the Protection of Vertebrate Animals Used for Research and Scientific Purposes» (Strasbourg, 1986), «General Ethical Principles of Conducting Experiments on Animals» (Ukraine, 2001), Law of Ukraine «On the Protection of Animals from Cruel Treatment» No. 3447-1U (Ukraine, 2006) [11].

RESULTS AND DISCUSSION

One month after the resection of the peritoneal cavity, dilation of the hepatic portal vein, pleurisy and dilation of the mesenteric veins and the visible venous bed of the small and large intestines, varicose veins of the esophagus, stomach, rectum, ascites, and splenomegaly were observed in experimental animals. The mucosa of the stomach, small intestine, large intestine, and rectum were full of blood, swollen, with single foci of point hemorrhages. The above indicated the presence of post-resection portal hypertension [12, 13]. When post-resection portal hypertension was combined with multiple organ failure, hepatargia, enteric, cardiac and renal failure appeared.

The quantitative morphological parameters of the venous vessels of the prostate gland of experimental animals obtained as a result of the study are presented in Table 1. A comprehensive analysis of the morphometric parameters of the vessels of the venous bed of the prostate gland shown in the table established that they all changed markedly in the conditions of post-resection portal hypertension.

It was established that the diameter of the post-capillary venules, from which the venous channel of the examined organ begins, increased with a statistically significant difference ($p<0.001$) from (12.85±0.06) μm to (17.54±0.09) μm in 2- and the experimental group (experimental animals with post-resection portal hypertension), i.e. by 36.5%.

When post-resection portal hypertension was combined with multiple organ failure, such expansion of the prostate gland capillary venules was more prominent and reached 38.5% ($p<0.001$). At the same time, the diameter of the post-capillary venules of the prostate was equal to (17.80±0,12) μm.

The structural rearrangement of the venules of the prostate gland in the simulated conditions of the experiment turned out to be similar. Thus, in control observations, the indicated quantitative morphological indicator was equal to (26.90±0.18) μm, and in animals with post-resection portal hypertension (35.10±0.21) μm. A statistically significant difference was established between the given morphometric parameters ($p<0.001$).

Table 1. Quantitative morphometric parameters of the prostate gland veins of the experimental animals (M±m)

Indicators	Groups		
	1st control	2nd experimental	3d experimental
Diameter of the post-capillary venules, μm	12,85±0,06	17,54±0,09***	17,80±0,12***
Diameter of the venules, μm	26,90±0,18	35,10±0,21***	35,70±0,21***
External diameter of the venous vessels, μm	40,56±0,42	47,60±0,45***	48,96±0,45***
Internal diameter of the venous vessels, μm	28,40±0,21	36,15±0,18***	38,56±0,18***
Thickness of the wall of the venous vessels, μm	12,16±0,12	11,45±0,12**	10,40±0,09***
Height of endothelial cells, μm	4,85±0,03	4,62±0,03**	4,40±0,02***
Diameter of the endothelial cells nuclei, μm	3,50±0,03	3,44±0,02	3,30±0,02**
Nuclear-cytoplasmic ratio	0,520±0,003	0,554±0,003***	0,562±0,002***
Relative volume of damaged endotheliocytes, %	2,30±0,03	18,86±0,15***	35,70±0,27***
Density of vessels of microcirculatory bed per 1 mm^2 of prostate tissue	3820,5±27,3	2846,3±26,1***	2735,4±25,2***

*Note. **-p<0,01; ***-p<0,001 comparatively to the 1-st group.*

At the same time, the last quantitative morphological indicator turned out to be increased by 30.5% compared to the same in the control group of laboratory sexually mature white male rats. It was established that when post-resection portal hypertension was combined with multiple organ failure, the diameter of prostate venules increased by 32.7% (p<0.001) compared to the control.

In the conditions of post-resection portal hypertension, the structure of the veins of the prostate gland also changed markedly, which was confirmed by the obtained morphometric parameters of their external and internal diameters and the thickness of the venous walls. Thus, the external diameter of the venous vessels of the studied organ in control sexually mature white male rats was equal to (40.56±0.42) μm, with post-resection portal hypertension this quantitative morphological indicator with a statistically significant difference (p<0.001) increased to (47.60±0.45) μm, i.e. by 17.3%. In the 3rd group of observations (combination of post-resection portal hypertension with multiple organ failure), the studied morphometric parameter reached (48.96±0.45) μm. It was established that the outer diameter of the venous vessels of the prostate gland in the specified group of animals exceeded the similar control indicator by 18.2% (p<0.001).

In the simulated experimental conditions, the internal diameter (lumen) of the venous vessels of the prostate also increased. In the conditions of post-resection portal hypertension, this morphometric parameter changed from (28.40±0.21) μm to (36.15±0.18) μm, that is, it increased by 27.3% (p<0.001). When post-resection portal hypertension was combined with multiple organ failure, the lumen of the venous vessels of the prostate gland increased by 35.7% and reached (38.56±0.18) μm with a high degree of statistically significant difference (p<0.001). The dominant increase in the inner diameter of the prostate veins compared to the outer diameter was accompanied by a decrease in the wall thickness of the studied vessels.

In the conditions of post-resection portal hypertension, the indicated quantitative morphological indicator decreased by 5.8% (p<0.01), in the combination of post-resection portal hypertension with multiple organ failure – by 14.4% (p<0.001).

It was also revealed that post-resection portal hypertension led to prominent structural rearrangement of the endothelial cells of the venous vessels of the prostate gland. This was confirmed by the change in their morphometric parameters. Thus, in the control observations, the height of the endotheliocytes of the venous vessels of the prostate gland was equal to (4.85±0.03) μm, in post-resection portal hypertension – (4.62±0.03) μm. A statistically significant difference (p<0.01) was found between the given quantitative morphological indicators. At the same time, the last morphometric parameter was smaller than the previous one by 4.7%, which indicated atrophy of the studied cells. When post-resection portal hypertension was combined with multiple organ failure, the investigated quantitative morphological indicator was equal to (4.40±0.02) μm. It was established that the given quantitative morphological indicator was lower by 9.3% (p<0.001) compared to the control. In the simulated experimental conditions, the morphometric parameters of the nuclei of the endothelial cells of the venous vessels of the prostate gland were also reduced. In the 2nd group of experimental animals with post-resection portal hypertension, the indicated quantitative morphological indicator was lower by only 1.7% (p>0.05) compared to the same control value. When post-resection portal hypertension was combined with multiple organ failure, the studied morphometric parameter was equal to (3.30±0.02) μm, which was statistically significantly (p<0.01) different from the similar indicator in the norm and decreased by 5.7% compared to it.

Under the conditions of the simulated experimental pathology, the ratio between the characteristicaj parameters of the nucleus and cytoplasm of the endothelial cells of

the venous vessels of the examined organ was significantly changed, which adequately was illustrated by the nuclear-cytoplasmic ratio in the indicated cells. Thus, in control observations, this morphometric parameter was equal to (0.520±0.003), in case of post-resection portal hypertension – (0.554±0.003). The last quantitative morphological indicator with a prominent statistically significant difference ($p<0.001$) differed from the previous one and exceeded it by 6.5%. In the 3rd group of observations (combination of post-resection portal hypertension with multiple organ failure), the nuclear-cytoplasmic ratio in the endotheliocytes of the venous vessels of the prostate reached (0.562±0.002). The given quantitative morphological indicator with a high degree of statistically significant difference ($p<0.001$) exceeded the same value in the norm by 8.1%. It should be noted that the found changes in the relationship between the characteristics of the nucleus and cytoplasm of the endotheliocytes of the venous vessels of the prostate gland in simulated experimental pathological conditions indicated their damage and disruption of cellular structural homeostasis [12, 13, 14].

The relative volume of damaged endothelial cells in the veins of the prostate gland in conditions of post-resection portal hypertension increased by 8.2 times ($p<0.001$), when post-resection portal hypertension was combined with multiple organ failure by 15.5 times ($p<0.001$) compared to the control. It is known that disruption of structural cellular homeostasis, damage to a significant number of endotheliocytes can lead to endothelial dysfunction.

The density of microcirculatory bed vessels per 1 mm^2 of prostate tissue was significantly reduced in post-resection portal hypertension, as well as in the case of its combination with multiple organ failure. It was found that in the 2nd experimental group of sexually mature white male rats with post-resection portal hypertension, the specified morphometric parameter with a statistically significant difference ($p<0.001$) decreased by 25.5%, when post-resection portal hypertension was combined with multiple organ failure - by 28.4% ($p<0.001$). Changes of the last quantitative morphological indicator indicated a significant violation of blood supply to the organ and violation of venous drainage, which aggravated various complications of the simulated pathology.

Using of light microscopy indicate in specimens of the prostate gland with post-resection portal hypertension, prominent vascular disorders, expansion of venous vessels, perivascular and stromal edema, foci of dystrophically, necrobiotically, apoptically altered endothelial cells/ Also epitheliocytes of glandular structures, myocytes, focal infiltrates and growth of connective tissue were observed. In some venous structures of the microcirculatory bed (postcapillary venules and venules), stasis, sludge, thrombosis, foci of diapedesis hemorrhages, plasmorrhagia of vessel walls and perivasal spaces were observed. Swelling of endothelial cells, their dystrophy, necrobiosis, desquamation and proliferation were also noted. This morphological features indicated the presence of hypoxia. Thinning of the wall of venous vessels and expansion of their lumen were observed optically. In places, thickening of the adventitia sheath of veins was observed.

CONCLUSSIONS

Post-resection portal hypertension in laboratory sexually mature white male rats leads to pronounced remodeling of the venous bed of the prostate gland, which is characterized by the expansion of the lumen of the vessels, thinning of their walls, atrophic, dystrophic and necrobiotic changes in endothelial cells, a violation of structural cellular homeostasis in them, endothelial dysfunction, hypoxia, dystrophic-necrotic changes in cells, stromal structures, infiltration and sclerosis. Morphological changes in the structures of the prostate dominated when post-resection portal hypertension was combined with multiple organ failure.

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CHANGES IN THE ULTRASTRUCTURAL ELEMENTS OF PERIODONTAL NEUROTROPHY UNDER CONDITIONS OF ACUTE SIMPLE COAGULATION DYSTROPHY IN THE EXPERIMENT

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ABSTRACT

Aim: To determine the role of damage to the ultrastructural elements of the periodontal nervous system in the pathogenesis of dystrophic periodontal disease.

Materials and Methods: The basis of the experimental part of the study was the preparation of ultrathin sections from blocks of gum tissue of white rats, which were prepared using the UMTP-3M device. The study and analysis of biopsy samples was carried out with the help of an electron microscope UEMV-100K.

Results: With the help of transmission electron microscopy, it was found that from the first minutes after the injection of hemolysate of isogenic erythrocytes into the rats, aggregates of erythrocytes, clumps of blood plasma, clusters of fibrin monomer masses, bundles of fibrin fibers, platelet and homogeneous were present in the connective tissue of the gums, and in particular in the lumens of hemocapillaries microthrombi, which confirms damage to the ultrastructures of the periodontium, which lead to the development of a pathological process, which is described when simple coagulation dystrophy is reproduced.

Conclusions: Coagulative damage to the ultrastructural elements of the periodontal nervous system is one of the important factors in the pathogenesis of dystrophic periodontal damage. Under these conditions, trophic disturbances occur, similar to those that occur when the integrity of the nerve is disturbed – neurotrophic mechanism of dystrophy.

KEY WORDS: Coagulation dystrophies, generalized decompensated thrombinogenesis, periodontium, nerves of the gingival mucosa membranes

INTRODUCTION

Many works in the modern medical literature are dedicated to the study of the mechanisms of periodontal tissue damage [1-9]. It is also known that the damage of parenchymal organs in many diseases has a coagulation-hypotrophic genesis [10-12]. As a result of the processing of scientific and informative material, protocols for providing therapeutic assistance to dental patients and taking into account our own experience, a classification of periodontal diseases is proposed, in which the varieties of coagulation periodontitis can be divided into the following types, of namely – coagulation periodontosis are distinguished: coagulation periodontosis (simple), inflammatory-coagulation periodontosis, immune-coagulation periodontosis, age-related coagulation periodontosis (physiological aging of the periodontium) [12-14]. One of the main mechanisms of the development of these periodontal diseases is the coagulation-hypotrophic mechanism. This coagulation-hypotrophic mechanism is responsible for the development of coagulation (degenerative) damage caused by the direct action of thrombin on periodontal structures and simultaneously includes three mechanisms of trophic reduction: enzymopathic, discirculatory and neurotrophic [10, 11, 15].

AIM

To determine the role of damage to the ultrastructural elements of the periodontal nervous system in the pathogenesis of dystrophic periodontal disease.

MATERIALS AND METHODS

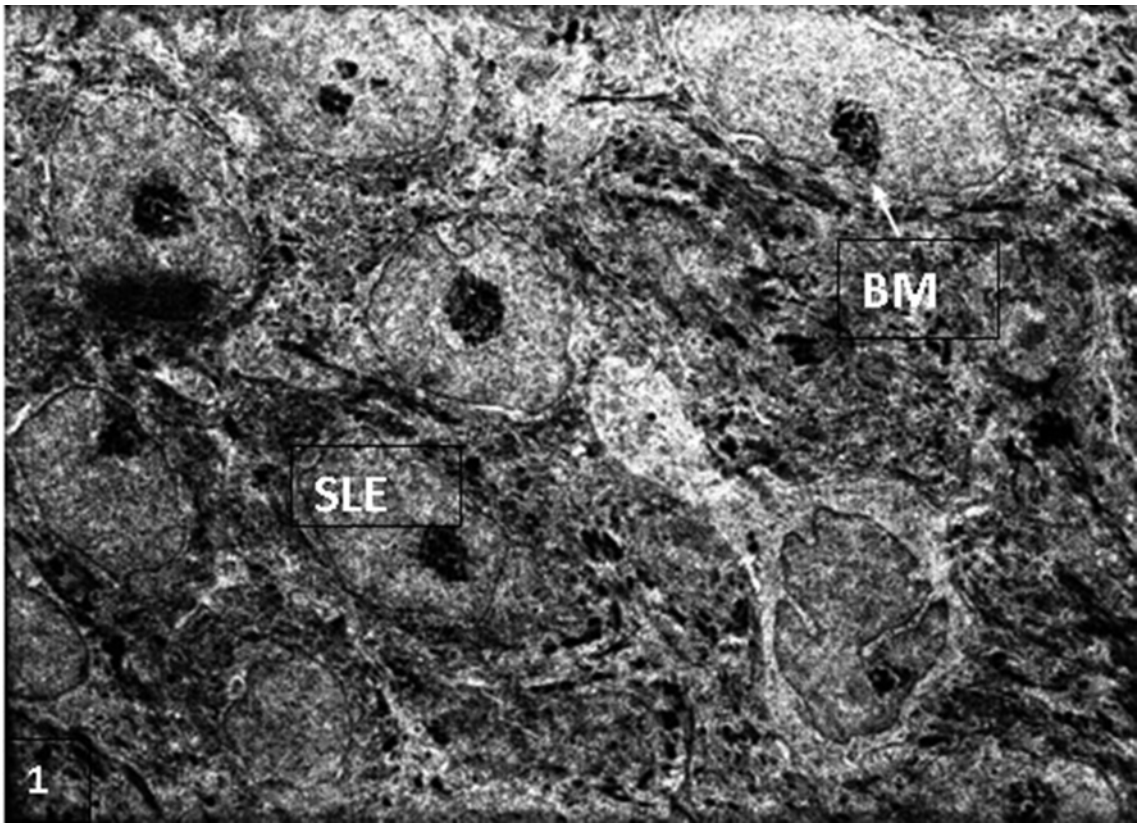
In an experiment on white rats, a model of acute simple coagulation dystrophy (generalized decompensated thrombinogenesis (GDT)) was reproduced by intravenous administration of hemolysate of isogenic erythrocytes in a dose of 25 ml/kg to white rats (55 rats) [16]. During

the research, the animals were killed by decapitation, at intervals of 15 and 30 minutes, and 2, 5, and 24 hours after the infusion of isogenic erythrocyte hemolysate, biopsies (tissue material of mucous membrane of the gums) were taken for the purpose of preparing electron microscopic samples for further studies. For the purpose of comparison, the gingival mucosa of the control group of 5 intact white rats was used. Bioptates of the gingival mucosa were fixed in a 2% solution of osmium tetraoxide in a 0.1 M phosphate buffer solution (pH 7.36) for 2 hours at (an ice-melting) temperature of 0 °C. Fixed blocks of gingival tissue were washed in chilled distilled water, dehydrated in solutions of increasing concentrations of ethyl alcohol and acetone, and soaked in a mixture of epon and araldite resins [17]. Ultrathin sections from blocks of gingival tissue were prepared using the UMTP-3M device. After that, the prepared sections were sequentially contrasted in solutions of uranyl acetate [18] and lead citrate [19]. Studying and photographing the material was carried out using an electron microscope UEMV-100K (Ukraine).

RESULTS

With the help of transmission electron microscopy, it was found that from the first minutes after the injection of hemolysate of isogenic erythrocytes into the rats, aggregates of erythrocytes, clumps of blood plasma, clusters of fibrin monomer masses, bundles of fibrin fibers, platelet and omogeneous were present in the connective tissue of the gums, and in particular in the lumens of hemo-capillaries microthrombic damaged organelles, precipitates, and coagulates were found in capillary endotheliocytes. The main substance and collagen fibers, which were adjacent to the capillaries, were disorganized. In the main substance, among the disorganized collagen fibers, there were mucoid and fibrinoid masses, and in the cells – precipitates, coagulates or continuous cytogel. Fibroblasts and macrophages had an increased electron density of the protoplast, significant numbers of autophagolysosomes were also found in them. Changes and degranulation of mast cells were observed, but this was accompanied by significantly less damage to non-cellular and cellular elements adjacent to them. At the same time, significant damage to the structures of epithelial cells was detected in the form of loosening (loss of contour) of the membranes of various organelles. An increase in the electron density of these cells and disruption of intercellular contacts were characteristic features. The most pronounced changes were found in the cells of the spinous, and especially the basal, layers of the epithelium, while they were less pronounced in the cells of the granular and horny layers. The state of the gum's mucosa ultrastructure of a white rat during the experimental simulation of simple coagulation dystrophy of the periodontium is shown in (Fig. 1).

The activity of mitosis at the cellular level decreased and was 10.25±0.57%, being at normal 16.67±0.41% (Fig. 2).



Disorganized cells of the spinous layer of the epithelium (SLE) and the basement membrane (BM) of the gums.

Fig. 1. The ultrastructure of disorganized cells of the spinous layer of the epithelium (SSC) and the basal membrane (BM) of the gingiva for 2 h of the experiment. Coll. x2000.

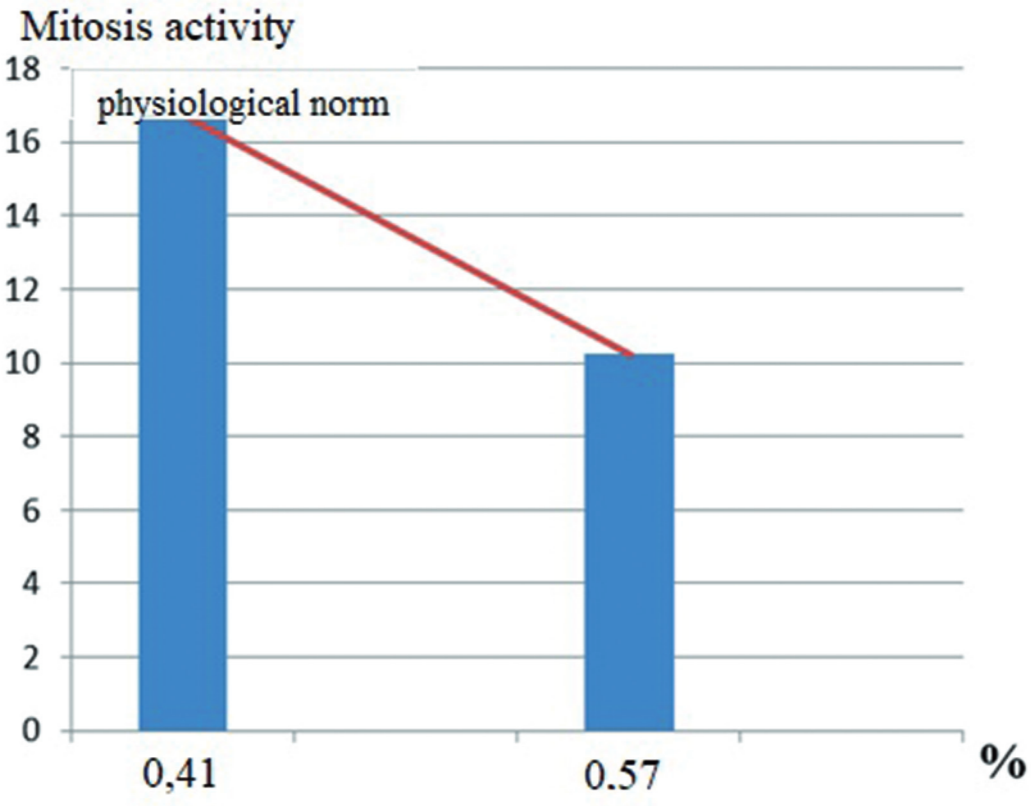


Fig. 2. Evaluation of mitotic activity compared to the physiological norm.

Mitosis is an important component of the process of growth, development of cells and tissues, and thus is an important component of restorative (reparative) processes. In the case of dystrophic processes, which were artificially induced in the periodontal tissues of experimental animals, a decrease in the mitotic activity of cells was established, as a result of which a decrease in the growth point of tissues was observed in the periodontium at the cellular level.

With the help of transmission electron microscopy, it was found that from the first minutes after the injection of hemolysate of isogenic erythrocytes into the rats, aggregates of erythrocytes, clumps of blood plasma, clusters of fibrin monomer masses, bundles of fibrin fibers, platelet and homogeneous were present in the connective tissue of the gums, and, in particular, in the lumens of hemo-capillaries microthrombi, damaged organelles, precipitates, and coagulates were found in capillary endotheliocytes. The main substance and collagen fibers, which were adjacent to the capillaries, were disorganized. In the main substance, among the disorganized collagen fibers, there were mucoid and fibrinoid masses, and in the cells – precipitates, coagulates or continuous cytogel. Fibroblasts and macrophages had an increased electron density of the protoplast, significant numbers of auto-phagolysosomes were also found in them. Changes and degranulation of mast cells were observed, but this was accompanied by significantly less damage to non-cellular and cellular elements adjacent to them. At the same time, significant damage to the structures of epithelial cells was detected in the form of loosening (loss of contour) of the membranes of various organelles. An increase in the electron density of these cells and a violation of intercellular contacts were characteristic findings. The most pronounced changes were detected in the cells of the spinous, and, especially, the basal layers of the epithelium, while they were less pronounced in the cells of the granular and corneous layers (Fig. 3). It was often possible to observe vacuolar dystrophy of epithelial cells (Fig. 3).

At the 5th hour from the beginning of reproduction of periodontal coagulation dystrophy, the walls of a number of capillaries were destroyed, which led to continuous interpenetration of ultrastructural components of the main substance of connective tissue and blood plasma. In most cells of the connective tissue, the cytoplasm was saturated with residual bodies, vacuoles, precipitates, and coagulates. Mast cells were found in small numbers, and their electron-bright cytoplasm contained small amounts of secretory granules. Such secretory granules resembled partially or almost completely emptied containers. At this time, intercellular contacts were broken in the epithelial part of the mucous membrane, represented by large intercellular spaces, in which polymorphonuclear leukocytes and small disintegrating lymphocytes were often detected. In some places of the mucous membrane, peeling of epithelial cells was noted. At the 24th hour after the onset of acute simple coagulation dystrophy of the periodontium, the changes in the mucous membrane of the gums mostly resembled the changes that were detected at the 5th hour, but some of them were more pronounced, the lysis of microthrombi

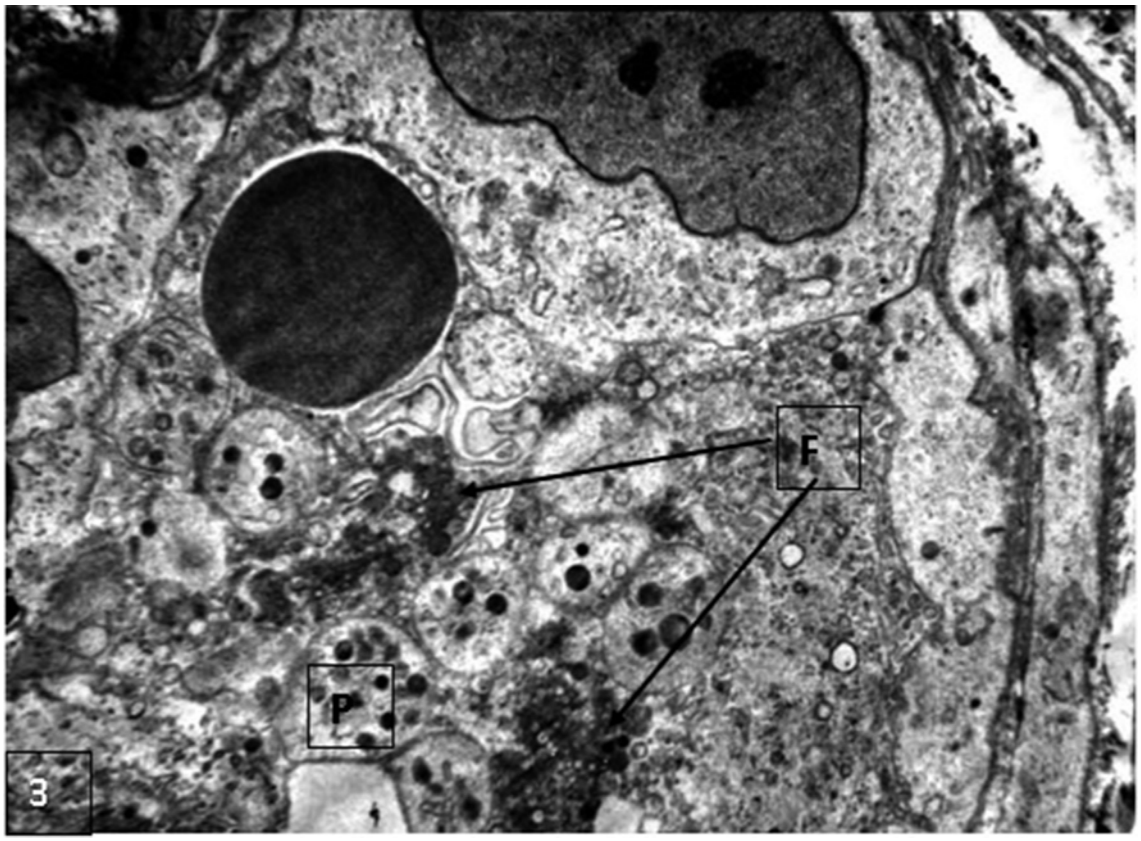
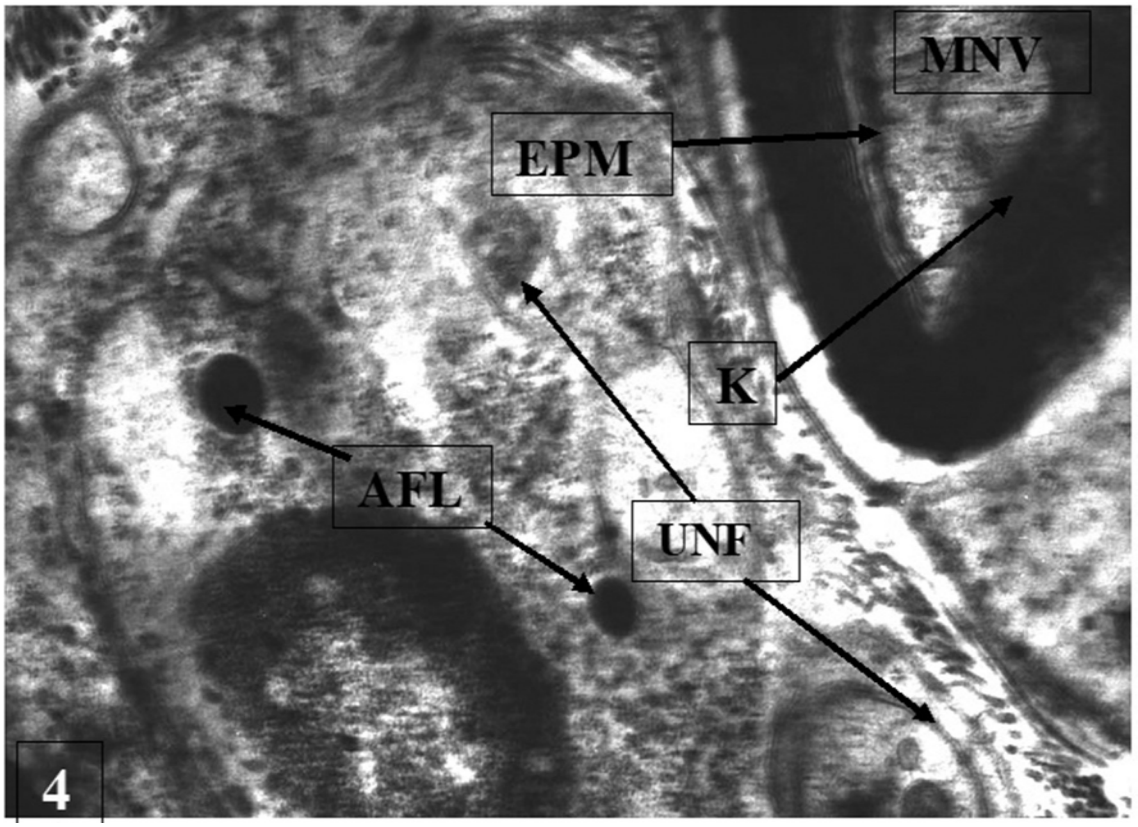
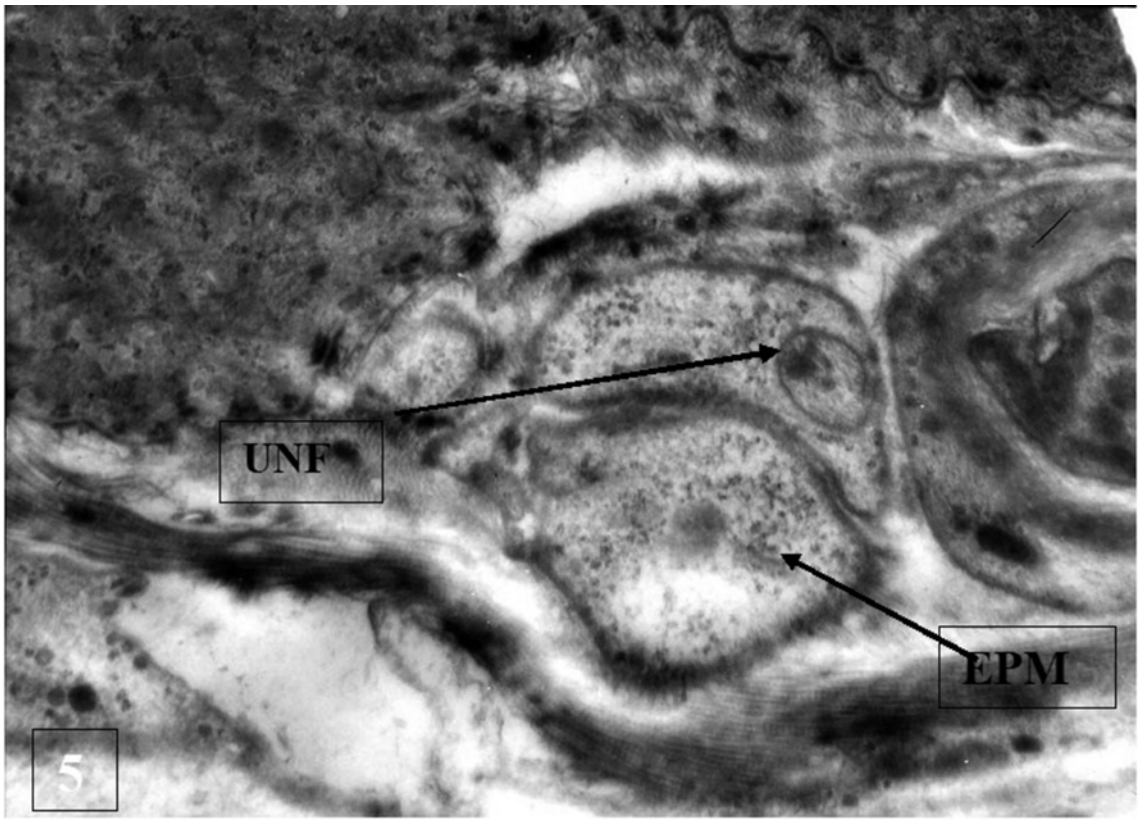


Fig. 3. Ultrastructure of a vessel of connective tissue, the lumen of which is filled with clusters of bundles of fibrin fibers (F), platelets (P), erythrocytes for 24 hours of the experiment. Coll. X2000.



Myelin nerve fibers (MNV), electron-dense precipitate masses (EPM), coagulates (K). Unmyelinated nerve fibers (UNF) Autophagolysosomes (AFL)

Fig. 4. Ultrastructure of myelinated nerve fibers (MNV), which have electron-dense disorganized axoplasm and mesaxons in the form of electron-dense masses of precipitates (P) and coagulates (K). The axoplasm of unmyelinated nerve fibers (BMNV) is limited by a plasma membrane that does not have clear contours. Autophagolysosomes (AFL) in the cytoplasm of a neuroleumocyte, at 15 min of the experiment. Coll. x23000.



Electron-dense precipitate masses (EPM), Unmyelinated nerve fibers (UNF)

Fig. 5. Ultrastructure of unmyelinated nerve fibers (BMV), the membranes of which do not have clear contours. The presence of precipitates (P) in the cytoplasm of a neuroleumocyte at 24 hours of the experiment. Coll. x17000.

and the disintegration of individual endotheliocytes were observed in the capillary lumens. A marked increase in secretory granules was found in individual mast cells.

All the damage in the ultra-structures we found were identified by a number of researchers as accompanying the development of increased thrombin formation and attributed to the pathological process described in the reproduction of simple coagulation dystrophy [1, 2, 4, 6, 7]. Therefore, as is known, the main active process in this case is the development of generalized decompensated thrombino-genesis, and the result of thrombin-induced changes in the structure of proteins, namely: the conversion of fibrinogen to fibrin (in the blood and in PST), actin polymerization (the conversion of G-actin to F in cells -actin) and denaturation of other proteins (enzymes, receptors, regulators and structural proteins), so in fact they are primary coagulation damage to organs. At the same time, significant damage to the ultrastructure of the nerves of the mucous membrane of the gums was revealed. Thus, already 15 minutes after the onset of reproduction of acute simple coagulation dystrophy of the periodontium, the cytoplasm of neurolemocytes contained precipitates and coagulates. The myelin layer of myelinated nerve fibers did not have a clear structural organization and orderliness of mesaxons and was often represented by local clusters of homogeneous electron-dense masses (Fig. 4).

Cytoplasm of axons with disorganized myelin sheaths was mainly represented by lysed fibers and filled with precipitates and coagulates of disintegrating organelles. Most of the unmyelinated nerve fibers were found to be in a state of disorganization and disintegration. Their axoplasm is electron light, and the plasma membrane is loose.

The cytoplasm of neurolemocytes, which included unmyelinated nerve fibers, was disorganized and saturated with electron-dense homogeneous masses (Fig. 5).

DISCUSSION

Coagulation damage to organs, according to the data in the modern literature, simultaneously includes three mechanisms of trophic reduction – enzymopathic, circulatory and neurotrophic, which during the next 24 hours causes a significant increase in damage to cell structures up to their disintegration (secondary dystrophic damage) [1, 2, 10, 13, 14, 16]. That is, in the test animals, under the conditions of the experiment, all gum damage characteristic of dystrophic periodontal damage and, in particular, periodontal disease, occurred. The obtained results, considering existence of the thrombin-plasmin system in all environments of the body [10, 11, 15] confirm and expand the previously substantiated coagulation-trophic theory of the pathogenesis of periodontitis [1]. Cell damage, according to this theory, develops in two stages: in the first – under the influence of

thrombin (primary coagulation damage), and in the second – as a result of a sharp disorganization of their trophic (secondary dystrophic damage). The cause of cell trophic disturbances, in turn, is: a) denaturation of intracellular proteins, enzymes and regulators, with a decrease in their biological activity; b) reduction of neurohumoral trophic influence on cells, on the one hand, as a result of non-perception of these influences by coagulation-damaged receptors of cells, and on the other hand, as a result of impaired passage of trophic impulses along coagulation-damaged internal nerve fibers. As a result, the nervous system cannot send and cells cannot perceive neurotrophic influences. We found similar ultrastructural damage to the gums during the ultrastructural examination of the gums of patients with periodontitis without clinical manifestations of inflammation. In particular, in the gingival stroma, there are microthrombi in the capillaries, mainly in the form of a homogeneous protein mass of increased electron density. There were also bundles of fibrin fibers or erythrocyte-platelet-fibrin microthrombi. Significant damage to nerve fibers and their synapses was recorded. They appeared in the form of damage to the myelin and non-myelin fibers of the gums, which undoubtedly created dystrophic effects on the periodontal tissues [12].

Precipitates, coagulates or continuous cytogel were found in the cells, next to which we found damage to membrane and non-membrane organelles. Frequent damage to the integrity of tissue basophils with their degranulation into the intercellular space was revealed. The main sign of damage to membrane structures (mitochondria, endoplasmic reticulum, Golgi complex, karyotheca and cytomembrane) was the loosening (loss of contour) of their membranes. The basement membrane is loosened and in many places there is a violation of lilosity. A number of areas of the surface layers of the epithelium are formed by flat-shaped electron-dense and electron-light cells, which are more typical of cells of the granular layer than of the stratum corneum, and there are also areas that often completely lack cells of the stratum corneum [12].

So, at the ultrastructural level, disseminated microthrombosis, mucoid swelling and fibrinoid transformation of the intermediate connective tissue and coagulation-dystrophic changes of periodontal tissues and cells were revealed. Therefore, taking into account the results of the studies highlighted in the literature [3,12,14,15] and similar lesions of the gums found at the ultrastructural level, presented by us, as a result of studies, on animals, have signs of coagulation-dystrophic damage caused by generalized thrombinogenesis, and by its the essence is actually a process of decompensated enhanced biocoagulation (cyto-histo-hemocoagulation).

CONCLUSIONS

Coagulative damage to the ultrastructural elements of the periodontal nervous system is one of the important factors in the pathogenesis of dystrophic periodontal damage. Under these conditions, trophic disturbances occur, similar to those that occur when the integrity of the nerve is disturbed (neurotrophic mechanism of dystrophy).

Under conditions of predominance of thrombinogenesis (thrombin action), irreversible changes in cells and nerve fibers can occur, and therefore, the physiological process turns into a pathological one with irreversible damage to the structures of cells and nerve fibers of the periodontium.

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AFFECTION ON CARIES AND ITS COMPLICATIONS OF TEMPORARY TEETH OF CHILDREN IN A REGION WITH EXCESS FLUORINE CONTENT IN DRINKING WATER

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ABSTRACT

Aim: The aim of the study was to determine the indicators of caries and its complications in the temporary teeth of children who permanently live in a region with a high fluoride content in drinking water.

Materials and Methods: It was examined with the definition of caries and its complications 277 children in the age range from 2 to 13 years, who were born and permanently live in the urban-type settlement of Mashivka. The fluoride content in the drinking water of the settlement was 1.7-2.5 mg/l.

Results: During the analysis of data from the survey of children who were born and permanently lived in the urban-type settlement of Mashivka, it was determined that the prevalence of caries of temporary teeth probably increases with age. Half of the 3-5-year-old children had caries-affected teeth, and temporary tooth caries reached the highest rates in 10-year-old children. It should be noted that a fifth of children in the youngest age group (3-5 years old) suffer from pulpitis and periodontitis of temporary teeth.

Conclusions: The conducted examination of children urban-type settlement of Mashivka confirms the opinion that the excessive content of fluorine in drinking water does not have a caries-protective effect, and the intensity of the process reaches the indicators characteristic of regions with its optimal content. Such a situation requires strengthening measures for both primary and secondary prevention of dental diseases.

KEY WORDS: children, periodontitis, teeth, caries, pulpitis, fluorosis

INTRODUCTION

A person's dental health is formed in early childhood and depends on the general state of the body and the influence of environmental factors. Environmental factors play one of the leading roles in incidence of caries. The compound and properties of drinking water used by the people affect the health of the population as a whole and the development of the dentition-maxillofacial system in particular [1]. Undoubted factors that determine impressionability to caries include the level of fluoride in the environment, especially in drinking water. The consumption of fluoride has both beneficial and harmful effects on health, and it depends on the level of its entry into the body. Fluorine reduces the incidence of caries, and if the population has provided with drinking water with optimal fluoride compound, it can prevent this pathology of the hard tissues of the teeth [2, 3]. However, the role of fluoride in the development of caries is unambiguous. When the concentration of this element in drinking water is low, the prevalence of the disease reaches of the high rates - up to 98-100% [4], while optimal fluoride content helps to reduce the level of morbidity. Excessive fluoride intake through the consumption of fluoride-rich artesian water and foods can lead to dental and bone fluorosis, ranging from staining and local areas of destruction of tooth enamel, to stiffness and pain in joints, changes in bone structure and calcification of ligaments. In addition, increasing the concentration of fluoride in drinking water above the optimal value does haven`t any anti-caries effect.

The high prevalence of complicated caries, namely periodontitis, indicates insufficiently effective dental prevention in general and imperfect methods of treatment of caries and pulpitis [5 - 8]. The development of therapeutic measures for children with pulpitis and apical periodontitis of temporary teeth in order to reduce the severity of the consequences is extremely important. An important stage for this is the preliminary study of the epidemiology of caries and the determination of the main risk factors in the region.

AIM

Thus, the purpose of the study was to determine the indicators of caries and its complications in the temporary teeth of children who permanently live in a region with a high fluoride content in drinking water (Mashivka, Poltava region, Ukraine).

MATERIALS AND METHODS

The study was conducted in the period from November 2019 to January 2020 and included 277 children who were born and permanently live in the city of Mashivka: 55 children aged 3-6 years (21 boys and 24 girls) who studied in kindergarten and 222 schoolchildren aged 7-13 (105 boys and 117 girls) who studied in a secondary school. The examination was conducted by only one permanent dentist. Calibration was carried out for all the indicators used in the study. In this clinical study, the number of temporary teeth with caries, the number of removed temporary teeth due to caries, the number of temporary teeth with fillings due to caries, dmf index (Caries index for primary teeth, d is for decayed teeth, m is for missing, f is for filled teeht), as well as the number of temporary teeth with complicated caries (According to the International Classification of Diseases (ICD-10)K04: Diseases of pulp and periapical tissues). The results of the examination made it possible to calculate the average number of temporary teeth affected by caries and its complications, as well as the frequency of caries and its complications.

The fluoride content in the drinking water of the settlement was 1.7-2.5 mg/l (according to the Regional Office of Water Resources in the Poltava Region of the State Water Resources Agency).

The study was conducted in accordance with the recommendations of the World Health Organization (WHO) for epidemiological studies using artificial lighting and a dental mirror and a dental probe [5]. The requirements of the Declaration of Helsinki, principles and norms of the Convention of the Council of Europe on Human Rights and Biomedicine, provisions of the current legislation and orders of the Ministry of Health of Ukraine were carried out during the study.

The Ethics Committee of the Poltava State Medical University granted ethical approval for the examination (protocol No. 38 dated October 10, 2019). The school participating in the study was informed and an informed consent form was explained to the parents to sign before the examination.

All schoolchildren, whose parents signed the informed consent, were examined. The criteria for inclusion in the study were: the age of the child from 3 to 13 years at the time of screening, who were born and permanently live in Mashivka; informed consent, completed and signed by parents. The exclusion criteria were: children who moved to Mashivka after birth; incorrect collection of data about oral health; failure to provide a signed consent form by the parents.

The results of the examination were recorded in patient's charts and statistically evaluated. For statistical analysis, continuous variables were described by number and frequency of occurrence. These variables were described as means, standard deviations, medians, quartiles, minimum and maximum values. Statistical differences between the two groups were tested using the Student's t test. Differences with p-value < 0.05 were considered statistically significant. Statistical evaluation of the research results was carried out using Statistica 10.0 software (Stat-Soft Inc., USA).

RESULTS

During the analysis of data from the survey of children who were born and permanently lived in the urban-type settlement of Mashivka, it was determined that the prevalence of caries of temporary teeth probably increases with age. Half of the children in the first age group (3-5 years) had teeth affected by caries, and the intensity of the process was 1.65+0.5 teeth per one examined patient. Children aged 6-8 years had a somewhat higher prevalence of caries in temporary teeth (62.1%; 57.5%; 62.9%), and the intensity of the process increases and fluctuates around 3 caries-affected teeth per one child (2.97± 0.57; 2.48±0.43; 3.04±0.44 teeth per examinee, respectively).

We determined the highest prevalence of caries of temporary teeth (almost 70%) in 10-year-old children, and the intensity of the process in them turned out to be quite high - 2.27±0.39 teeth per one examined. From the age of 11 years, there is a gradual decreasing in the prevalence of caries in temporary teeth - from 42.4% in 10-year-olds to 10.3% in 13-year-olds. This reduction in the intensity of the process is associated with physiological changes in the teeth. The intensity of caries of temporary teeth relays in the same direction as the prevalence - from 1.27+0.42 teeth per one examined in 10-year-olds to 0.21+0.49 teeth per one examined in 13-year-old children.

It should be noted that a fifth of children in the youngest age group (3-5 years old) suffer from pulpitis and apical periodontitis of temporary teeth with a fairly high intensity - 0.42±0.15 teeth per one examined child (Table 1). In 7-year-old children, the prevalence of caries complications decreases with a simultaneous increasing in its intensity. In our opinion, this situation is related to the change of the affected temporary incisors and the growing involvement of temporary molars with the majority of chronic periodontitis. The level of intensity of complicated caries increases as children grow older. Thus, in 8-year-old children, the intensity of caries complications of temporary teeth is the highest and reaches of 3 teeth per one examined. There is a gradual decrease in indicators from 0.54±0.2 among 9-year-olds to the level of 0.07±0.2 teeth per one examined among 11-12-year-olds. Such dynamics of caries are associated with the physiological change of carious temporary molars to permanent premolars. It should be noted that all children who had cases of complicated caries of temporary teeth belonged to II-III groups according to the degree of caries activity. The level of intensity tends to decrease with age, and it is associated with both premature removal of such teeth and physiological changes in the teeth.

The increase in the share of complicated caries in the structure of dental morbidity in children has caused considerable concern in recent years. The decline in the implementation of sanitation in the work of children's dentists, the cancellation of dispensary work in schools and kindergartens led to insufficient implementation of primary prevention and inadequate secondary prevention, which, in turn, leads to an increase in the specific weight of caries complications, especially in temporary teeth. Despite the anti-caries effect of fluoride, its excess level no

Table 1. Indicators of caries of temporary teeth and its complications among the children of the urban-type settlement of Mashivka, M+m

Age, years	Amount of children	Prevalence of complicated caries, %	Intensity of complicated caries, M+m
3-5	26	19,23	0,42±0,1
6	29	24,6	0,62±0,1
7	40	27,5	0,78±0,3
8	27	28,5	0,41±0,2
9	35	25,7	0,54±0,2
10	29	13,79	0,31±0,2
11	33	15,15	0,21±0,1
12	29	6,89	0,07±0,2
13	29	7,0	0,07±0,1

longer has such an effect, and this leads to the occurrence of fluorosis of the teeth and other negative consequences for the body as a whole. There is high fluoride content in drinking water of some settlements in Poltava region. Among them is the urban-type settlement of Mashivka, where the fluoride content in drinking water ranges from 1.7 to 2.5 mg/l. According to the data obtained in our study, 6-year-old children have a high incidence of caries in their temporary teeth - the prevalence is about 62% with an intensity of almost 3 carious teeth per one examined child. Complications of caries of temporary teeth in children of this age group were detected by us in 24.6% of examined children at the level of intensity - 0.62±0.1 teeth.

DISCUSSION

In our earlier studies among children of Poltava and its suburbs (fluoride content in drinking water is about 1.2 mg/l), it was determined that the prevalence of caries of temporary teeth ranges from 66.54 to 53.59%, with an intensity level of 2.14±0.14 to 1.76±0.12 teeth per one examined child [9]. That is, with almost the same prevalence of the process, the intensity of caries of temporary teeth was higher in children who consumed drinking water with high fluoride content.

When comparing our data with the results of research by other scientists who conducted similar research in other regions of Ukraine, some differences were identified. Thus, as a result of a study conducted among children aged 6-7 years in the city of Kharkiv (optimal fluoride content in drinking water), it was determined that the prevalence of caries of temporary teeth was 54.6% with an intensity level of 4.19±0.29, which was determined as an intermediate level. In the structure of the CS index, the components "C" - temporary teeth affected by caries, which are subject to treatment or removal, and "S" - sealed temporary teeth, were equal and accounted for 51% and 49%, respectively. That is, the data of these researchers indicate a lower prevalence of caries of temporary teeth with a significantly higher level of its intensity [10].

Both the level of intensity and the prevalence of caries and its complications of temporary teeth are much higher in children in the western parts of Ukraine, where the drinking water is poor in fluoride content. Thus, among 6-year-old children living in Bukovina, caries of temporary teeth was diagnosed in 91.83% of cases, and the average value of intensity of caries of temporary teeth is 5.19±0.30; 13.62% of temporary teeth with complicated caries were found, and the share of prematurely removed temporary molars was 4.39% [11].

A retrospective analysis conducted by a team of scientists confirmed the high prevalence (96.9%) and intensity (14.9±1.9) of caries in children aged 5-6 years in the Zakarpattia region (the fluoride level in the water is 0.1–0.3 mg/l) and significant intensity of its complications (3.8 ± 0.05 teeth). High rates of prevalence, level of intensity of caries and its complications are directly linked by researchers to the insufficient intake of fluorine and iodine in the human body, which leads to an imbalance in the processes of enamel de- and remineralization, which leads to the destruction of the enamel crystal lattice and the appearance of defects in the hard tissues of the teeth with their subsequent destruction [12].

High incidence rates were also determined in children of the Ternopil region, which is characterized by a low fluoride content in drinking water. Thus, during the analysis of indicators of caries damage to temporary teeth in the examined children, it was established that the prevalence of caries in boarding school children is 96.4% with an intensity of damage CS=3.4, and in children of a general education school this indicator corresponds to 94.2% with CS=3.1 [13].

Therefore, our examination of children who live permanently in regions with high fluoride content and the comparison of our results with the data of studies conducted in other regions of Ukraine that differed in fluoride content confirms the opinion that excessive fluoride content in drinking water is not has a caries-protective effect, and the intensity of the process reaches the levels inherent in regions with its optimal content.

CONCLUSIONS

The analysis of the examination data of the children of the urban-type settlement of Mashivka indicates a low level of their dental health, taking into account the indicators of caries and its complications of temporary teeth. Such a situation requires strengthening measures for both primary and secondary prevention of dental diseases.

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REVIEW ARTICLE

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HIV CRIMINALIZATION'S ORIGINS, ENFORCEMENT, AND SOCIAL IMPACTS

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ABSTRACT

This article aims to raise awareness and stimulate serious discussion about the ineffectiveness of HIV criminalization and its impact on human rights and public health and to propose improvements in criminal law regulation. The study is based on the empirical and analytical data of the Joint United Nations Programme on HIV/AIDS, the World Health Organization, legal acts, drafts legal acts, legal practice, and statistics of Ukraine, legal acts of the USA, Germany, Estonia, Latvia, Lithuania, and Poland. In total, 21 laws, drafts of laws, other documents, and 26 court decisions were analyzed. Dialectical, comparative, analytical, synthetic, systemic, sociological, induction, and deduction research methods were applied.

The criminalization of HIV stems from a lack of awareness among policymakers and society about advances in medical science and ways to control the epidemic. Such regulation is ineffective, leads to stigmatization of people living with HIV, and has a negative impact on the epidemic. Causing harm to a person's health by intentionally infecting a person with a severe infectious disease could be criminalized under the general norm on bodily harm, excluding the stigmatization of patients with certain nosologies.

KEY WORDS: public health, criminal law, human rights, stigmatization, bodily harm

INTRODUCTION

Ending the epidemics of AIDS by 2030 is one of the targets of the UN Sustainable Development according to the plan of action for people, planet, and prosperity "Transforming our World: The 2030 Agenda for Sustainable Development". This plan was approved by all countries-member of the 70th session of the UN General Assembly in New York (September 2015), which hosted the UN Sustainable Development Summit [1].

Political Declaration on HIV and AIDS: Ending Inequalities and Getting on Track to End AIDS by 2030, adopted by the United Nations Member States at the United Nations General Assembly High-Level Meeting on AIDS (June 2021), aims to achieve this goal [2]. One of the inalienable obligations that States have undertaken is to commit to urgent and transformative action to end the restrictive and discriminatory laws, policies and practices, stigma, and multiple and intersecting forms of discrimination, including based on HIV status and human rights violations that perpetuate the global AIDS epidemic.

At the same time, many countries, including Ukraine and Poland, have laws that criminalize people living with HIV for intentional or reckless transmission of HIV to another person, as well as for the very fact of creating a risk of such transmission when the consequences have not yet occurred. Not being narrow specialists on this problem, lawyers, as a rule, consider their existence quite justified since criminal law should respond to the behavior of people who create a danger to other members of society. At the same time, the issues of the effectiveness of HIV criminalization and its compliance with modern achievements of medical science in the field of prevention and combating the epidemic do not find due attention in legal science.

On the part of representatives of medical science, as well as international organizations working in the field of combating HIV/AIDS, there is evidence that the stigmatization of people living with HIV through criminal law not only does not contribute to the reduction of HIV transmission but, on the contrary, leads to an increase in their number, which negatively affects the epidemic situation.

In addition, the criminalization of HIV is an obvious manifestation of discrimination based on health status, which cannot be considered acceptable in a democratic society. Therefore, there is a need to decriminalize the very fact of placing a person in danger of being infected with HIV, as criminalizing such behavior violates human rights and negatively affects public health.

AIM

This article aims to raise awareness and stimulate serious discussion about the ineffectiveness of HIV criminalization

and its impact on human rights and public health and to propose improvements in criminal law regulation.

MATERIALS AND METHODS

The study was conducted in 2023 based on empirical and analytical data from the Joint United Nations Programme on HIV/AIDS, the World Health Organization, normative acts, draft normative acts, legal practice and statistics of Ukraine, and legal acts of Germany, Latvia, Lithuania, and Poland. In total, 21 laws, draft laws, other documents, and 26 court decisions were analyzed.

In the first stage of the research, dialectical and analytical methods were used to study the origins of HIV criminalization, as well as the development of relevant legal acts in Ukraine and some states of the USA. Subsequently, the current legislation on HIV criminalization in Ukraine was studied. Then, the legislation of Ukraine was compared with the relevant legislation of Germany, Estonia, Latvia, Lithuania, and Poland using the comparative method. At the next stage, using analytical and systematic methods, the positions of medical scientists - experts in the field of HIV/AIDS - expressed in scientific articles on the ways of HIV transmission and the impact of HIV criminalization on the epidemic situation were analyzed. Further, using sociological and analytical methods, as well as methods of induction and deduction, the statistics of application of Article 130 of the Criminal Code of Ukraine (after this - CCU) "Infection with HIV or any other incurable contagious disease" for the last ten years were analyzed, as well as 26 judgments of Ukrainian courts, issued based on Article 130 of the CCU. In the next stage, analytical and systematic methods were used to analyze the positions of Ukrainian lawyers on the criminalization of HIV, as well as experts from international organizations working in the field of HIV/AIDS prevention and treatment. In the final stage, conclusions and recommendations were drawn.

REVIEW AND DISCUSSION

ORIGINS AND CURRENT SITUATION WITH HIV CRIMINALIZATION

Criminal law has traditionally been regarded by a significant proportion of politicians and society at large as an effective way of addressing severe social problems. The reaction of many countries to the emergence of HIV in the early 1980s, the development of which led to the deadly disease AIDS, was no exception. After the first cases of HIV infection were registered in the United States in 1981, the morbidity and mortality of AIDS patients increased dramatically [3]. At that stage, medical science did not have sufficient information about both the ways of HIV transmission and ways to prevent the development of the disease. There was fear and panic among the population about the danger of contracting a deadly disease for which there was no cure. To stop the spread of the deadly virus, many countries around the world enacted criminal laws that severely penalized people living with HIV for virtually any action that could lead to a threat of transmission to another person. Criminal punishment was provided for both intentional and negligent infection with HIV and for placing a person in danger of being infected in the absence of such consequences.

Researchers provide data that as of 2022, 82 countries have HIV-specific criminal laws in place. Since the first documented prosecutions in the 1980s, 81 countries have pursued HIV criminalization cases-under HIV-specific laws in 35 countries and under other laws of general application in 48 countries (with a few jurisdictions applying both HIV-specific and general laws). [3]

Thus, in the United States, the response to the demands of active voters, religious groups, and politicians was the adoption throughout the country of laws that criminalized the behavior of HIV-positive people who allegedly exposed others to the risk of contracting the virus [4]. American researchers note that "in 1990, passage of the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act ushered in a new era of federal HIV legislation. States that received federal funding through the CARE Act (e.g., for testing, surveillance systems, treatment, etc.) were required to have legal mechanisms to prosecute HIV-positive individuals who knowingly exposed others to the virus [4]".

In Ukraine, HIV was first criminalized in 1987 by supplementing the 1960 Criminal Code with Article 108-2, "Infection with the Human Immunodeficiency Virus," the first part of which established a penalty of up to five years imprisonment for knowingly putting another person at risk of HIV infection, and the second part of this article established a penalty of up to eight years imprisonment for infecting another person with HIV by a person who knew that he or she had an infection caused by this virus. [5]

During the following codification of criminal legislation in Ukraine in 2001, the criminalization of HIV was retained. Up to the present time, Article 130 of CCU punishes willful placing of a person in danger of being infected with HIV (part 1), infection of another person with HIV by a person who was aware of himself/herself being a circulator of this virus (part 2), infection of two or more persons or a minor (part 3) and willful infection of another person with HIV (part 4). The maximum penalty for offenses under this article ranges from three years of imprisonment (part 1) to ten years of imprisonment (part 4) [6]. It is noteworthy that only part 4 of article 130 of CCU provides for punishment for intentional acts that led to the infection of another person with HIV. When committing the crime provided for in part 1, infection of another person does not occur, and when committing the crimes provided for in parts 2 and 3, the punishment is established for HIV infection of another person through negligence.

It should be noted that Article 130 of the Criminal Code of Ukraine also penalizes placing a person in danger of being infected with any other incurable contagious disease dangerous to human life. However, this provision cannot be validly applied in Ukraine because, for more than 30 years of the existence of this article, the Ministry of Health of Ukraine has not developed a list of incurable contagious diseases dangerous to human life. There is no such list in the documents of the World Health Organization either.

Despite this, there is a vicious practice in Ukraine of punishing people on Article 130 of CCU for placing a person in danger of being infected with any other incurable contagious disease dangerous to human life. This situation does not regard the fact that modern medicine does not consider tuberculosis an incurable disease.

Therefore, to prevent violation of human rights in the application of criminal law and taking into account the achievements of modern medical science, the existence of this provision needs urgent revision. Poland Penal Code establishes penalties for a person who knows that he is infected with HIV and exposes another person to the infection. Thus, according to Art. 161 (§ 1) whoever, knowing that he or she is infected with HIV or affected by a disease venereal or infectious disease, a serious incurable or real life-threatening disease life, directly exposes another person to infection with such virus or such disease, shall be subject to a penalty of imprisonment from 3 months to 5 years. According to § 3 of this Article, if the perpetrator of the act specified in § 1 exposes several persons, it shall be punishable by imprisonment for a term of one to ten years. [7] It should be noted that in addition to the problematic nature of criminal punishment for exposure to HIV, attention should be paid to the use of the term "venereal disease" by the Polish legislator. A similar problem exists in Ukraine (Article 133 of CCU. The concept of "venereal disease" is outdated and is not used by WHO in the 10th and current 11th versions of the International Statistical Classification of Diseases and Related Health Problems (ICD). The ICD currently uses the term "sexually transmitted diseases," which includes a wide range of diseases that can be transmitted in other ways, and a significant proportion of which do not pose a severe risk to human health. [8] All this shows the groundlessness of retaining in the criminal law the norm providing for punishment for infection with a venereal disease.

In Latvia, Criminal Law also consists of the HIV criminalization. According to Section 133, for a person who knowingly commits infection of a person with human immunodeficiency virus or hepatitis B or C virus, the applicable punishment is the deprivation of liberty for a period of up to five years or temporary deprivation of liberty or probationary supervision, or community service, or fine. [9]

The other attitude has countries that do not have any special criminal law provisions about HIV criminalization. Thus, for example, the criminal legislation of Germany [10], Estonia [11], and Lithuania [12] do not have special regulations about HIV but use general provisions about serious bodily harm or violation of the regulations governing the control of epidemics or communicable diseases.

THE VALIDITY AND EFFECTIVENESS OF THE HIV-CRIMINALIZATION FROM THE POINT OF VIEW OF THE MEDICAL SCIENCE

Based on their experience in the field of HIV/AIDS prevention and treatment, as well as the current state of medical science in this area, health professionals have a negative attitude toward HIV criminalization. Of particular concern is the disregard by legislative and law enforcement bodies in many countries for the achievements of medical science, which results in the criminalization of actions of people living with HIV that either could not lead to HIV transmission to another person at all, or the risk of such transmission is close to zero. The application of criminal law contrary to the achievements of medical science not only leads to unjustified restriction of human rights and freedoms stigmatization of people living with HIV but also undermines efforts to combat the HIV epidemic.

Thus, in July 2018, twenty authoritative scientists from regions worldwide – specialists in the field of HIV published an «Expert Consensus Statement to address the use of HIV science by the criminal justice system» (after this - Expert Consensus Statement). As the publication's authors point out, a detailed analysis of the best available scientific and medical research data on HIV transmission, treatment effectiveness, and forensic phylogenetic evidence was performed and described so it may be better understood in criminal law contexts.

Based on scientific proof, evidence has been presented that the actions most often considered by courts as offenses that pose a risk of HIV transmission are, in fact, either not likely to result in HIV transmission at all or have an extremely low probability. Thus, the authors of the Expert Consensus Statement scientifically substantiate that HIV transmission during a single episode of sex, biting, or spitting ranges from no possibility to low possibility. In addition, the use of modern treatment methods has the effect that the amount of the virus in the body of a person living with HIV is reduced to a level undetectable by medical tests, which makes it impossible to transmit it to another person in particular through unprotected sexual contact. However, this circumstance is not considered when addressing the issue of criminal punishment for putting at risk of HIV infection [13].

In July 2023, WHO published a policy brief on " The role of HIV viral suppression in improving individual health and reducing transmission." Among the key messages of this paper are those that emphasize the zero or negligible risk of HIV transmission through sexual intercourse by people on regular antiretroviral therapy, namely:

"People living with HIV who have an undetectable viral load using any WHO-prequalified combination of sample and testing platform, including dried blood spot samples, and continue taking medication as prescribed have zero risk of transmitting HIV to their sexual partner(s).

People living with HIV who have a suppressed but detectable viral load and are taking medication as prescribed have almost zero or negligible risk of transmitting HIV to their sexual partner(s)" [14].

Taking into account the scientific evidence presented, it is a gross violation of human rights to criminalize people living with HIV for actions that not only did not lead to but objectively could not lead to HIV transmission or the probability of such transmission was extremely low and approached zero.

The said Expert Consensus Statement also draws attention to the fact that criminal law does not consider the fact that

since the discovery of HIV in the early 80s, medical science has achieved significant results in the treatment of diseases caused by the presence of this virus. Thus, the authors point to "the positive health impact of modern antiretroviral therapies that have improved the life expectancy of most people living with HIV to a point similar to their HIV-negative counterparts, transforming HIV infection into a chronic, manageable health condition" [13]. This situation raises the question of the need to reconsider the attitude to HIV infection as a serious harm to human health.

Another critical aspect of the Expert Consensus Statement is the scientific basis for the fact that "the use of scientific evidence in court found that phylogenetic analysis alone cannot prove beyond reasonable doubt that one person infected another although it can be used to exonerate a defendant" [13]. Since there is no precise science-based methodology to provide evidence that one person transferred HIV to another person, there is a very high likelihood of miscarriage of justice and criminal punishment of the innocent.

Prepared and published by twenty scientists, the Expert Consensus Statement was subsequently supported by another 71 scientists from regions worldwide, a list of which is published in Supplementary Material to this Statement – S1. Endorsers of the Expert Consensus Statement [13].

In the same year, scientists from the USA, Thailand, Australia, and Switzerland published a scientific article, "Addressing HIV criminalization: science confronts ignorance and bias" [15], in which they expressed support for the position described in the Expert Consensus Statement. The authors of this article also focused on the negative impact of HIV criminalization on public health. Thus, researchers indicate that "no data support HIV criminalization as a supposed deterrent to protect innocent people from becoming HIV positive. On the contrary, criminalization of HIV transmission creates an unjust public health environment where individuals living with HIV may be fearful about disclosing their status, which may delay their own engagement in care. In a world where highly effective tools exist to enhance the lives of people living with HIV and to curtail HIV transmission through the ongoing use of effective antiretroviral medication, any disincentive to engage in care is undesirable from a public health and human rights standpoint" [15].

In 2022, the article "When Law and Science Part Ways: The Criminalization of Breastfeeding by Women Living with HIV" was published, the authors of which, based on the evidence provided, claim that "the criminalization of breastfeeding by people living with HIV is unjustified. Yet, we are witnessing a wave of criminal prosecutions, particularly in Africa. Legal mechanisms are being mobilized to punish and shame rather than protect human rights. In these circumstances, gains in health research have not been translated into gains for women's rights and children's well-being." In addition, the researchers express strong support for the scientific consensus that "HIV criminalization threatens the health and well-being of people living with HIV and jeopardizes the goals of ending HIV discrimination and, ultimately, the epidemic. Not only do punitive laws targeting people living with HIV lack a scientific evidence base, they perpetuate stigma and serve as barriers to HIV prevention, treatment and care" [16].

In 2023, UNAIDS Reference Group on HIV and Human Rights published a statement, "Decriminalization and the end of AIDS: keep the promise, follow the science, and fulfill human rights" [3]. This statement says that "states have unanimously committed to the Sustainable Development Goals of ending AIDS as a public health threat by 2030 and to achieving gender equality and just and inclusive societies. In the United Nations General Assembly's Political Declaration on HIV of 2021, they recognized that ending inequalities is essential to the goal of ending AIDS and adopted the targets of the Global AIDS Strategy 2021-2026, including the abolition of criminal and other punitive laws, policies and practices targeting key populations affected by HIV." UNAIDS Reference Group on HIV and Human Rights demands that states fulfill their obligations. The aspect of HIV-criminalization calls for "abolish or reform relevant laws that are used to criminalize HIV transmission, exposure or non-disclosure, ensuring that the law, in whatever form, allows for criminal liability only in cases of actual, intentional transmission at most" [3].

JUDICIAL STATISTICS AND JUDICIAL PRACTICE OF UKRAINE ON THE HIV-CRIMINALIZATION

As already noted, in Ukraine, HIV is criminalized in Article 130 of CCU, "Infection with HIV or any other incurable contagious disease," which establishes criminal punishment for placing in danger of being infected, as well as for intentional and negligent infection with HIV or other incurable infectious disease.

Over the last ten years, from 2013 to 2022, 78 offenses under Art. 130 of CCU, at the same time, 23 proceedings were sent to the court with the charge, and the rest of the cases were terminated [17]. It is very doubtful that such activity of the justice system could have a significant impact on curbing the HIV epidemic, given that Ukraine had the second highest rate of newly diagnosed HIV infections in the WHO European Region in 2021 after the Russian Federation at 37.1 per 100,000 population. The total number of newly infected with HIV for the period from 2013 to 2021 amounted to 139,393 people [18].

Analysis of the Unified State Register of Court Decisions [19] showed that since 2006, 22 first-instance court sentences and four judgments of appellate courts issued under Article 130 of CCU are publicly available. Out of the total number of verdicts, Article 130 of CCU was applied in three verdicts in connection with placing in danger of being infected with tuberculosis infection, in 16 - placing in danger of being infected with HIV, and in three - HIV infection by negligence.

As already noted, the application of Article 130 of CCU to cases of endangering tuberculosis, which is classified as an incurable contagious disease dangerous to human life, is an obvious violation of the principle of legality. There is no normative act in Ukraine that would establish a list of incurable contagious diseases dangerous to

human life, and the fact that tuberculosis is incurable is not indisputable. In those sentences in which criminal penalties were imposed for placing of a person in danger of being infected with tuberculosis, the defendants and their defense counsel agreed with the charge and did not challenge its illegality; these sentences were not reviewed on appeal. These circumstances, combined with the lack of professionalism of the judges and prosecutors, led to an unjust judgment.

16 sentences that imposed criminal penalties on HIV-infected persons under Part 1 of Article 130 of CCU for placing of a person in danger of being infected with HIV that did not result in the transmission of the virus can be divided into the following four groups:

1. Failure to disclose HIV-positive status when donating blood
2. Biting and spitting
3. One-time or attempted sexual contact during the commission of rape or other crimes
4. Regular sexual contact with a partner

Failure to disclose HIV-positive status when donating blood took place in two of the sentences studied under Article 130 of CCU. In one case, the convicted person explained that he decided to donate blood due to his difficult financial situation; in the second case - a person wanted to be re-tested for HIV because he had doubts about the diagnosis. It should be noted that since Ukrainian legislation provides for mandatory testing of donor blood for infections, including HIV, such behavior not only did not but also could not lead to the transmission of HIV to another person.

Biting and spitting were qualified under Article 130 of CCU as placing of a person in danger of being infected with HIV in five of the sentences studied. Even though modern medical science considers such actions as those that exclude the possibility of HIV transmission to another person, or, under certain circumstances, the risk of such transmission is extremely low and close to zero [13, 14], Ukrainian courts continue to consider such behavior as placing of a person in danger of being infected with HIV, which is an apparent violation of human rights.

One-time sexual contact or attempted sexual contact during the commission of rape or other crimes occurred in five of the sentences studied. In three cases, the rape was committed by a person previously diagnosed with HIV; in one case, there was voluntary sexual contact followed by open possession of the victim's money and gold jewelry; in one case, there was attempted sexual contact during which the victim broke free and ran away, but the court did not classify such acts as sexual violence. In none of these cases of sexual contact, was HIV transmitted to the victim. This situation is another confirmation of the correctness of the opinion of HIV experts that the probability of HIV transmission through a single sexual contact is extremely low and close to zero [13]. There is no doubt that perpetrators of rape or other crimes should be criminally punished, but the validity of punishment for placing of a person in danger of being infected with HIV is not undisputed.

Regular sexual contact with a partner that did not result in transmission from an HIV-infected person occurred in 4 of the sentences studied. In 2 of these cases, the defendants claimed that they had informed their partner that they had HIV, which was not disproved in court by any evidence other than the partner's objections. In 3 convictions, there was information that the convicts were in treatment and on antiretroviral therapy, one of whom gave birth to a healthy child during this period. However, there was no information in the sentences about the amount of virus in the blood of these persons, taking into account the antiretroviral medicines and whether there was a risk of sexual transmission of the virus to other persons.

In 3 of the 22 sentences studied, criminal punishment was imposed for *negligently infecting another person with HIV*. For example, in one case, a person was convicted under Part 3 of Article 130 of CCU for HIV infection that caused the death of two people - a husband and a child. At the same time, the death of the husband, caused by diseases caused by HIV infection in the AIDS stage, occurred less than two years after the convicted person learned of her HIV infection, which, considering the average duration of HIV infection, casts doubt on the evidence of which of the spouses was first infected with HIV. As for the vertical transmission of HIV from mother to child, this fact was established in court, and the perpetrator refused to administer antiretroviral therapy to the child [20]. In two other sentences, criminal punishment was imposed based on Part 2 of Article 130 of CCU for HIV infection that occurred as a result of prolonged sexual contact during cohabitation. At the same time, there was no evidence beyond a reasonable doubt that the convicted person was the source of HIV transmission to the victim, as the court considered as evidence only the victim's testimony and the fact that the convicted person knew that he or she had HIV.

JUSTIFICATION OF HIV CRIMINALIZATION FROM THE PERSPECTIVE OF LAWYERS AND POLITICIANS

Despite the consolidated position of the medical community, which has demonstrated the unfoundedness of HIV criminalization and such a problematic application of Article 130 of CCU, there is a contrary opinion among lawyers who are not explicitly involved in this issue.

Thus, on 19.06.2023, draft law No. 9398, "On Amendments to the Criminal Code of Ukraine on Improvement of Criminal Liability for Infection with Infectious Diseases or Infection by their Causative Agents" was submitted to the Verkhovna Rada of Ukraine. This bill proposes to exclude from CCU Article 130, "Infection with HIV or any other incurable contagious disease," which should result in the decriminalization of creating a risk of HIV infection [21]. The Main Scientific and Expert Department of the Verkhovna Rada of Ukraine, in its opinion on this draft law, points out that the decision to decriminalize the act of placing of a person in danger of being infected with HIV is unjustified in given the large number of people living with HIV in Ukraine, as well as one of the highest rates of increase in the number of infected people in Europe [22]. A similar opinion on the validity of

criminalization of placing of a person in danger of being infected with HIV was given by the Main Scientific and Expert Department of the Verkhovna Rada of Ukraine on the draft law No. 6365 dated 01.12.2021 - "Draft Law of Ukraine "On Amendments to Article 130 of the Criminal Code of Ukraine on Reduction of Stigmatization and Discrimination against People Living with HIV" [23].

The opinion that criminalization of placing of a person in danger of being infected with HIV at the current stage of Ukrainian development will contribute to the fight against its spread is expressed by some authors and on the pages of legal journals. For example, this conclusion was reached by K. D. Yanishevska in a scientific article published in 2020 [24]. However, as can be seen from the list of references, the author is not familiar with the position of representatives of medical science - experts in the field of HIV, and the conclusion about the validity of HIV criminalization and its effectiveness is speculative and not scientifically proven.

It should be noted that the position on the necessity of HIV criminalization is quite widespread not only among representatives of legal science but also in society in general, as well as among some politicians. However, this position shows that its authors are unaware of the negative impact of HIV criminalization on the fight against the epidemic, as well as of the systematic gross violations of the rights of people living with HIV when applying criminal penalties for putting them at risk of HIV infection.

However, Ukraine, which has the second highest number of new HIV infections in Europe, is unable to ensure wide coverage of testing to detect this infection. This situation is especially true for key groups of people at high risk of HIV infection. An example of this is people serving prison sentences or in pre-trial detention. Thus, according to a study conducted in Ukrainian prisons in 2021, "approximately 20-30% of newly arrived detainees and prisoners refuse to take the test (72% of respondents believe so); 12% determined this indicator at the level of 40%; 8% - at the level of 50% or more; 7% - at the level of 10%". [25] This situation was repeatedly encountered by one of the authors of this article, who, as a representative of CO "100% LIFE", the largest patient organization in Ukraine, participated in providing counseling to prisoners during their HIV testing. The majority of prisoners who refused to be tested for HIV argued that in case of a positive result, they would immediately face restrictions on their rights, in particular, the threat of criminal punishment for placing of a person in danger of being infected with HIV. Such persons, having a reasonable suspicion of HIV, decided to refuse testing until their health condition significantly deteriorated, and they needed emergency medical assistance.

The attitude towards people living with HIV as a source of danger to others and the unfounded criminalization of their habitual, everyday behavior, contrary to the findings of modern medical science, leads to a set of negative consequences both for these people and society as a whole. In particular, the groundless fear of people being infected with HIV has the consequence of excluding people living with HIV from clinical trials. Such people are involved only in clinical trials of medicines intended for HIV prevention and treatment [26], while they are not involved in clinical trials of other medicines [27]. As a consequence, the impact of new medicines on people living with HIV and the compatibility of new medicines with antiretroviral therapy are not investigated. All of this indicates a lack of public concern for the health of people living with HIV, who, at certain stages of the disease, are highly vulnerable to a significant number of diseases.

The negative impact of unjustified and disproportionate restrictions on human rights on the epidemic situation is not unique to the HIV epidemic. The same situation was recorded during the COVID-19 pandemic when unprecedented restrictions on human rights and freedoms undertaken by States were widespread. Thus, Latvian scientists on this issue conclude that "an important element in the case of successful management of the COVID-19 pandemic prevention is the communication with patients as part of society. When patients' rights to freedom, life, and health are violated or pretend to be violated, patients may become proactive and try to protect their interests and rights. ... States should show that they are open to provide explanation and meaningfulness of decisions made. It is important for the public to understand why they should comply with and execute the decisions made" [28].

CONCLUSIONS

HIV criminalization, which emerged as a response to the emergence of a previously unknown deadly infection in the early 1980s, currently exists either in the form of special laws that criminalize HIV transmission or in the form of general laws that criminalize infection with a hazardous infectious disease as serious bodily harm or violation of the regulations governing control of epidemics or contagious diseases. At the same time, such punishment is established either only for an intentional act that had the consequence of infecting another person with HIV, or for both intentional and negligent acts that led to such consequences, or (for example, in Ukraine) for the mere fact of creating a risk of infection with HIV even if such infection did not occur.

Thus, there is currently a consensus among representatives of medical science that criminalization of HIV not only does not contribute to curbing the epidemic but also has the opposite effect, as it leads to the fear of people disclosing their status, delaying timely treatment. It is unacceptable to apply criminal law to people living with HIV for actions that not only did not but could not lead to HIV transmission to another person or had a very low probability of such transmission. Criminal penalties are only permissible for intentional acts that result in the transmission of HIV to another person. At the same time, it should be taken into account that, thanks to the achievements of medical science, HIV has now been transformed into a controlled chronic disease, in which the life expectancy of most people who use antiretroviral drugs does not differ from the life expectancy of people who are not infected with HIV.

Thus, the analysis of the practice of application of Article 130 of the CCU shows the validity of the conclusions of scientists - specialists in the field of HIV prevention and treatment - that criminal punishment for putting in danger of HIV infection and HIV infection by negligence is mainly applied unreasonably, because either in reality such danger did not exist or it was extremely low, or the fact of HIV infection by the accused was not brought beyond reasonable doubt. Such application of the criminal law is a violation of the rights of people living with HIV.

Among Ukrainian lawyers who are not specifically involved in the problem of HIV criminalization, as well as among a significant part of politicians, there is an opinion about the necessity of such criminalization as a factor of containment of the HIV epidemic. The study showed that this position results from a lack of awareness of the achievements of modern medical science in this area. Lawyers and politicians who are experts in this field insist on the need to take urgent measures to decriminalize HIV, as such criminalization violates the rights of people living with HIV and also negatively affects the epidemic situation.

All this shows the groundlessness of HIV criminalization from the point of view of both medical science and the effectiveness of the application of criminal law norms and their compliance with the principle of proportionality of limitation of human rights and freedoms in a democratic society. Therefore, it is necessary for the authorities of states that still criminalize the very fact of placing of a person in danger of being infected with HIV to take urgent measures to eliminate such norms from the criminal law. Only intentional acts that cause serious harm to the health of another person by infecting him or her with a serious infectious disease, which should include HIV, should be criminalized. Criminalization of behavior related to the transmission of only one type of infection, an example of which is available in the criminal laws of certain countries (including Ukraine, Latvia, and Poland), is inadmissible, as it leads to discrimination and stigmatization of patients by individual nosologies.

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REVIEW ARTICLE

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HISTORY OF ORIGIN, ADVANTAGES AND DISADVANTAGES, VECTORS OF APPLICATION OF THE DIAPHONIZATION METHOD: CURRENT STATE OF THE PROBLEM

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ABSTRACT

The article deals with the method of diaphonization, which consists in clarification and staining of tissues, organs and whole organisms for long-term storage in the form of preparations as one of the modern methods of morphological research and, in general, a powerful tool for studying the internal structure and topography of organisms. The authors have analyzed the history of the diaphonization method, its advantages and disadvantages. Its advantages include the ability to study the internal anatomy without destroying the object, detailing structures, preserving samples for further research, and the possibility of combining with other modern research methods. Despite its advantages, the diaphonization method also has certain limitations and disadvantages (possible deformation of structures, loss of color, time and space complexity, and limitations in application to certain types of organisms). With its three main application vectors (clinical, experimental, and botanical), the diaphonization method is an essential tool for researchers in many fields, which continues to evolve and find new applications, improving the overall scientific picture of understanding the structure of organisms and contributing to scientific progress. The article also highlights the importance and prospects of combining the diaphonization method with other techniques to determine a more accurate picture of the relative location and structural features of certain tissues, organs, and systems.

KEY WORDS: diaphonization, morphology, history of origin, advantages and disadvantages, clinical medicine, experimental medicine, botany

INTRODUCTION

It is a common fact that methods of morphological research can be rightly considered the basis for many branches of medicine and other natural sciences as a way to analyze the structure and its normal or pathological variants in organisms. Due to this, it is a constantly relevant issue to modernize, update and improve the existing methods of morphological research, their further development and improvement, taking into accounts the characteristics of research objects and the possibilities of modern scientific progress. Among a number of currently available methods of morphological research, we consider the method of diaphonization to be one of the most noteworthy as a relevant and modern method that can be used at different levels and in combination with other modern methods to form a more complete anatomical picture and obtain new information about the object of study [1-3].

AIM

The purpose of the study was to analyze the history of the origin, advantages and disadvantages, vectors of application of the diaphonization method based on the literature data.

MATERIALS AND METHODS

The articles were searched in open electronic databases of scientific literature. The following words and phrases were used for the search: "diaphonization", "history of diaphonization", "advantages of diaphonization", "disadvantages of diaphonization", "vectors of diaphonization application", "diaphonization in clinical medicine", "diaphonization in experimental medicine", "diaphonization in botany". The methods of abstraction, generalization, induction, deduction, explanation, and classification were used in our literature review.

REVIEW AND DISCUSSION

Diaphonization is a method that consists in reducing or "removing" the optical color of the objects under study in order to achieve their transparency while maintaining their morphological structure, which is mainly studied in the finished sample [4] (Fig. 1). Another name for the

Fig. 1. Newborn guinea pig after diaphonization.

diaphonization method is the "cleaning and staining method", which actually explains the essence of the method, which consists in enzymatic decolorization of the preparation and subsequent staining of its bone and cartilage structures with dyes. Sample preparation, proportions of working solutions, processing time and method of storage are determined by the characteristics of the tissues and the ratio of their various types in the preparation. Currently, small laboratory vertebrates are most often used for research using this technique, because due to their size and tissue characteristics, diaphonization on this type of preparation takes less time and is more effective (transparency is more expressed and the structures under study are more visible) compared to larger organisms.

The discovery and application of this method was an important step for research on normal and pathological anatomy. The method of diaphonization developed by Schultze in 1897 has been improved more than once by many scientists [5]. For example, in 1991, the German anatomist Spaltegolz proposed one of the methods of achieving transparency of anatomical specimens based on optical laws [6]. Its essence was to achieve transparency by placing previously prepared preparations in a solution with a refractive index equal to that of the tissue or organ under study. Also, the method of diaphonization, which can now be considered a classic, was developed in 1977 by scientists G. Dingerkus and L.D. Uhler [3]. It is according to this methodology that the essence of diaphonization is defined and updated protocols are still being created to take into account the characteristics of the tissues under study.

We have identified three main vectors of application of diaphonization (clinical, experimental and botanical), each of them having its own characteristics, prospects and features. It is worth noting that this classification is based on existing scientific publications describing the use of diaphonization for the study of certain objects [7].

The use of diaphonization for the preparation of tooth samples for the study of their tubular-root system was started by Robertson [8], who improved the current Spaltegolz protocol, taking into account the characteristics of tooth tissues. This technique is considered to be the basic one for research in clinical odontology and is currently being actively improved and widely used by scientists. With its help, by decalcification, purification and staining of preparations, the visibility of the system of roots and tubules of the tooth is achieved with the naked eye. Favorable factors for this are the small size and relatively easy accessibility of human teeth. Finished preparations, in addition to macroscopic studies, can also be examined under a microscope, combining diaphonization with various types of microscopy [7].

The mentioned above method has also become the basis for some other methods of dental examination, the

attractiveness of which, similar to the classical method of diaphonization, is the ability to accurately preserve the original location of canals, roots and cavities of the tooth without changing their topographic features. In addition, this method is often combined with modern technologies, such as electron microscopy, computed tomography, etc. The use of the diaphonization method in clinical practice allows to identify the topographic features of tooth parts, which is especially important for morphological studies or in the process of teaching students, as well as in clinical practice when working with extracted teeth. Accordingly, determining the relative position of canals, roots and cavities of the tooth, especially in atypical variants of their topography, can be useful in diagnosing disorders not only of a particular tooth but also of the entire dentition or jaws [8, 9].

Among the promising applications of diaphonization, it should also be mentioned its use in para-endodontic surgery, i.e. an alternative method to endodontic surgery for research, for example, leakage during filling. In this case, it is the use of diaphonization that simplifies the visualization of the tooth structure and the assessment of dye leakage between different materials in the root canal. In this case, the tooth to be examined is prepared: dentin is removed and old fillings, if any, are removed, and a dye or contrast solution is applied to the boundaries of the dentin and filling material to help highlight the boundary between these materials. To analyze the internal structure of the root and dye leakage, diaphonization is used in combination with special light that is transmitted through the tooth, and its intensity varies depending on the properties of the materials. In this case, the image of the internal anatomy of the root and the place of the dye leakage can be displayed on a screen or other visual device. This allows the dentist to see the structure of the root canal and measure the leakage rate at the interface between dentin and filling material. The data obtained in this way can be analyzed by the dentist to determine the quality of the filling, identify possible leaks that may require additional treatment, and improve the overall diagnosis and treatment of dental problems.

As for the experimental vector of diaphonization, as already mentioned, it is mainly used for studies of small laboratory animals (mice, rats, guinea pigs, rabbits), and the object of study is the corpses of such animals. Here it is important to mention the importance of the bioethical aspect in this context: it is significant that the method of diaphonization can be used on the bodies of animals that died in a "natural" way, which does not require causing harm and suffering to animals, i.e., violation of bioethics and rules for the use of laboratory animals in research [7]. Animals that have died as a result of diseases can be used for research, which allows them to be used in pathomorphological studies. At the same time, the bodies of animals that did not die as a result of disease can be used to create preparations intended to study normal anatomy and morphology, for example, as a kind of standard for comparing the corresponding structures in normal and pathological conditions.

According to the scientific literature available to us, the most common objects of experimental research using diaphonization are nervous, bone, cartilage structures and blood vessels [2, 10-12]. In particular, when studying bone and cartilage structures in laboratory animals, it is possible to investigate the degree of ossification of certain bone structures [11]. Also, based on the degree of ossification of the structures under study, it is possible to determine, for example, the age of the animal, or to diagnose calcification disorders, which can, accordingly, contribute to the diagnosis of disorders of not only osteogenesis but also hormonal and vitamin metabolism [12]. Such studies can be conditionally attributed to microscopic studies, while morphological changes in the topography of certain bone structures (as seen with the naked eye) are macroscopic. Among the studies on this topic, we can, for example, mention the work of Atanasoff and others. [5], where young male sturgeons are the object of study. Thus, using the diaphonization method and by combining it with computed tomography to obtain more accurate data, it is possible not only to identify certain pathologies in bony fish, but also to determine the causes of their occurrence, which, for example, may be due to changes in the diet of fish, their migration, and the influence of various environmental factors (temperature, water salinity, etc.). By analyzing the latter, it is hypothetically possible to determine and predict the effects of environmental changes on fish populations, which determines the use of the diaphonization method as an interdisciplinary research method that is relevant not only in the field of zoology and botany but also on a more global level.

Among the significant studies on the application of the diaphonization method in experimental practice, one should highlight the work devoted to the study of the characteristics of the auditory tube in pigs [13]. The object of study in this work is primarily non-standard, due to which the possibilities of diaphonization as a method of morphological research are expanded. The author also noted the high accuracy of diaphonization, which allows to notice the smallest morphological studies of the auditory canal without violating its integrity and surrounding structures, which is especially important given its relative topographic "inaccessibility".

Angiological studies by diaphonization primarily involve combining this method with methods of filling vessels, because the tissues of organs, the blood supply of which is to be investigated, enlightened by diaphonization, act as a kind of background for the vessels, which can be made more visually contrasting and visible by filling them with appropriate substances, the choice of which depends on the purpose and further course of the experiment [3]. Thus, it becomes possible to visualize for further research the peculiarities of branching and relative location of vessels, as well as their pathological disorders (ischemia, thrombosis, aneurysms, etc.). The results of such studies can be used not only for zoological research, but also in the field of experimental medicine. In the latter case, we mean, for example, the idea of using small (i.e., more

accessible for research by diaphonization) animals as a kind of model for understanding the mechanisms of angiotherapy methods under development in order to avoid the risks of unforeseen complications due to the use of the corresponding method in humans without prior experimental testing [14, 15]. In addition, the ability to observe the effectiveness of a particular vascular treatment method on the drug can contribute to the development of new methods or the improvement of existing ones. At the same time, the diaphonization method, due to the possibility of volumetric visualization without the use of screens and artificial changes in the location of vessels, is the most visual for such studies.

The study of blood vessels by combining diaphonization and computed tomography is also effective and promising, as it contributes not only to the study of blood vessels in vitro, but also to achieving greater depth of penetration and resolution [10], as well as to the digitalization and digitization of the results obtained, which will facilitate the dissemination of experimental results and expand the boundaries of scientific discussion. Thus, the architecture of blood vessels can be studied more comprehensively, which contributes to the understanding of physiological and pathological processes in organs and systems of the body.

In general, the experimental vector of diaphonization has connections with various fields of science other than anatomy and morphology. Due to the fact that this method allows to study organs, bones, cartilage and other structures without the use of invasive procedures, it becomes possible to compare the anatomical features of different species and study their changes, for example, through the prism of evolution [16]. The study of anatomical features by means of diaphonization can help to reveal the adaptation and specialization of organs and tissues associated with certain environmental conditions [17]. Thus, the study of anatomy using diaphonization can help to establish more accurate differences between different species and groups of animals, which can be useful for their classification and systematics in paleontology, etiology, etc. In addition, diaphonization can help study the development of animal embryos and fetuses at different stages. This can help establish the timeframe for the development of various tissues and organs. Also, diaphonization can be used to study the functional aspects of animal tissues and organs, primarily, for example, blood vessels or nervous structures [4, 10]. In addition, as mentioned above, diaphonization can be used in medical research to create models for studying the anatomical aspects of animals in order to conditionally project the results onto the human body to improve diagnostic and treatment methods [18, 19].

As for the botanical vector of using diaphonization, it, like the other vectors, allows us to study the internal structure of plants in greater detail and without damaging the samples, which is important for various aspects of botanical research. That is, in botany, diaphonization can help study the internal structure of plant leaves and stems, including cellular structures, vessels, fibers, and other components [20]. There are a number of studies on the use of diaphonization in botanical research, which describe in detail the differential differences of this area of application of the method and describe the technology and results of specific studies [21-23]. In general, it is worth noting that the study of the internal structure of plants using diaphonization helps to understand how they adapt to different environmental conditions, and also allows us to monitor the development and differentiation of tissues during different stages of plant growth. In general, in botany, the method is used to solve various scientific problems and deepen understanding of the functioning of plant systems.

By analyzing and testing the existing protocols for conducting experiments using the diaphonization method [4, 7], we were able to identify certain functional and general features of the diaphonization method, which define it as a multifunctional, relevant, and promising method of morphological research. Among them, for example, it is worth noting the relative atraumatic nature of the method, which allows for research in general without violating the integrity of the object and without physically destroying it for future study [3]. In addition, under the right conditions, finished preparations have a fairly long shelf life, which facilitates their use for scientific and educational purposes. This is also facilitated by the rather high detail of the objects prepared using the diaphonization method. It makes it possible to study quite small structures (vessels, nerves, small organs) with a fairly high level of visualization, moreover, in a three-dimensional format, which is especially important for future physicians to understand the topographic and spatial relations of certain structures and parts in the body [1, 8].

The advantages of the research technology itself include cost-effectiveness, which is ensured by the relative availability of materials required by the research protocol. In addition, the use of complex and highly specialized equipment is not required to obtain finished products, which also simplifies the methodology. However, combining diaphonization with other technologies, including, for example, digital technologies, significantly expands the effectiveness and prospects of research. Important features of the method include its relative versatility, i.e., the ability to process organisms of different classes (fish, amphibians, reptiles, mammals), which is, however, limited by the size of the research object. Also, the diaphonization method is a relatively safe research method that does not require contact with hazardous substances or harmful fumes for a long time. The finished products are stored in closed containers and do not require direct contact with the product. This greatly simplifies the visualization of the finished product, makes it possible to use the method for educational purposes, and protects the researcher from deterioration of health during the preparation and dissection of samples.

However, like any research method, the diaphonization method has certain drawbacks. Among them are color loss, possible changes in tissue structure, which, although insignificant, can distort the results of research, which, however, requires further study and experimental

confirmation. Another peculiarity is the static nature of the method, i.e., the impossibility of using it to study the dynamic manifestations of the organism, which can, however, be studied by comparing similar samples. Also, diaphonization can be limited for large organisms or organisms with a complex structure, such as large and dense bones or exoskeletons, which narrows the choice of research objects. However, these shortcomings, in our opinion, are only certain features of the method that should be taken into account when conducting experiments using it to achieve the highest quality and most accurate results.

The success of diaphonization may depend on the type and concentration of solutions, the duration of its implementation, and the storage conditions of the drugs used, which may require appropriate optimization and testing [2]. However, in this regard, special attention should also be paid to the plasticity of the method, i.e. the possibility of changing it in order to optimize it in accordance with the histochemical characteristics of the tissues or organism that is the object of study. This creates really significant prospects for further development and improvement of the diaphonization method, which we see as one of our scientific tasks.

CONCLUSIONS

The method of diaphonization has a long history, which testifies to its importance in the study of anatomy and morphology of various tissues, organs, systems, and organisms. From early attempts to isolate internal organs and achieve their transparency to the modern use of chemical solutions, the diaphonization method continues to evolve and improve. The diaphonization method is extremely useful for scientific research in many fields. Its advantages include the ability to study internal anatomy without destroying the object, detailing structures, preserving samples for further research, and the ability to combine with other modern research methods. Despite its advantages, the diaphonization method also has certain limitations and disadvantages (possible deformation of structures, loss of color, time and space complexity, and limitations in application to certain types of organisms). With three main vectors of application (clinical, experimental and botanical), the diaphonization method is an important tool for researchers in many fields, which continues to evolve and find new applications, improving the overall scientific picture of understanding the structure of organisms and contributing to scientific progress.

PROSPECTS FOR FURTHER RESEARCH

The prospect for further research is, firstly, the application of the diaphonization method together with the methods of filling the vessels in order to study the anatomy and topography of the vessels supplying the brain in humans and some experimental animals; secondly, determination of the histological and histochemical features of various tissues of humans and experimental animals after the application of the diaphonization technique; thirdly, determination of the anatomical features of the jaws in experimental animals in normal conditions, in modeling fractures and contractures.

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REVIEW ARTICLE

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STATE OF ORGANIZATION OF PROVIDING ONCOLOGICAL MEDICAL CARE TO THE POPULATION OF UKRAINE

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ABSTRACT

Aim: The purpose of this work is to study the state of organizational factors in the provision of oncology care to the population of Ukraine and to determine the needs of the population in oncology care.

Materials and Methods: The following materials were used in study: a report on diseases of malignant neoplasms; report on medical personnel; report on contingents of patients with malignant neoplasms. The used methods were: bibliosemantic, content analysis, analytical, statistical and graphical methods.

Conclusions: The oncological control system in Ukraine is represented by institutions of various levels. The number of specialized beds is increasing from 8,587 in 2015 to 9,088 in 2021. there is a tendency to decrease the total number of medical personnel by 12% and the number of general practitioners - family medicine by 1.5%. During the period from 2015 to 2021, the contingent of patients with neoplasms increased by 21-24%. The rate of neglect of cases of malignant neoplasms registered in Ukraine during 2022 was 22.4%, which is 1.4% more than in 2021.

The system of oncology medical care of Ukraine is at a sufficient level, but there are certain difficulties caused by certain difficulties of the primary health care sector due to the decrease in the number of medical specialists. In the modern context, there are difficulties caused by the difficult migration situation of the population against the background of Russia's military aggression against Ukraine.

KEY WORDS: oncology medical care, staffing of the health care system, incidence, structure of malignant neoplasms

INTRODUCTION

The World Health Assembly "Cancer Prevention and Control in an Integrated Approach" (2017) recognized that cancer is the second leading cause of death worldwide. Most of the cases of death from oncological pathology fall on the percentage of countries with a low and middle income level. Oncological diseases are a threat to the health of the population. According to WHO forecasts, the number of new cancer cases may increase to 21.6 million by 2030. In accordance with paragraph 3 of the Sustainable Development Goals proclaimed by the resolution of the United Nations General Assembly in 2015 (ensuring healthy lifestyles and promoting well-being for all at all ages), the task was set to reduce mortality from non-communicable diseases by one third by 2030 and the set task of ensuring coverage of the population with health care services [1].

In 2020, cancer caused the death of more than 10 million people in the world. The most common types of cancer in the structure of causes of death are: lung cancer (1.8 million deaths); colon and rectal cancer (916,000 deaths); liver cancer (830,000 deaths); stomach cancer (769,000 deaths); breast cancer (685,000 deaths). Every year, 400,000 children are diagnosed with cancer [2, 3].

All countries face the important task of strengthening the health care system at the national and regional levels in the interests of increasing the availability of oncological care and of monitoring the burden of oncological diseases [4, 5].

WHO notes that attention should be paid to the fact that if people have access to primary and specialized medical care systems, it will be possible to detect oncological diseases at an early stage, with their effective treatment and even complete healing. Cancer should not be a death sentence for anyone, anywhere. It is also noted that even in low-income countries, it is possible to achieve progress in this direction [2].

In Ukraine, more than 130,000 new cases of malignant neoplasms are detected every year, and more than 60,000 patients die from this pathology. Along with this, more than 1 million people with an oncological diagnosis are constantly registered at the dispensary [6].

The fight against malignant neoplasms is one of the most important health care problems in Ukraine, the relevance of which is determined by the constant increase in its incidence, difficulties in timely diagnosis, high cost and complexity of treatment, high level of disability and mortality [7].

It has been proven that primary prevention and conducting preventive examinations of the most common types of malignant neoplasms can significantly increase the level of early detection and timely treatment of such diseases and save state budget funds, as well as reduce the number of cancer patients in Ukraine [8].

AIM

The purpose of this work is to study the state of organizational factors in the provision of oncology care to the population of Ukraine and to determine the needs of the population in oncology care.

MATERIALS AND METHODS

To achieve the goal, the following materials were studied: a report on diseases of malignant neoplasms (form No. 7); report on medical personnel (form No. 17); report on contingents of patients with malignant neoplasms (form No. 35). The retrospective search was five to seven years (2015-2022).

The following methods were used during the research: bibliosemantic (for the analysis of modern scientific literature), content analysis (for the analysis of normative and legal documents regulating the work of the oncology service), analytical and statistical methods (for the processing of indicators of the work of the oncology service) and a graphical method (for accompanying visualization of results).

REVIEW

The oncological control system in Ukraine is represented by institutions of various levels. The main oncological institution of the Ministry of Health of Ukraine is the National Cancer Institute, which carries out scientific and methodological management of oncological institutions, develops and implements modern methods of diagnosis and treatment of cancer patients. On its basis, the National Oncology Registry of Ukraine was created, prepared in accordance with the order of the Ministry of Health of Ukraine dated January 22, 1996 No. 10 "On the creation of the National Oncology Registry of Ukraine". The National Oncology Register unites a network of regional registers on the basis of regional (city) oncology institutions that work using a single information technology.

The main statistical indicators that indicate the prevalence of malignant neoplasms are morbidity and mortality rates.

The principle underlying the state system of cancer registration in Ukraine provides for mandatory filling in of regulated medical documents. In order to support the oncology registration system, the following medical registration documents were approved and regulated by the Ministry of Health of Ukraine in different years:

"Report on a patient diagnosed with cancer for the first time in his life..." (form No.090/o), which is of a signal nature and provides communication between general treatment and oncology institutions. Such a document is filled out for each new case of malignant neoplasm and is mandatory for all medical institutions of Ukraine. Within three days, it must be sent to the regional (city) oncology dispensary at the place of registration of the patient.

"Extract from the medical record of an inpatient with a malignant neoplasm" (form No.027-1/o), which is filled out by all medical institutions of Ukraine in case of detection or confirmation of the diagnosis of a malignant neoplasm.

"Protocol on the detection of a neglected form of malignant neoplasm in a patient" (form No.027-2/o), which is also filled out by all medical institutions in the case of detection or confirmation of a malignant neoplasm in the neglected stage (IV stage - all localizations of malignant neoplasms (C 00 - C 97 according to ICD-10, as well as the III stage of the process for visual localization of tumors).

The main internal accounting document of the oncology service of Ukraine is the "Registration card of a patient with a malignant neoplasm" (form No.030-6/o), which is formed on the basis of the above-mentioned primary medical documents. For the registration of cases of death from malignant neoplasms, the source document is the "Medical Death Certificate" (form No.106/o).

WHO notes that investment in human resources in the field of health care is one of the important components of strengthening and ensuring the effectiveness of health care and social protection systems in the conditions of today's challenges and international crises [9].

The network of health care institutions of Ukraine, in which assistance is provided to cancer patients, is represented by various health care institutions. Against the background of an increase in the incidence of oncology, the number of specialized (oncology) beds is increasing from 8,587 in 2015 to 9,088 in 2021.

Analyzing the staffing of the health care system of Ukraine as a whole and the oncology service separately, it was determined that recently in Ukraine there has been a tendency to decrease both the total number of doctors and individual oncology specialists with the only exception being a slight increase in the total number of oncology specialists (Table 1).

As can be seen from the given data, during the period covered by the study, staffing has relatively minor fluctuations in the indicator of the population's supply of doctors. However, for 2017-2022, there is a tendency to decrease the total number of medical personnel by 12% and the number of general practitioners - family medicine by 1.5% (Fig. 1). Such changes can have a negative impact on the initial diagnosis of precancerous conditions and directly oncological diseases, since they are initially detected during examination and treatment for other diseases.

At the same time, analyzing the provision of the population by oncology service specialists, a slightly different picture is observed. There is an increase in the total number of oncologists (from 0.17 per 10,000 population in 2017 to 0.19 per 10,000 population in 2022). At the same time, there is a slight decrease in the availability of radiologists (Fig. 2).

A total of 1,105,152 people were registered with malignant neoplasms in Ukraine in 2022, including 393,452 men and 711,700 women. In general, when conducting research on the contingent of patients with oncological pathology, an increase in the number of people with detected malignant neoplasms is observed throughout time. During the period from 2015 to 2021, the contingent of such patients increased by 21-24% (Table 2).

To determine the status of the organization of the diagnostic and treatment process, the main indicators were studied.

Table 1. Staffing of the oncology care service for the population of Ukraine (2017-2022)

Profile	2017		2018		2019		2020		2021		2022		Visibility (%) (2022 to 2017)
	abs	per 10000	abs	per 10000	abs	per 10000	abs	per 10000	abs	per 10000	abs	per 10000	
All doctors	159600	37,8	157550	37,53	154816	37,10	147616	35,64	144112	35,15	137759	33,60	88,8
Oncologists	718	0,17	729	0,17	708	0,17	714	0,17	752	0,18	776	0,19	111,7
Oncologists--surgeons	669	0,16	680	0,16	697	0,17	676	0,16	695	0,17	650	0,15	100
Oncologists--gynecologists	248	0,06	241	0,06	250	0,06	254	0,06	239	0,06	230	0,05	100
Radiologists	431	0,10	426	0,10	408	0,10	390	0,09	384	0,09	383	0,09	90
Doctors of general practice	14728	3,49	14814	3,53	15029	3,60	14797	3,57	14 367	3,50	14092	3,44	98,5

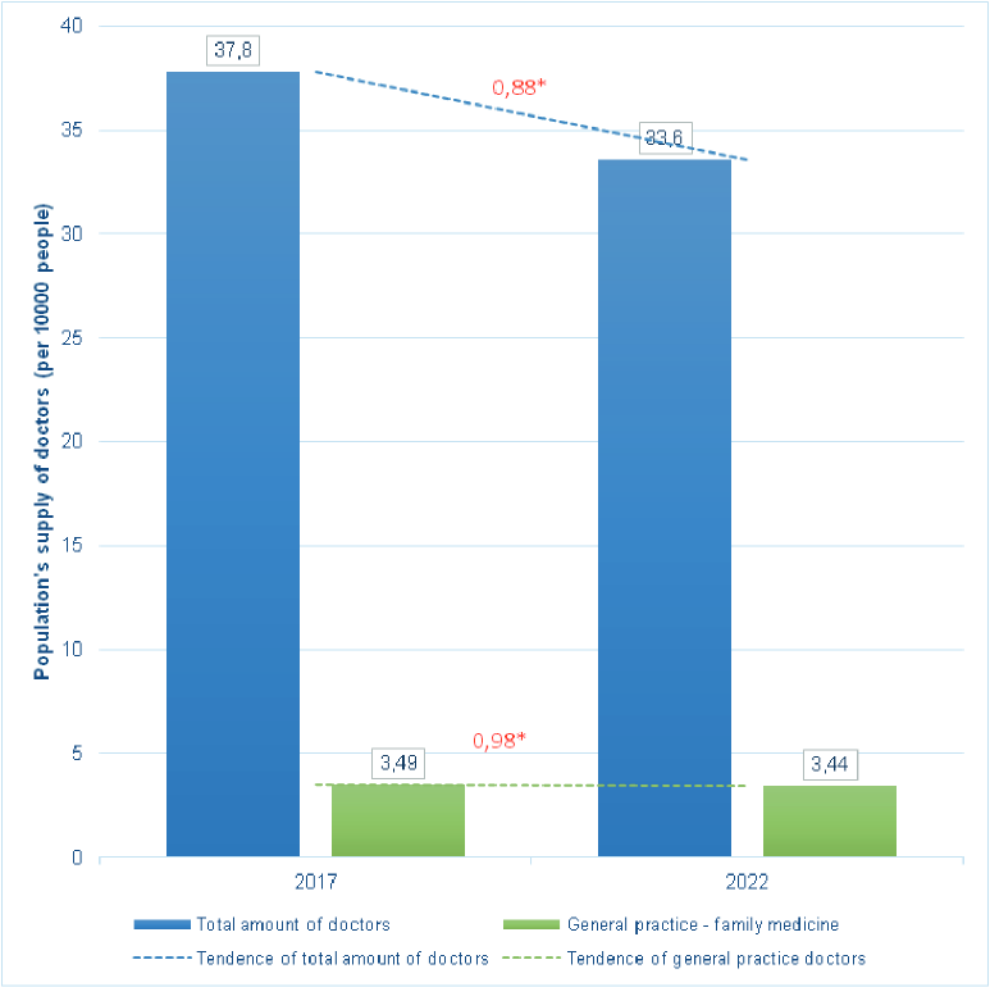

Fig. 1. Changes in staffing of the total number of doctors in the field of medical care of Ukraine. *Visibility index (relation between 2022 and 2017 in population`s supply of doctors).

Table 2. Contingent of patients with malignant neoplasms who were registered with an oncologist (per 100,000 population)

	2015	2020	2021	Visibility (%) (2021 to 2015)
Ukraine	2249,4	2665,0	2784,0	123,76
Rural population	1963,4	2280,0	2385,3	121,48
Urban population	2378,8	2836,0	2960,2	124,44
Population (0-17 years old)	73,6	87,5	90,8	123,36

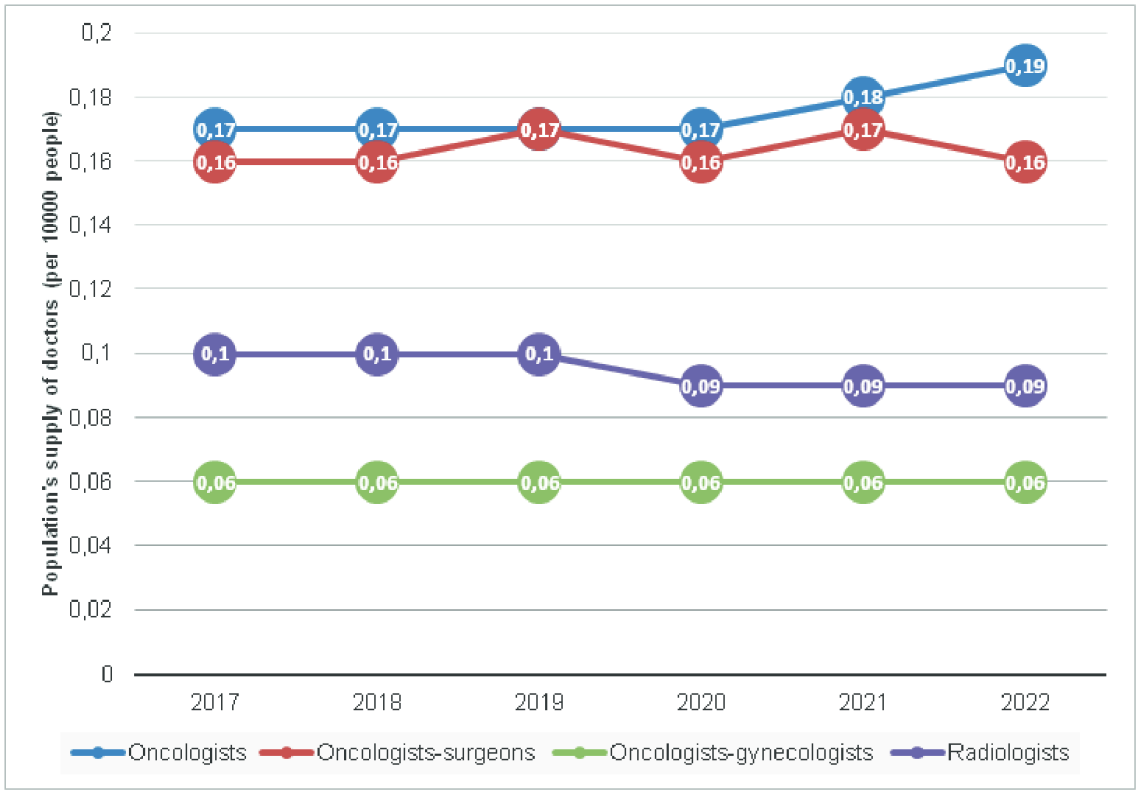

Fig. 2. Changes in staffing of the oncology service of Ukraine.

Table 3. Incidence of malignant neoplasms among the population of Ukraine (per 100,000 population)

	2015	2020	2021	Visibility (%) (2021 to 2015)
Ukraine	313,6	263,0	279,6	89,15
Rural population	300,6	246,0	260,0	86,49
Urban population	319,5	270,5	288,0	90,14
Male population	323,8	270,6	284,4	87,83
Female population	304,9	256,4	275,2	90,25
Working-age population	126,9	125,7	131,9	103,94
Population (0-17 years)	13,2	10,5	11,0	83,33
Children (0-14 years)	3,8	3,5	3,3	86,84

The state of diagnosis was characterized by the indicator of neglect of cases of malignant neoplasms - detection of the disease in the 4th stage or in the 3-4th stage with visual localization. The rate of neglect of cases of malignant neoplasms registered in Ukraine during 2022 was 22.4%, which is 1.4% more than in 2021.

At the same time, analyzing the incidence rates of oncological pathology during 2015-2021, there is a tendency to decrease the overall incidence rate in Ukraine by 11%, from 313.6 per 100,000 population in 2015 to 279.6 per 100,000 population in 2021. A similar picture is observed when analyzing indicators separately by group, depending on gender, age group and place of residence. The only opposite trend is inherent in the incidence rate of malignant neoplasms among the working-age population, where it increased by 4%, from 126.9 per 100,000 population in 2015 to 131.9 per 100,000 population in 2021 (Table 3).

It should be noted that since 2022, due to large-scale military operations on the territory of Ukraine, the collection of information on cancer patients, both newly discovered and those who were already registered, was difficult or partially interrupted.

As can be seen in Figure 3, in some regions of Ukraine, when comparing the incidence rates of malignant neoplasms in 2021/2022, it can be seen that in a number of regions there is a sharp decrease in the incidence rate, which is due to the conditions of hostilities in these regions and the outflow of refugees from these regions.

According to the National Health Service of Ukraine, the main most common oncological pathologies for which medical assistance was provided as part of the packages in 2022 are malignant neoplasms of the breast, prostate, rectum, ovary, sigmoid colon, upper lobe of the bronchus or lung, and endometrium (Cancer - register 2023).

Examining the structure of oncological diseases in men, it was noted that in 2022 the highest rate was noted for prostate cancer (12.9%), non-melanoma malignant skin neoplasms (9.2%), bladder cancer (7.1%), cancer colon (6.7%) and rectal cancer (6.3%) (Fig. 4).

In women, the first places in the structure of the incidence of oncological pathology are non-melanoma malignant neoplasms of the skin (16.2%), uterine body cancer (12.3%), cervical cancer (8%), thyroid cancer (6%) and melanoma of the skin (4.7%) (Fig. 5).

DISCUSSION

The organizational and methodological management of the oncology service of Ukraine is carried out by the National Cancer Institute of the Ministry of Health of Ukraine. The functions of oncology medical institutions include diagnosis, treatment and monitoring of cancer patients, as well as registration of disease cases in the region of activity, which ensures the maintenance of an information base for the assessment of morbidity and mortality from malignant neoplasms in Ukraine.

The primary importance for the high-quality work of the System is the standardization of documents, which will optimally ensure the work of the entire oncology service and includes the development and implementation of modern legislative and medical-technological documents based on the best clinical guidelines implemented from European and adapted to the conditions of the domestic health care system [10].

In our study, a clear trend towards a decrease in the total number of doctors was determined, which is consistent with similar data presented in the works of domestic scientists, who note the presence of a global trend towards a decrease in the number of doctors and nurses, as a result of which the state of health of the population and the level of organization of medical care in countries with a low development index is at risk due to a possible reduction in the scope of provision and a decrease in the availability of medical care [11, 12].

In the conditions of war and limited financial resources, the state continues to finance the medical system. The Government of Ukraine adopted the Program of Medical Guarantees for 2023, in which, along with such important types of assistance as rehabilitation in outpatient and inpatient conditions for adults and children; of psychological support at the primary level, funds are allocated for oncological assistance to the population [13].

Types of free medical care for cancer patients include:

– emergency medical care and first aid - at the pre-hospital stage by emergency medical aid stations (departments), emergency medical aid points in a life-threatening condition;

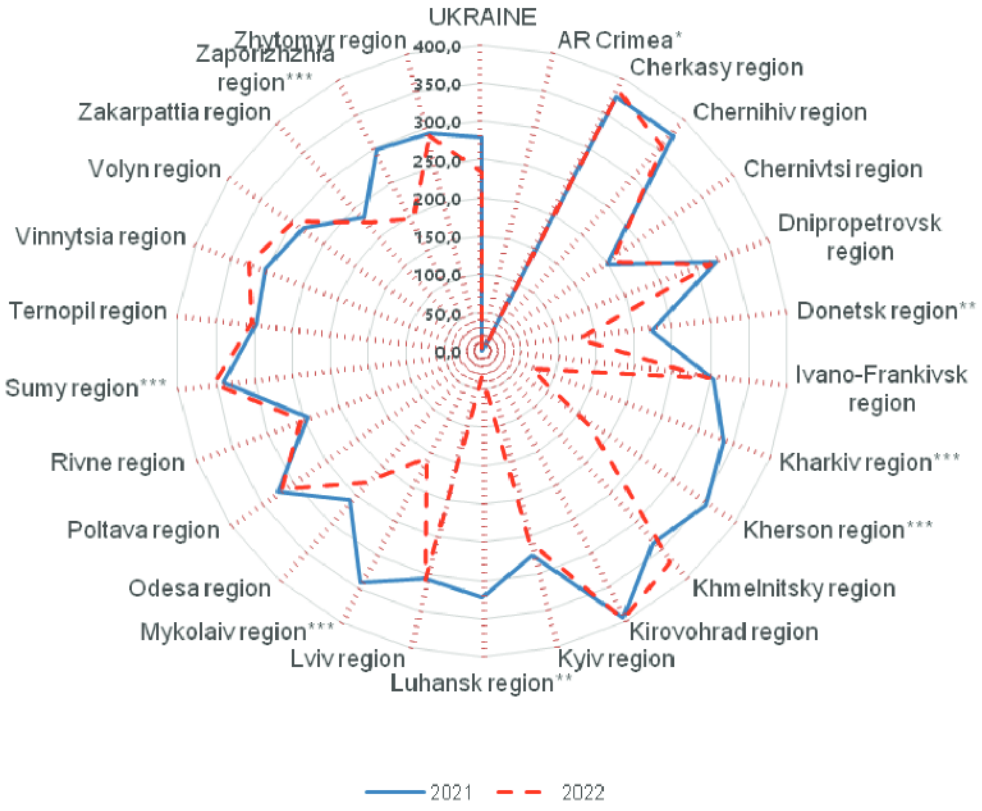

Fig. 3. Incidence of malignant neoplasms in Ukraine in 2021-2022. * - occupied territory since 2014; ** - territory partially occupied since 2014 and active hostilities since 2022; *** - the territory partially occupied since 2022 and where active hostilities are taking place.

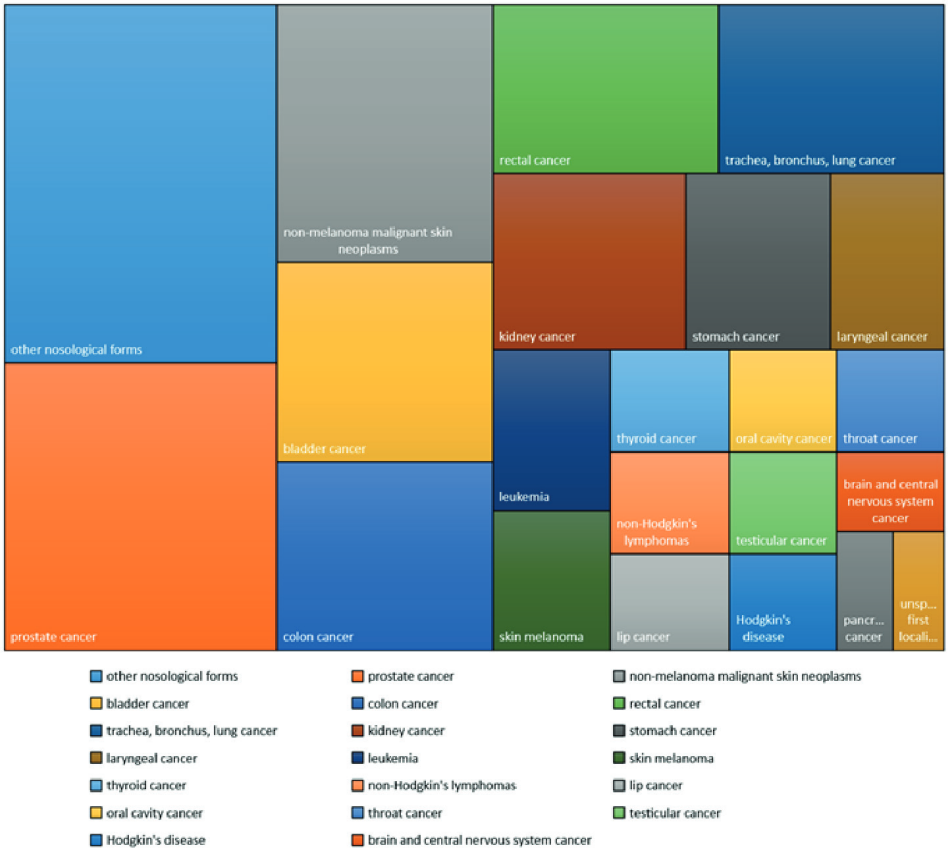

Fig. 4. The structure of malignant neoplasms in the male population in 2022.

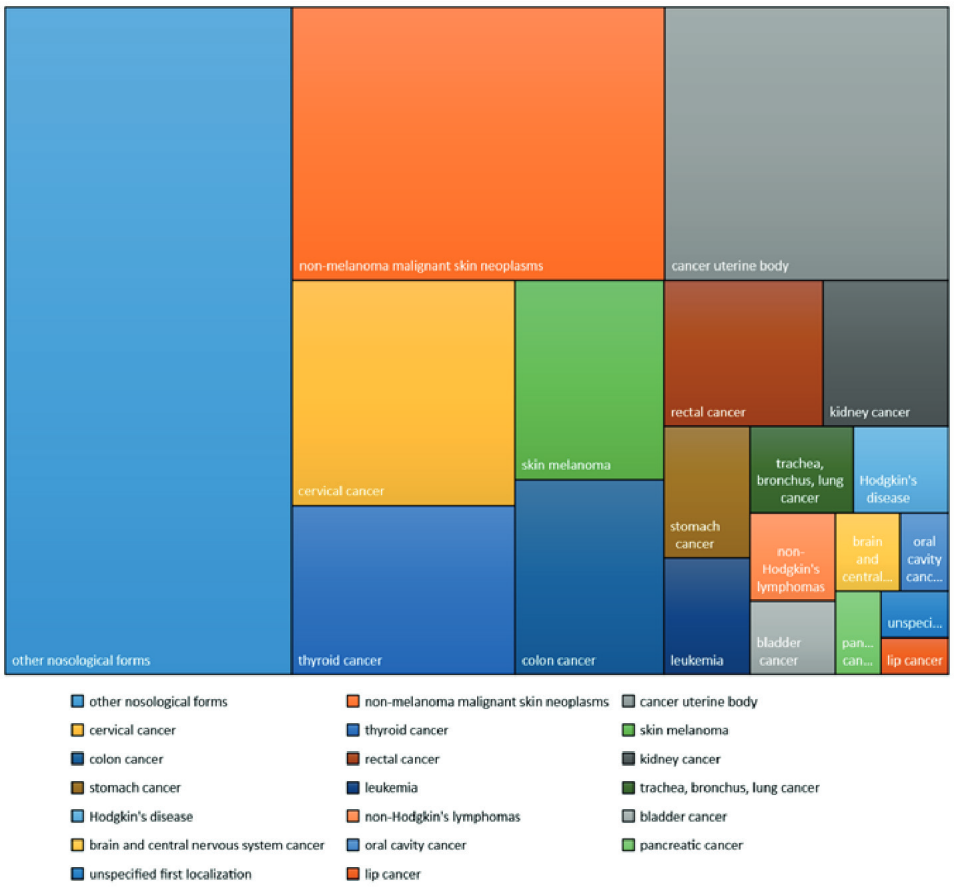

Fig. 5. The structure of malignant neoplasms in the female population in 2022.

– primary medical care
– specialized outpatient polyclinic medical care;
– inpatient medical care - in case of an acute illness and in urgent cases when intensive treatment, round-the--clock medical supervision and hospitalization are required, including for epidemic indications, for children, pregnant women and women in labor, patients referred by medical and social expert commissions, medical and advisory commissions;
– sanatorium-resort assistance to persons with disabilities and patients in specialized and children's sanatoriums;
– medical and social examination of disability.

Thus, the Medical Guarantee Program covers all types of medical care for oncology patients (diagnostic services, treatment, rehabilitation and palliative care). In order to optimize the timely detection of the most common malignant neoplasms, six examinations for the early detection of oncology are free upon referral: mammography, cystoscopy, hysteroscopy, bronchoscopy, colonoscopy and gastroscopy). These studies are recommended to the population after they reach a certain age: after 40 (mammography, colonoscopy) and 50 years (all others) [14].

Every patient with a confirmed oncological diagnosis has the right to free treatment in outpatient or inpatient settings. The treatment process is accompanied by free laboratory and instrumental studies (MRI, CT, etc.), as well as drugs, intensive therapy, oxygen support, pain relief [15].

The level of neglect of malignant neoplasms largely characterizes the level of oncological vigilance and literacy of primary and specialized doctors, as well as the diagnostic activity and capacity of the medical field as a whole. Along with the neglect indicator, attention should also be paid to the relative number of cases of diseases, the stage of which cannot be determined due to the absence or inaccuracy of the necessary identifying data in the signal medical documents.

CONCLUSIONS

So, as a result of the conducted research, it was determined that, against the background of constant improvement of medical care for cancer patients, some complications continue to be observed. First of all, due to the fact that the number of doctors of other specialties (therapists, general practitioners, others) decreases, the availability of medical care decreases and the possibility of early detection of oncological diseases worsens. At the same time, it should be noted a stable situation with a tendency to improve in the staffing of the oncology service.

The analysis of the accounting documentation makes it possible to establish a sufficient level of measures for the accounting and analysis of oncological patients. However, it is necessary to take into account that during the last period of time, the accounting of patients has difficulties, which is due to military aggression against Ukraine and the conduct of hostilities on its territory.

In Ukraine, the Program of Medical Guarantees has been adopted, which provides the maximum level of treatment and diagnostic possibilities for cancer patients.

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THE IMPACT OF THE INTRODUCTION OF ARTIFICIAL INTELLIGENCE TECHNOLOGIES ON THE CURRENT HUMAN RIGHTS AND FREEDOMS CONCEPT

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ABSTRACT

Artificial Intelligence (AI) has undeniably transformed the landscape of healthcare, offering unparalleled potential to enhance patient care, streamline diagnostics, and improve overall healthcare outcomes. As AI continues to make its way into the medical field, it has raised crucial questions about regulation, ethics, and patient safety and that is guiding us to the core question – how that will impact current human rights and freedoms concept, and is this concept ready for such an impact? The aim of the research is to identify and evaluate the potential impact of AI introduction in healthcare on modern human rights and freedoms concept, and on the basis of discovered complexities to propose ways to eliminate them. This study was conducted during June-October of 2023. Through a broad literature review, analysis of international and state regulation acts, scientific researches and opinions of progressive-minded people in this sphere this paper provide a guide to understanding the impact of AI introduction in healthcare on current human rights and freedoms concept. It is based on dialectical, comparative, analytic, synthetic and comprehensive methods.

KEY WORDS: artificial intelligence, healthcare, medical devices, software, EU artificial intelligence act

INTRODUCTION

Artificial Intelligence (AI) has undeniably transformed the landscape of healthcare, offering unparalleled potential to enhance patient care, streamline diagnostics, and improve overall healthcare outcomes. As AI continues to make its way into the medical field, it has raised crucial questions about regulation, ethics, and patient safety, and that guides us to the core question – how that will impact current human rights and freedoms concept, and is this concept ready for such an impact?

AIM

The aim of this research is to identify and evaluate the potential impact of AI introduction in healthcare on modern human rights and freedoms concept, and on the basis of discovered complexities to propose ways to eliminate them.

MATERIAL AND METHODS

This study was conducted during June-October of 2023. Through a broad literature review, analysis of international and state regulation acts, scientific researches and opinions of progressive-minded people in this sphere this paper provide a guide to understanding the impact of AI introduction in healthcare on current human rights and freedoms concept. It is based on dialectical, comparative, analytic, synthetic and comprehensive methods.

REVIEW AND DISCUSSION

The modern paradigm of ensuring human rights and freedoms is reflected in international and regional human rights conventions, such as the Universal Declaration of Human Rights [1], the International Covenant on Economic, Social and Cultural Rights (including General Comment No. 14, on the right to health) [2], the International Covenant on Civil and Political Rights [3], as well as regional human rights conventions such as the African Charter on Human and Peoples' Rights [4], the Inter-American Convention on Human Rights [5] and the European Convention on Human Rights [6]. In general, despite the relative modernity of this system, there are certain nuances that affect its effectiveness, including the fact that the above fundamental documents do not cover all countries of the world (due to regional regulation, reservations or nonratification for one reason or another), the fact that the protection of rights and freedoms is largely implemented through national legislation at the general and constitutional levels. An additional challenge to the further development of the system of human rights and freedoms is also posed by certain manifestations of technology development, especially artificial intelligence (hereinafter – AI) technologies, which, as a result of their implementation, can both contribute to the improvement and strengthening of such a system and pose threats and undermine the basic established principles of rights and

freedoms. These problems are becoming a subject of interest not only for the scientific community, but also for the highest political circles, where, in particular, the UN High Commissioner for Human Rights determines [7] that along with the potential positive effect of the introduction of high technologies in the medical field, additional risks may arise in the form of dehumanizing approaches to medical care, threats to the confidentiality of patient data, etc; [8] The United Nations Secretary-General, in response to the growing collection and use of data on the COVID-19 pandemic, called on governments to "put human rights at the center of legal frameworks and legislation on the development and use of digital technologies" [9] that was reflected in the scientific researches also [10]; the Council of Europe continues to explore the possibility and potential elements of a legal framework for the development and use of digital technologies in line with its standards on human rights, democracy and the rule of law; non-governmental organizations do not stand aside either [11]

The context of human rights, bioethics, and privacy in terms of the potential for introducing AI into the medical field can also be found in Article 8 of the European Convention on Human Rights: the right to respect for private and family life, home and correspondence [12]; the Oviedo Convention on Human Rights and Biomedicine, which covers the ethical principles of individual human rights and responsibilities [13]; the Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data [14] and the guidelines for the protection of individuals with regard to the processing of personal data in the world of big data prepared by the Convention's Advisory Committee [14]. In 2019-2020, the Council of Europe established a special Committee on AI to consult with stakeholders to identify opportunities and potential elements of a legal framework for the development and application of AI in line with the Council of Europe's standards on human rights, democracy and the rule of law. In addition, in 2019, the Council of Europe released the Guidelines on Artificial Intelligence and Data Protection [15], the European Commission on the Efficiency of Justice's ethical charter includes five principles related to the use of artificial intelligence for healthcare [16].

A significant part of the regulatory framework is made up of international and national acts related to the protection of personal data, which is itself a trend of our time. And given the fact that the functioning and development of AI itself is absolutely dependent on input data, this regulatory area will certainly also be affected by the intensification of AI implementation in all spheres of life, including medical relations. Among the key such system-forming acts are the following: The General Data Protection Regulation (GDPR) of the European Union (EU); in the United States, the Health Insurance Portability and Accountability Act; in addition, a number of recommendations and regulations that relate not to data in general, but to medical data directly should be noted.

Analyzing the above-mentioned regulations, individual governmental and nongovernmental recommendations and guidelines on the use of AI technologies, we can conclude that there is currently no unity in defining a system of relevant principles, but we can generalize certain priority fundamental areas that are certain "points of intersection" for many of them. Among them are transparency, justice, fairness, integrity, non-crime and responsibility, while some researchers [17] rightly emphasize that other principles, such as confidentiality, solidarity, respect for human dignity, sustainability, are currently underrepresented. This lack of a system of principles for the use of AI in general certainly affects the use of AI in medical practice, and we do not even have a pre-established vision of such a system. Instead, there are positive developments in the concept of the principles of use of technologies in the medical field in general [18; 19; 20], which certainly does not provide all the necessary guidelines for the implementation of such a complex and unique technology as AI, but it allows us to predict a certain vision and trends in the prospects for the relevant legal support of such a field. And the determining guidelines for the introduction of AI in the medical field should be proper and comprehensive documentation, transparency, risk management that meets the requirements of the healthcare sector, requirements for data quality, analytical and clinical validation, confidentiality and protection of personal data, etc.

The most acute aspect of the issue of AI implementation in medical practice in the context of the impact on human freedom is that the combination of these two components inevitably poses a number of difficult tasks that are on the verge of law and ethics. Some aspects of the above analysis have been studied in a separate research paper [21], so now we will shift the focus to the part that is directly related to the impact of the introduction of AI in medical practice on the system of ensuring human rights and freedoms. So, what ethical and legal challenges will be (and are already being) faced in the process of integrating AI into medical/pharmaceutical activities?

DECIDING ON THE APPROPRIATENESS/NECESSITY OF USING AI IN A PARTICULAR AREA

The novelty of the technology itself provokes potential risks of overestimating the results of its application and not taking into account the associated risks [22]. The AI technology itself may not meet the standards of scientific validity and accuracy currently applied to medical technologies, which are a long-standing standard. For example, the digital technologies developed in the early stages of the COVID-19 pandemic did not necessarily meet any objective standard of performance that would justify their use [23]. And the emergency situation itself does not and should not justify the deployment and implementation of untested technologies, given the potential impact on the lives and health of a large number of people.

Secondly, the benefits of AI can potentially be overestimated due to the erroneous failure to take into account digital and economic diversification between countries and relevant institutional features, which makes the potential effect of their implementation radically different between developed and least developed countries. This is primarily due to the critical importance of data quality, which is the "entry point"

of AI technology. Ensuring data quality among countries with different levels of economic development cannot be a priori the same, or at least comparable. Next, the predictive nature of the results of using AI in medical practice (e.g., predicting the susceptibility to certain diseases of a particular person or group of persons), despite the generally positive social effect, may lead to the marginalization of such persons/groups of persons, disproportionate provision of medical services, etc. (precisely because they have an increased risk of diseases such as HIV/AIDS).

And finally, even if we conditionally leave aside the above moral and ethical obstacles, we should take into account not only the technological but also the economic effect of AI implementation (both in terms of the cost of the technology itself and its impact on economic processes, the labor market, employment, etc.) For each specific scenario and technology, these forecasts and prospects may be ambiguous and far from obvious, and will vary based on many factors.

PROCESSING OF PERSONAL DATA

The collection and use of health data (clinical trials, laboratory results, medical records, etc.) is the basis of medical and pharmaceutical practice, and the amount of such data and sources of its approval have recently increased tremendously. Different types of data, collectively known as Biomedical Big Data, form a separate large-scale ecosystem that includes data from standard sources (medical services, healthcare, research) and other auxiliary sources (environmental data, lifestyle data, socioeconomic, behavioral and social data, etc.), which is associated with the digitalization of society, the proliferation of IoMT devices, etc.

The development of a successful AI system for use in healthcare relies on the critical need for high-quality data both to train the AI algorithm and to validate the algorithmic model and the resulting training results. And one of the problems with health data is its quality, which, combined with the fact that training data will always have one or more systemic biases due to underrepresentation by gender, age, race, sexual orientation, or other characteristics, will significantly affect the reliability and validity of the AI model's results. [24]

There is also a risk that a lack of confidentiality may harm a person, for example, through future discrimination based on their health status, transfer of such data to third parties, etc. One of the main problems is the vulnerability of data during its exchange or transfer, especially in the context of cybercrime or accidental disclosure. This becomes especially relevant for stigmatized and vulnerable groups who may be subject to discrimination or punitive measures in case of misuse of their data, including children. Accumulated data about a child can lead to future "delayed" discrimination, and it is important to consider children's right to privacy and autonomy in choosing health care.

The COVID-19 pandemic has accelerated efforts to collect data, track individuals' status, and create digital IDs to store health information. This was driven by the need to control the spread of the virus and take effective measures to minimize public health risks. Some of the measures that have been implemented or strengthened during the pandemic include:

Collecting and sharing health data: Many countries have implemented systems for collecting and sharing health data, such as COVID-19 test results or immunity to the virus. This helps to monitor the spread of the disease and take appropriate measures to control contagion.

Digital IDs and mobile apps: Some countries are using digital IDs or mobile apps to provide proof of vaccination or COVID-19 test results. This can be used to control access to certain spaces or services and to ensure safety in public places.

Contact tracing: Contact tracing technologies, such as Bluetooth apps or QR codes, have been used to detect and alert people who may have been in contact with COVID-19 patients. This helps to detect and contain the spread of the virus faster.

However, the introduction of such measures has also raised some controversial issues regarding privacy and data confidentiality.

Another risk in this context concerns the use of health data that may go beyond the scope of the original purpose/purpose and be used for an unlawful purpose (a purpose not covered by the original purpose and consent of the patient). This is the socalled "excess behavioral data" [25], which raises serious ethical and legal concerns in the context of protecting human rights and freedoms. This "repurposing" of data is a problem that has become even more urgent with the use of AI in healthcare. For example, in 2021, the Singapore government admitted that data from the COVID-19 tracking program (Trace Together) could be used for criminal investigations [26], despite previous promises to ensure the privacy of such data. Legislation restricting the use of such data was introduced, allowing its use only in the most serious criminal investigations with appropriate penalties for illegal use, but the approach to regulation itself has created (or rather exposed) a dangerous and wide-ranging precedent that is clearly at odds with the current system of standards for the protection of rights and freedoms. Such data can also be (and is) transferred to [27] companies that use it to develop AI in the marketing of goods and services or for forecasting used, for example, by insurance or technology companies. It is clear that disclosure of medical data has an irreparable effect (unlike, for example, disclosure of financial data) that cannot be compensated for in the form of material compensation, as the effect has much greater and more multifaceted consequences for the individual.

"DIGITAL DISCRIMINATION"

This phenomenon means an uneven distribution of access, use, or impact of information and communication technologies among different groups and categories of the population. It should be noted that we are currently seeing the cost of digital technologies falling, but statistics show that this does not directly correlate with the fairness of the distribution of access to them.[28] One fifth of the world's population, for example, still does not use mobile Internet services due to financial inaccessibility or distrust

of the technology itself. And the criteria for such "digital discrimination" are gender, geography, culture, religion, language, and generation, and it - "digital discrimination" - undoubtedly affects the prospects and effect of the use of AI, which as a technology has the potential to both reduce and, on the contrary, enhance the effect of such "digital discrimination."

DECISION-MAKING AUTONOMY

At present, we can talk about the complete replacement of human functions by AI mostly in routine medical/pharmaceutical activities (accounting, categorization, etc.) and a more assistive (non-autonomous) approach in forms of medical activities that pose a threat to life and health. But in any case, the ultimate purpose of AI is to maximize automation of the area where it is implemented, so the issue of expanding the scope of AI in medical practice is solely a matter of time and the state of technology development.

Delegation of clinical judgment and decision-making from humans to AI raises the question of the legitimacy of such delegation, as legislation increasingly recognizes the right of individuals not to be influenced by solely automated decisions when such decisions will have a significant effect on them (which obviously includes the healthcare sector). Therefore, we can currently speak of achieving only a conditional level of automation or assistance, and in general, strange as it may seem, the medical sector, despite its openness to technology, is one of the slowest technological sectors today in the context of the introduction of AI technologies.

The problem of human-computer interaction is ethically complicated, as doctors will have to rely on AI judgments, which are decisions based on black-box algorithms (i.e., the effect when it is not possible to trace and verify the entire algorithm from data input to output). Therefore, it may be questioned whether doctors can be forced to act in accordance with the decisions made by such "black box" algorithms, and thus AI technologies should be transparent and understandable [29], which we have mentioned above as a key guiding principle for the implementation of the technology.

THE ISSUE OF LIABILITY IN THE USE OF AI TECHNOLOGIES

One of the expected results of the successful implementation of AI in medical practice is a reduction in the level of medical errors, since according to research, even in developed countries, this indicator is far from ideal. [30] At the same time, the need for a fundamental revision of the concept of liability for harm in the implementation of medical activities using AI technologies becomes apparent, as this raises certain aspects of controllability, including their opacity, dependence on human influence, interaction, discretion, scalability, ability to generate ideas and software complexity.

The problem of control is one of the obstacles to establishing liability in the context of AI, as it involves a "plurality" of subjects: the developer of the AI software system, the healthcare professional as its operator, and the AI system itself (as a relatively autonomous entity), while developers may bear limited liability for AI systems that operate autonomously and develop in such a way that their activity and its results cannot be fully predicted. This creates a liability gap that can be passed on to the injured party or healthcare provider who uses the technology but has no direct influence on its design, configuration, or development. We have considered some aspects of this complex ethical and legal issue in our previous work [31], concluding that the concept of liability in this case, as a multilayered phenomenon, depends on a number of determinants, including the state of development of a particular technology, the degree of medical intervention, the national concept of legal liability regulation of a particular state, etc.

THE ETHICS OF DELEGATING RESOURCE ALLOCATION AND PRIORITIZATION TO AI

Assistance and automation in decision-making when using AI in medical activities will undoubtedly face ethically complex issues that directly affect the foundations of the concept of human rights, in particular when it comes to decision-making in conditions and according to the input rules of limited time, resources, etc. (i.e., circumstances that significantly affect the "fairness" of the decision, whatever it may be). And this problem will be multiplied by the risk that the data in both traditional databases and machine learning training sets may be biased from the outset.

Such bias can lead to the allocation of resources that discriminate against people on certain grounds, and certain forms of bias and discrimination can not only come from the entire data set, but can also be deliberately included in algorithms due to the desire to take into account the specifics of a particular area (which can have both positive and negative results). One example is the situation with the distribution of COVID-19 vaccines in a medical facility in California, USA, based on a formula based on programmed rules, which allocated a critically small number of available doses to those healthcare workers most at risk of contracting the virus, while prioritizing "higher ranking" doctors with a low risk of COVID-19. [32]

In other words, technologies that are designed with a focus on neutral and efficient use of resources may jeopardize human dignity and equal access to treatment. And decisions on whether to provide access to certain costly treatments or interventions (if made by AI based on such biased data) will be based on projected life expectancy, quality of life, etc., i.e., based on data that is inherently biased. [33]

The same risks apply to the predictive use of AI, where risks are associated with the use of AI for predictive purposes that affect patient care or resource allocation by a facility or health system. Predictive technologies may be inaccurate because the AI technology bases its recommendations on an inference that optimizes health markers rather than identifying the underlying underlying need of the patient. For example, an AI-powered mobile app developed by DeepMind to predict acute kidney failure produced two false positives for every one correct result and therefore did not improve patient outcomes. [34]

Prediction-based technologies, which are considered to be more accurate and efficient than conventionally "old technologies," question the patient's freedom of choice even outside of their interaction with a doctor. The use of AI in combination with incentives can turn, for example, a simple mobile application for promoting a healthy lifestyle into a technology for powerful control over [35] a person's decisionmaking in everyday life (while formally not directly influencing the person's will).

AI, THE LABOR MARKET, AND HEALTHCARE EMPLOYMENT

Automation, as a key consequence of the introduction of AI in medical practice, brings to the surface two opposing trends that coexist as its inevitable result: automation as a relief of medical staff from routine functions (and the ability to focus on highly professional aspects of medical care), and automation as a replacement of human labor, and thus a reduction in the need for a certain number of specialists and professions. [36] The introduction of AI will definitely require the "digitalization" of knowledge, skills, and abilities of medical professionals. The requirement for digital literacy will not be limited to clinical care, but will apply to healthcare professionals in the areas of public health, surveillance, environment, prevention, protection, education, diet, nutrition, and all other social determinants of health that can be supported by artificial intelligence. All healthcare professionals in these areas should be trained and retrained to use AI to support and facilitate their duties.

The challenges here may be that, on the one hand, healthcare professionals who already have to process large amounts of information to meet the standards of care may be regularly required to acquire new competencies in the use of AI-enabled technologies in their daily practice. Such continuing education may not be available to all healthcare professionals (due to limited financial and technical resources). On the other hand, the acquisition of "digital" skills in the use of AI technologies may gradually replace the need to obtain and update primarily "medical" skills (analysis of cardiograms, fluorograms, X-rays, etc.).

At some point, doctors may not be able to perform such a task without "computer assistance," and AI systems will have to be "taught" to use the medical knowledge base that has been operated by healthcare providers. This dependence on AI systems could, in the worst case, immobilize the healthcare system if the AI system fails or is compromised [37].

As the use of AI increases, the nature of medical practice and healthcare delivery will fundamentally change. As noted above, this could give healthcare providers more time to care for patients or (if patients interact more frequently and directly with AI), result in physicians spending less time in direct patient contact and more time administering technology, analyzing data, and training in the use of new technologies.

AI, BIAS, AND DISCRIMINATION

Such manifestations of social relations as discrimination and prejudice are an integral part of many processes and phenomena, including the use of predictive AI technologies in such areas as lending, insurance, criminology, etc. (when, based on input data, the relevant institutions draw a conclusion about the likelihood of an insured event/loan repayment/crime recurrence, etc.) And this certainly cannot avoid the use of AI in medical practice. At the same time, these phenomena of bias/discrimination are not negative factors or inappropriate practices in themselves, because, for example, the association of representatives of certain nations with certain healthy/harmful habits that affect health, or statistical differences in life expectancy based on gender, etc. are quite objective patterns that have a completely logical explanation and justification.

However, it should be borne in mind that when we talk about AI, we are primarily talking about "training", primary data, and the extent to which it reflects the real ratio of certain types will determine how effective the AI algorithm will be in general. Roughly speaking, in societies where there is some social discrimination, there will a priori be less relevant medically relevant data on those segments of the population that are subject to such discrimination. Existing biases and entrenched discrimination in healthcare delivery and healthcare structures and practices are reflected in the data that trains AI models, and manifest in the recommendations made by AI-driven technologies. The consequence is that recommendations will be irrelevant or inaccurate for populations excluded from or underrepresented in such data (which is also a consequence of implementing AI technology that is "trained" in one environment but used in another).

Turning to the definition of regulatory guidelines that should serve as a roadmap for the development of the legal framework, it should be noted that the use of AI in healthcare poses a number of challenges that cannot be addressed within the framework of existing and established ethical principles, legislation, and policies, in particular because the risks and opportunities of using AI are not yet well understood and will change over time.

In addition, many principles, laws and standards have been developed by developed countries based on their visions and expectations, but the technology definitely needs to be scaled up globally, and the least developed countries will face challenges and problems that are currently difficult to predict and foresee.

The system of risk management for the introduction of AI technologies in the medical sphere itself, although largely adapted to the existing concept of legal support, will require a number of modifications and innovations, some of which we intend to discuss briefly in the following. In the area of human rights impact, the regulatory guidelines on AI in healthcare delve into the intricacies of ensuring that the development and implementation of AI systems comply with fundamental human rights principles. These guidelines are intended to create a comprehensive regulatory framework that protects and promotes human rights in the context of AI in healthcare.

An important aspect of these recommendations is the emphasis on nondiscrimination and equity. To reduce

bias and promote equity, regulators should proactively address potential disparities arising from AI systems. This involves scrutinizing the data, algorithms, and decision-making processes used in medical AI to prevent any discriminatory practices that may disproportionately affect certain groups or individuals based on race, gender, age, or socioeconomic status. Proactively combating these biases aims to promote equal access to healthcare services and mitigate the perpetuation of existing inequalities, which in turn requires rulemaking and interpretation based on the existing concept of ensuring rights and freedoms

Privacy and data protection also play an important role in the regulatory framework that should be tailored to the introduction of AI in the medical field. Robust regulations are needed to protect patients' privacy and safeguard their personal health information. This involves implementing strict measures to ensure compliance with relevant data protection laws, enforcing strict access controls, and strengthening security measures to prevent the unauthorized use or disclosure of confidential medical information. By implementing robust data protection mechanisms, individuals can be assured that their personal information is handled with the utmost care and that their privacy rights are respected when AI systems are used in healthcare settings.

The importance of informed consent and individual autonomy cannot be overstated. It is crucial to empower patients to make informed decisions about the use of their medical data in AI applications. This requires the establishment of clear and transparent informed consent processes that allow individuals to actively participate in decisions about the collection, storage, and use of their personal health information. By providing patients with comprehensive information about how AI systems make decisions that affect their health, they can exercise their autonomy and maintain control over their own data.

In cases where human rights may be violated, accountability and remedial measures are imperative. It is important to establish mechanisms that hold stakeholders accountable for any potential human rights violations caused by the use of AI systems in healthcare. This includes establishing mechanisms to ensure stakeholder accountability. This includes empowering people to raise concerns, seek redress, and take legal action in situations where harm has been caused by algorithmic decisions or data misuse. Building accountability and remedies into the legal framework ensures that human rights and freedoms are respected and protected.

Conducting ethical reviews and impact assessments plays an important role in identifying and addressing potential human rights implications. Ethical reviews assess ethical considerations related to AI systems, taking into account the principles of privacy, autonomy, non-discrimination, and fairness. Impact assessments aim to determine the broader social impact of AI applications, especially on vulnerable populations. Thorough ethical review and impact assessments provide regulators with valuable information on the potential risks and benefits of AI in healthcare, enabling them to make informed decisions and ensure the protection of human rights. Such a position is widely supported by a number of researchers [38].

The integration of human oversight and accountability is vital to achieving the right balance between AI capabilities and ethical considerations. Human oversight ensures that healthcare professionals retain an important role in decision-making processes, providing their expertise and knowledge to protect human rights. By prioritizing human-centered values, healthcare systems can effectively utilize AI technologies while adhering to ethical standards and protecting individual rights.

The European Union has recently passed the Artificial Intelligence Act [39] which is the first comprehensive set of regulations for the artificial intelligence industry. The act proposes requiring generative AI systems to be reviewed before commercial release and seeks to ban real-time facial recognition. The law takes a risk-based approach to regulating AI, where the obligations for a system are proportionate to the level of risk that it poses. The regulation also provides the legal basis for the use of personal data collected for other purposes for developing certain AI systems in the public interest within the AI regulatory sandbox. The act gives citizens the right to file complaints against providers of AI systems and makes a provision for an EU AI Office to monitor enforcement of the legislation. It also requires member states to designate national supervisory authorities for AI. These small steps towards establishing of regulative framework for AI using make us closer to the milestone where the concept of human rights should be carefully revised to consider the technological changes and their impact in general and on the healthcare in particular.

CONCLUSIONS

By implementing these comprehensive regulatory guidelines into the governance of AI in healthcare, policymakers and stakeholders can help create an environment that not only maximizes the potential benefits of AI, but also prioritizes the protection and promotion of human rights. Such an approach promotes the responsible and ethical use of AI technologies, ensuring that they are used for the benefit of society while respecting and protecting the fundamental rights of every individual.

All in all, AI has the potential to solve many global healthcare problems, but achieving this goal is still far from being achieved. This requires a proper system of data infrastructure standardization, intact privacy and patient consent systems, and other important aspects that go beyond the current privacy model. Leading institutions such as the FDA and EMEA are currently taking only the first steps in this direction. However, achieving widespread adoption of AI in healthcare will require deeper efforts and the development of an effective regulatory paradigm that guarantees human rights and their protection in this new technological landscape. The European Union has recently passed the Artificial Intelligence Act is a proper way of highlighting modifications needed and regulative frameworks necessary to make use of AI suitable for such a sensitive sphere as healthcare.

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CASE STUDY

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CEREBRAL TOXOPLASMOSIS IN THE COURSE OF HIV INFECTION – CASE STUDY

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ABSTRACT

The aim of our study is to draw attention to the need to take into account HIV infection and its complications, such as CNS toxoplasmosis, in the differential diagnosis of people presenting with impaired consciousness. We analyzed our patient's medical records and available statistical data on HIV infection, as well as literature on nervous system involvement in the course of AIDS. In our paper, we present the case of a 43-year-old male who was admitted to a neurological ward due to impaired consciousness. Diagnostic imaging and laboratory tests were conducted, and patient was diagnosed with toxoplasmosis in the course of AIDS. HIV infection is a global public health problem. In the absence or ineffectiveness of treatment, it leads to profound immunodeficiency and, consequently, opportunistic infections. One of them is the reactivation of the latent *Toxoplasma gondii* infection. It is the most common cause of extensive cerebral lesions in patients infected with the HIV virus. In these cases, MRI reveals numerous scattered ring-enhancing lesions. The symptoms are non-specific: headaches, impaired consciousness, convulsions, behavioral changes, and focal neurological deficits. The onset of neurological symptoms may be the first clinically relevant manifestation of AIDS. It is key to diagnose such patients as soon as possible and treat them accordingly.

KEY WORDS: HIV, AIDS, neurotoxoplasmosis, cerebral toxoplasmosis

INTRODUCTION

The human immunodeficiency virus (HIV), which belongs to a subgroup of retroviruses, has an affinity for cells with CD4 receptors: T helper cells, macrophages, and microglial cells. This causes an immune deficiency, which, untreated, leads to acquired immunodeficiency syndrome (AIDS), defined as HIV infection with either a CD4 count of less than 200 cells/l or the occurrence of an indicator condition (list of such conditions was made by the CDC) [1]. The infection is transmitted *via* sexual contact (the majority of those cases are MSM (men who have sex with men), *via* blood contact, from infected mother to fetus during pregnancy, during childbirth, or *via* contact of mucous membranes with infectious material.

Despite numerous social campaigns, forms of prophylaxis, and easily accessible treatments, the consequences of HIV infection are still a global issue. It is estimated that in 2021 approximately 38.4 millions of people were infected with HIV worldwide, of whom only 28.7 million received antiretroviral therapy (ART) [2]. Data for 2022 has not been verified yet, but available epidemiological reports show a significant increase in the number of new cases compared to the same period in 2021. In Poland in 2021 there were 16.9 thousand people with confirmed HIV infection; 14.5 thousand of those treated with ART [3]. In 2022, another 2,384 cases of infection were registered in Poland (more than twice as many as in 2021) [4].

HIV is a neurovirulent virus that easily crosses the blood-brain barrier and reaches the CNS, causing an inflammatory reaction. Neurological disorders are diagnosed in 30–40% of patients with AIDS, and in 10–20% of those are the first manifestations of the illness [5]. Nervous system diseases in AIDS patients can be caused either by a virus's direct impact on neural cells, by immunodeficiency, or by a side effect of treatment. The first group includes HIV-associated neurocognitive disorders (HAND), myelopathies, peripheral neuropathies, aseptic meningoencephalitis, and myopathies. Immune deficiency leads to opportunistic infections (progressive multifocal leukoencephalopathy [PML], CNS cryptococcosis, CNS toxoplasmosis, CNS tuberculosis, and neurosyphilis) and to neoplastic diseases (primary CNS lymphoma) [6].

AIM

The aim of our study is to draw attention to the need to take into account HIV infection and its complications in the differential diagnosis of people presenting with impaired consciousness. We will present this based on the case of a patient diagnosed with CNS toxoplasmosis in the course of untreated AIDS.

CASE STUDY

A 43-year-old male Ukrainian citizen was admitted to the neurological ward from the ER due to impaired consciousness. Medical history was impossible to obtain.

According to the patient's wife in the previous week he has had several headaches and impaired consciousness - he had been confused and hadn't been able to perform everyday activities. The intensity of those symptoms fluctuated during the day. Moreover, in the last 6 months, the patient had lost 20 kilos and had hemorrhoids inflammation. Negative history of exposure to infectious agents.

A CT head scan taken in the ER demonstrated hypodense areas of different sizes in both cerebral hemispheres, the ventricular system was not dilated and without midline shift, narrow sulci of the brain convexity were compressed near cerebral lesions (Fig. 1).

On admission, the patient's general condition was satisfactory; he was both hemodynamically and respiratorily stable. In the neurological examination, the patient was conscious, oriented toward himself, and his location, but not as to time; psychomotor retardation was present as well as photophobia, dorsiflexion tendency of both halluxes was observed and also he had nuchal rigidity. Besides that, there were no signs of focal CNS damage.

Due to suspicion of a neuroinfection, a lumbar puncture was performed. Cerebrospinal fluid examination showed signs of inflammation in the CNS (cytosis 15/mm^3, protein 1.23 g/L, albumin 677.1 mg/L). The PCR method didn't detect any typical pathogens. Empirical broad-spectrum antibiotics (ceftriaxone and vancomycin) and anti-edematous drugs were given.

In the next few days, the patient's general condition deteriorated, and passive oxygen therapy was needed. In neurological examination, the patient opened his eyes in response to voice and in response to pain, he had nuchal rigidity and small, non-reactive pupils. Muscle tension was increased in all four limbs, without evident signs of paresis. Babinski's sign was positive bilaterally. Tendon reflexes were brisk and symmetric.

Three days after admission to hospital, a control CT scan with contrast showed irregular cortico-subcortical hypodense areas (more severe on the right side), also visible in deep brain structures in both cerebral hemispheres and within the left cerebral peduncle, also with cerebral sulci compression. No contrast enhancements. The ventricular system was asymmetrical (compressed frontal horn of the left lateral ventricle) but not dilated, and without a midline shift. Pericerebral fluid spaces were narrow, particularly on

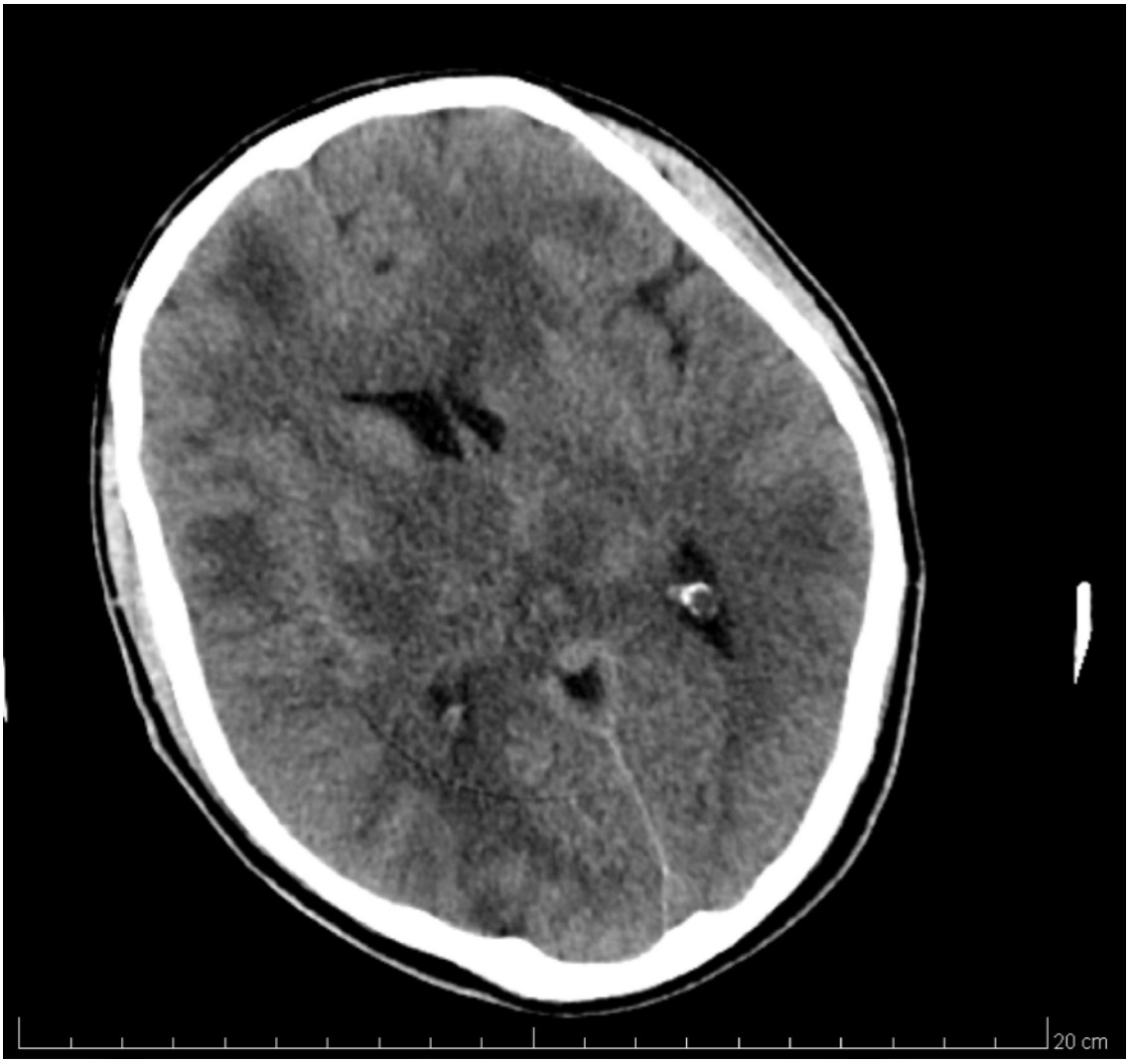

Fig. 1. Head CT scan on admission with multiple areas of hypodensity.

the right side - signs of cerebral oedema.

Due to the patient's unclear medical history and the results of a CT scan, tests for HIV, CMV, and Toxoplasma gondii infections were done. The screening HIV test result was positive (a blood sample was sent to a reference laboratory for confirmation), as well as tests detecting anti-CMV IgG antibodies and anti-*Toxoplasma gondii* IgG antibodies (high avidity index in both tests).

Since the 5th day of hospital stay, the patient's condition has been severe; he was unconscious and on high-flow passive oxygen therapy. Head MRI with contrast showed numerous areas of increased signal (in T2 and STIR sequences) of diameter varying from 15 to 40 mm within cortical and subcortical white matter in both hemispheres, with signs of oedema causing pressure on the ventricular system (Fig. 2), and with signs of ring enhancement (Fig. 3). A similar area of about 12 mm in diameter could be observed on the right side of the brain stem. Signs of a slight signal decrease in the DWI sequence. Asymmetrical ventricular system, slightly narrowed, with no significant midline shift. Subarachnoid space was not dilated. The signal and width of the corpus callosum and infratentorial structures were normal.

Based on the results of diagnostic imaging and laboratory tests, *Toxoplasma gondii encephalitis* due to HIV infection was suspected; cotrimoxazole was given.

On the 7th day of hospitalization, the patient became respiratory insufficient, despite the use of high-flow passive oxygen therapy. In neurological examination: unconscious, nuchal rigidity, constricted non-reactive pupils. Eyeballs turned upward and to the right. Muscle tension increased in all four limbs. Tendency to withdraw from painful stimuli. Babinski's sign was positive bilaterally. After a consultation with an anesthesiologist, the patient was intubated and moved to the ICU.

During the ICU stay, the HIV infection was confirmed, and stage 3 AIDS was diagnosed (CD4 count 4,3 cells/mm^3). After consulting with a clinic for acquired immunodeficiencies, the patient was given ART regimen (dolutegravir, emtricitabine, or tenofovir). Cotrimoxazole treatment was continued and tailored therapy for *Acinetobacter baumannii*-related pneumonia was started.

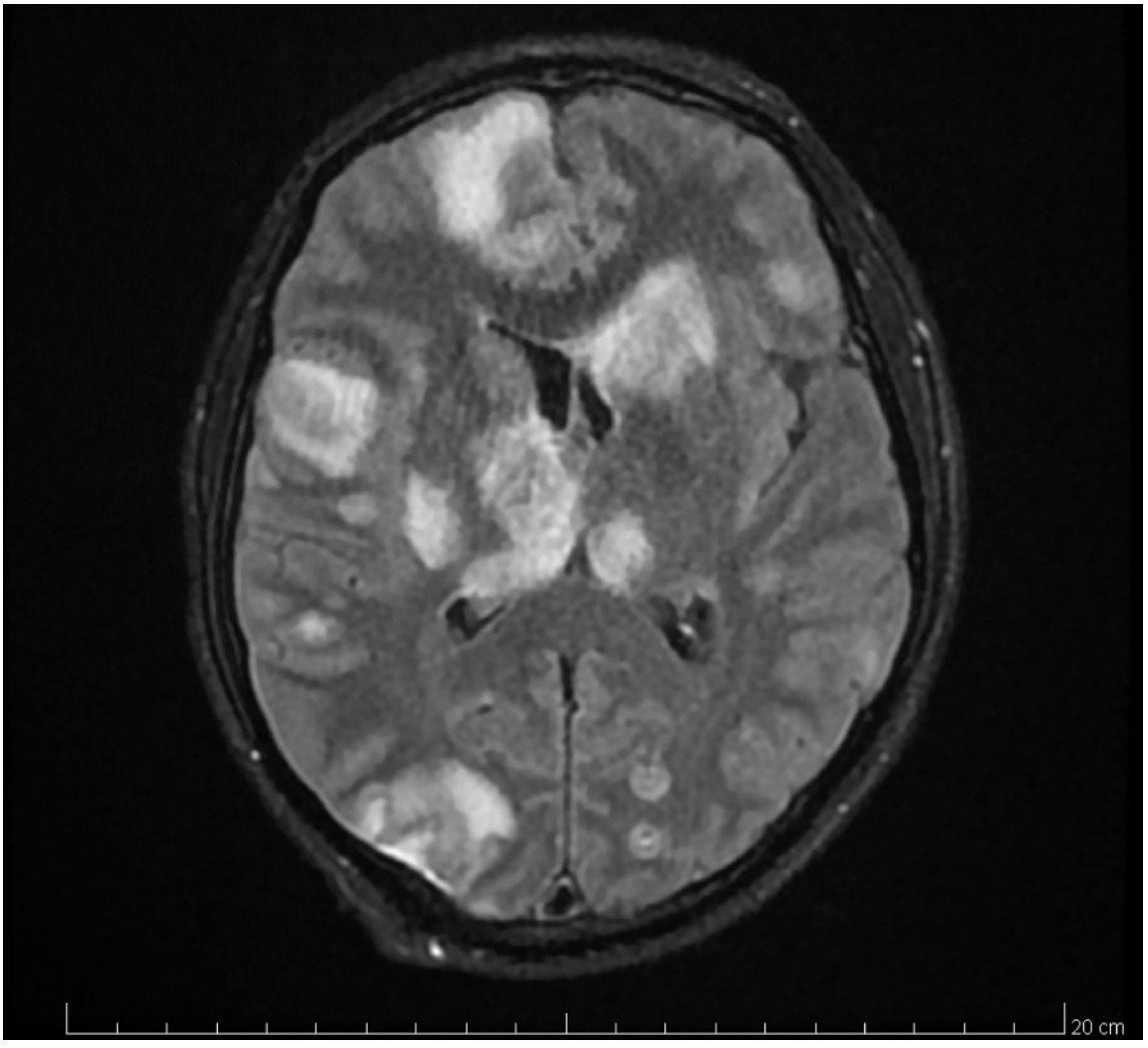

Fig. 2. Hyperintense areas in the T2 FLAIR sequence.

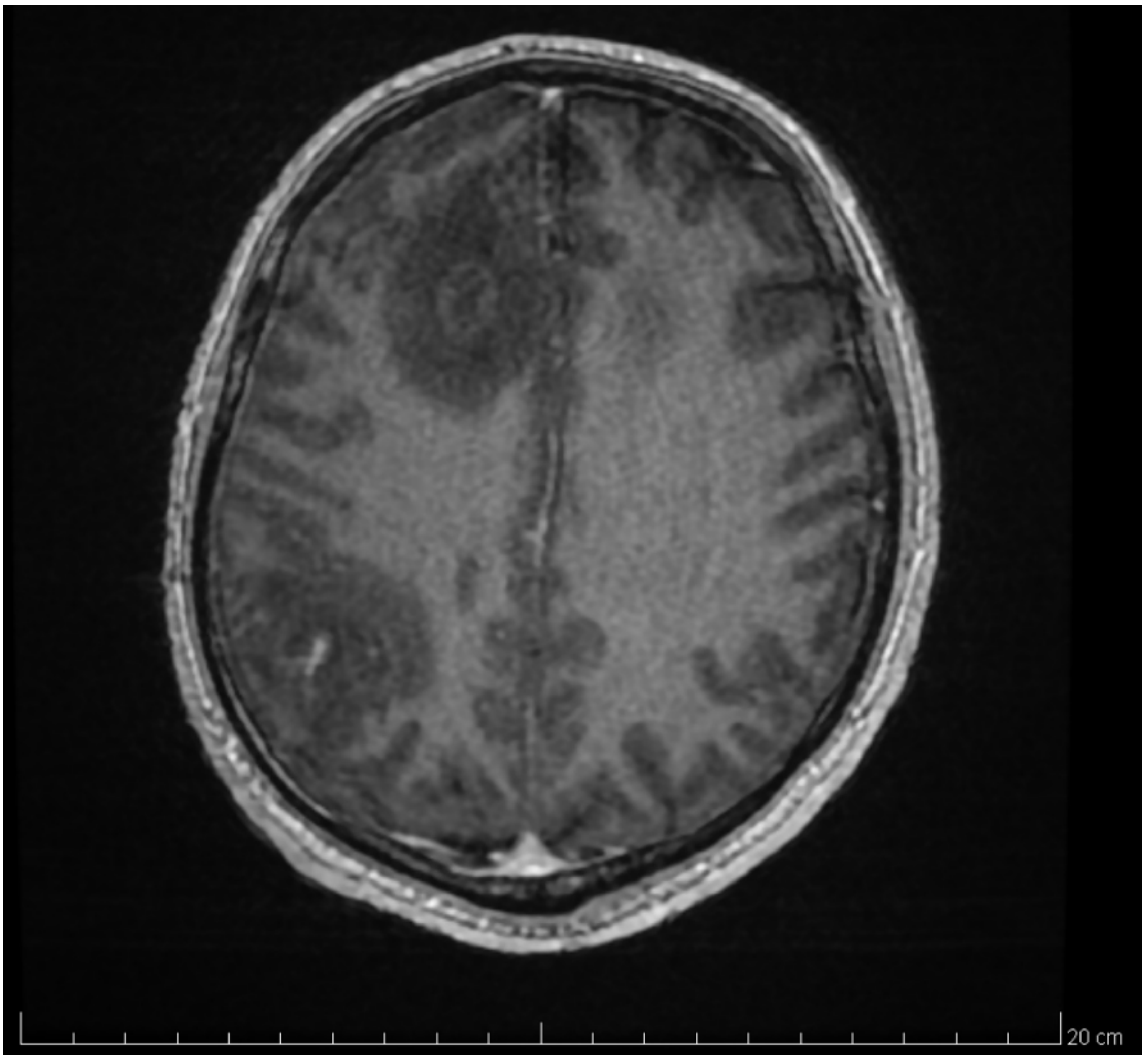

Fig. 3. Ring-enhancement of the lesions in the T1 sequence after contrast administration.

The patient's condition gradually improved, and after 11 days he was extubated and moved back to the neurological ward, in serious but stable general state. In neurological examination: conscious, without verbal contact, doesn't obey commands. Negative meningeal signs. Symmetrical and reactive pupils. Cranial nerves' examination showed no abnormalities. Flaccid paralysis of both lower limbs and the left upper limb. In the right upper limb muscle tension was increased, and motor strength was 4/5, based on Medical Research Council (MRC) muscle power scale. Reduced tendon reflexes in both lower limbs and left upper limb. Besides that, there were no abnormalities.

After 6 days, the patient's condition deteriorated again; he developed a fever and became respiratorily unstable. Empirical antibiotics were given. On the 10th day after moving from the ICU, the patient was unconscious, meningeal signs were negative, pupils were equal and reactive, and flaccid paralysis of all four limbs were present. 2 days later, due to respiratory failure, septic shock, and multiple organ system failure, he was consulted with an anesthesiologist and disqualified from re-treatment in the ICU, given the neurological state and lack of response to treatment. After 31 days from admission to the hospital patient died due to respiratory and circulatory failure.

DISCUSSION

Toxoplasmosis is caused by the protozoan parasite *Toxoplasma gondii*. The final hosts are cats and others felidae. In their digestive tract, sexual reproduction of the parasites takes place, and oocysts are formed, which are excreted in the feces and accidentally eaten by other animals [7]. Humans can get infected by consuming raw or undercooked meat containing *T. gondii* tissue cysts or by ingesting water, fruits, or vegetables contaminated with oocysts [8]. More uncommon causes include transplacental transmission from mother to fetus, blood transfusion, or organ transplant.

It is estimated that *T. gondii* infections afflict one third of the world's population [8]. In over 80% of immunocompetent people, the infection is asymptomatic or causes temporary lymphadenopathy, splenomegaly, malaise, fever, or a sore throat [7].

gondii infection is particularly dangerous for the fetus of seronegative mothers, who have their first contact with this parasite during pregnancy or during reactivation of the infection in immunocompromised pregnant women. The chance of transplacental transmission increases from <20% in the first trimester to approximately 80% at the end of pregnancy, while the severity of complications for the fetus is inversely proportional; in the case of transmission at the beginning of pregnancy, it can lead, e.g., to miscarriages and significant mental retardation [7]. The classic triad of symptoms of congenital toxoplasmosis (*hydrocephalus*, *chorioretinitis*, and intracerebral calcifications) occurs only in some cases of infected newborns [9].

Another group in which *T. gondii* can cause very serious symptoms are people with immunodeficiency. Reactivation of latent *T. gondii* infections in immunocompromised patients may lead to cerebral toxoplasmosis, which is the most common cause of extensive cerebral lesions in HIV/AIDS patients. Before the era of antiretroviral therapies, it was estimated that cerebral toxoplasmosis was the cause of death in up to 30% of AIDS patients in Europe [10]. Typical symptoms are headaches, focal neurological deficits, impaired consciousness, convulsions, behavioral changes, cranial nerve palsy, ataxia, and vision impairment [11].

When toxoplasmosis is suspected, MRI is the preferred method for brain imaging. Most common are numerous ring-enhancing lesions in the basal ganglia (48%), frontal lobes (37%), and parietal lobes (37%), with perilesional oedema. Less frequently, lesions are located in other parts of the brain. In 15% of patients, MRI reveals a single lesion [11].

The differential diagnosis should include primary CNS lymphoma and other infectious diseases, such as tuberculosis, cryptococcosis, aspergillosis, and microsporidiosis [7].

Cerebral toxoplasmosis is diagnosed based on a positive response to empirical treatment in patients with a suspected *T. gondii* infection. Treatment consists of pyrimethamine with sulfadiazine or cotrimoxazole. After the initial phase (lasting 6 weeks or until the patient's condition shows significant improvement), maintenance therapy is given until the CD4 count is above 200 cells/μl. Brain imaging should be performed after 2 weeks of treatment to assess the effectiveness of therapy. In the event of a lack of clinical or radiological improvement after 10–14 days of treatment, it is recommended to perform a brain biopsy to confirm the diagnosis [11].

It is also worth keeping in mind the possibility of the coexistence of another neuroinfection during the treatment of HIV-infected patients suffering from cerebral toxoplasmosis; in this group of people, the most common co-pathogen is CMV [12].

The introduction of antiretroviral drugs into widespread use has significantly reduced the incidence of cerebral toxoplasmosis among HIV-infected people, but it is still an important cause of mortality in this group, especially in low- and medium-income countries [11].

CONCLUSIONS

The onset of neurological symptoms may be the first clinically relevant manifestation of AIDS. In patients presenting non-specific neurological symptoms or with unclear or suspicious results of brain imaging, it is recommended to include the possibility of HIV infection in the process of differential diagnosis. It is key to diagnose coexisting indicator conditions as soon as possible and treat them accordingly, because when left untreated, they can even lead to death in a short period of time.

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CASE STUDY

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TREATMENT OF STRESS-INDUCED URINARY INCONTINENCE BY TVT-O METHOD (CLINICAL CASE)

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ABSTRACT

Stress urinary incontinence (SUI) is one of the most common diseases accompanied by loss of control over the activity of the bladder. Women are more susceptible to this pathology than men due to the peculiarities of the structure of the genitourinary system, as well as due to pregnancy, childbirth, gynecological operations, and age. Incontinence occurs when a woman coughs, sneezes, laughs, lifts weights, runs, etc. It leads to social isolation and significantly reduces the quality of life of patients.

The article analyzes the case of a patient who was in the gynecological department of the Uzhhorod City Maternity Hospital of the Uzhhorod City Council and complained of urinary incontinence during coughing, sneezing, laughing, and physical exertion. A full clinical and laboratory examination, physical examination, and consultation with narrow specialists were conducted. According to the research data, a diagnosis of stress urinary incontinence was made. Urethropexy with a synthetic loop (TVT-O operation) was performed using the Gynecare TVT Obturator System Tension-free Support for Incontinence. The complex treatment included antibacterial, antithrombotic and infusion therapy.

The effectiveness of the result of surgical treatment was evaluated taking into account subjective and objective criteria for the restoration of anatomical parameters and functional parameters, as well as the patient's quality of life during dynamic follow-up for 2 years. We noted the high efficiency of surgical treatment of stress urinary incontinence using synthetic material.

KEY WORDS: stress urinary incontinence, sling surgery, TVT-O surgery

INTRODUCTION

In the modern world, due to the improvement of socio-economic conditions of life and its increasing duration, medical and social problems associated with stress urinary incontinence (SUI) are becoming increasingly relevant [1]. As defined by the International Committee on Urinary Incontinence (ICUI), stress-induced urinary incontinence (SUI) is sudden involuntary urination during coughing, laughing, or physical activity due to a sudden increase in abdominal pressure. Despite the fact that this condition is not life-threatening or fatal, it has a significant impact on a woman's physical, psycho-emotional, and social status. According to European and American statistics, from 10 to 70% of the female population aged 40-60 years report symptoms of stress urination [2].

The pathomorphology of urinary dysfunction is based on a disturbance in the relationship between the bladder neck and the pubic junction and vagina due to a disturbance in the tone of the pelvic floor muscles with a consistent protrusion of the bladder neck and urethra («vaginal hammock»). As a result of increased abdominal pressure during coughing or physical exertion, the pressure in the bladder increases, which is transferred to the urethra and leads to uncontrolled urination. The risk factors for stress-induced urinary incontinence are age, obstetric complications, exhausting physical work, history of surgical treatment of the genitourinary system and pelvic organs, obesity, diabetes mellitus, and a large number of childbirths [3].

From the pathophysiological point of view, stress urinary incontinence is divided into two types: 1) anatomical – due to prolapse (hypermobility) of the vesicourethral segment and intact sphincteric apparatus of the urethra and bladder neck as a result of weakening of the musculo-fascial support of these organs (occurs in 90-95% of patients with SUI); 2) insufficiency of the urethral sphincter (with or without urethral hypermobility) as a result of endocrine atrophy of the urethral submucosa in postmenopausal women or damage to the urethral sphincter after pelvic surgery, trauma, radiation therapy, neurogenic diseases (occurs in 5-10% of patients with PBS) [4].

It is proposed to classify POP as follows (the type of pelvic organ prolapse according to Baden-Walker is indicated in parentheses): SUI grade I, type I – the patient loses urine only in an upright position, there is no pelvic organ prolapse. SUI I, type IIA (cystocele I, rectocele I) – the patient loses urine only in an upright position and has initial degrees of prolapse of the anterior and posterior vaginal walls. SUI grade II, type III – the patient loses urine in vertical and horizontal positions, the urodynamic parameters of the urethral sphincter are below normal, there is no pelvic organ prolapse. POP II, type IIIA (cystocele II, rectocele II, metrocele II) – the patient loses urine in vertical and

horizontal positions, the urodynamic parameters of the urethral sphincter are below normal, there is a prolapse of the anterior and posterior walls of the vagina, as well as the uterus to the vaginal ring [5].

Among all types of urinary incontinence in women, stress incontinence (urinary incontinence during stress) accounts for about 50-80%, urgency incontinence – 10-20%, mixed incontinence – 15-30%, and all other types – up to 5%. Diagnosis and treatment of various forms of urinary incontinence remains one of the main problems of urogynecology.

Today, there is no surgery that can provide 100 percent success in surgical correction of stress urinary incontinence in women. This is due to the complex anatomical structure of the lower urinary tract of a woman who is exposed to traumatic (childbirth, surgery on the anterior vaginal wall, etc.), physical, psychological and hormonal influences throughout her life, as well as to the multicomponent mechanism of regulation of the function of the vesicourethral segment in normal and pathological conditions, including urinary retention. The mechanism of urinary retention in women under stress is a complex and multifactorial system in which each anatomical element contributes to its successful functioning [6]. Various techniques, both conservative and surgical, are used to combat stress urinary incontinence. However, only surgery can cope with serious manifestations of the disease. The «gold standard» in surgical urogynecology is the TVT-O or TVT Obturator operation. This operation is the safest compared to other techniques and can be used in the treatment of stress incontinence [7].

The above and the importance of this problem prompted us to describe a clinical case of stress urinary incontinence in a woman.

SURGICAL INTERVENTION

A synthetic loop urethropexy (TVT-O operation) was performed using the Gynecare TVT Obturator System Tension-free Support for Incontinence (ETHICON, inc. Johnson & Johnson Company, USA). The complex treatment included antibacterial, antithrombotic and infusion therapy.

CASE STUDY

A 53-year-old woman turned to the UMPB UMD Department of Gynecology with complaints of urinary incontinence during coughing, sneezing, laughing, and physical exertion. She considers herself sick for 7-8 years, when she first noticed symptoms during physical activity. For the last year, she has been experiencing urinary discharge with any abdominal wall tension.

Family and allergic history is unremarkable. Occupational history is burdened by constant physical labor at factories.

Obstetric and gynecological history – 4 pregnancies, 3 natural births, 1 spontaneous abortion at 8-9 weeks. The delivery was complicated by cervical and vaginal tears. Menstrual function: menarche since the age of 15, the cycle was regular, menstruation was moderate, not painful. Currently, she has been in menopause for 3 years. Previous surgeries: appendectomy in childhood.

During the objective examination of the patient, the general condition was considered satisfactory. The patient has a regular body structure. Increased BMI. The skin and mucous membranes are pale pink in color. Lymph nodes are not palpable. The pharynx is clean, the tongue is not coated. The thyroid gland is not enlarged. The mammary glands are soft, not painful. Symptoms of peritoneal irritation are negative. At the Uzhhorod City Maternity Hospital of the Uzhhorod City Council, the gynecological department, in order to diagnose stress urinary incontinence, the following was done assessment of complaints, patient's medical history, pelvic ultrasound, vaginal examination with determination of the «coughing impulse» symptom, voiding test (Valsalva), cystometry, urethrocystometry assessment of the residual urine volume after urination, assessment of the frequency and volume of urine output, general and bacteriological urinalysis, clinical and laboratory tests (complete blood count, coagulogram, biochemical blood test), consultation with a therapist, neurologist.

Gynecological status: The external genitalia are properly developed. The introitus vagina is free. The cervix is cylindrical, the external os is closed, atresia of the os. There is an insufficiency of the urethral sphincter, it is gaping. The uterus is not enlarged, not painful to palpation, movable. Appendages on both sides are unremarkable. Parameters are free, vaults are deep. Vaginal discharge is mucous. On the gynecological chair, urine leakage on exertion was detected, cough test and Valsalva test were positive.

At the stage of preoperative preparation, clinical and laboratory examinations were performed, and the patient was consulted by other specialists, namely: a general practitioner, anesthesiologist, and neurologist. Examination by a therapist: Ischemic heart disease. Cardiac insufficiency I. Condition after ischemic stroke (2008). Adipositas of the second stage. Conclusion of the neurologist: neurological causes of urinary incontinence were excluded, no acute neurological disease was detected.

Normal results of general and bacteriological urinalysis and neurological examination, the presence of anatomical pelvic support disorders and urinary leakage during exertion, positive cough test and Valsalva test, normal cystometry and urethrocytometry, normal residual urine volume, normal bladder capacity and sensitivity, absence of involuntary detrusor contractions allow to make a diagnosis of stress urinary incontinence.

Admission to the operation has been obtained. The patient was familiarized with the scope of the operation and informed consent was obtained. Surgical treatment was performed as planned. A synthetic loop urethropexy (TVT-O operation) was performed using the Gynecare TVT Obturator System Tension-free Support for Incontinence (ETHICON, inc. Johnson & Johnson Company, USA). The complex treatment included antibacterial, antithrombotic and infusion therapy.

In aseptic conditions, under spinal anesthesia, the puncture points of the suburethral sling were marked 1 cm above the urethra and at the intersection of the inguinal fold and the transverse line. We install a Foley catheter. In the

projection of the urethra, 1 cm below the external sphincter, make a vertical incision 1.5-2 cm long. We take the edges of the wound on the Alice clamp and pull them aside. Next, we hydroprepare the vaginal walls in the direction of the descending branch of the pubic bone at an angle of 45° on both sides. After that, we separate the tissues with a sharp and blunt method, also at an angle of 45° until you feel the touch of the pubic bone. The procedure is repeated on both sides. In the formed tunnels, to protect the bladder, we alternately place a grooved probe along which, using a deshan-like conductor, we pass a mesh implant through the septum and enter the skin at the intersection of the direct projection of the clitoris and the iliac crease. This manipulation is performed on both sides. We place a clamp between the urethra and the strip, on which the implant is fixed to determine the degree of tension. We cut off the ends of the implant above the skin. The vaginal mucosa is sutured with vicryl sutures. Separate knotted vicryl sutures are placed on the skin in the area of the incisions. Gauze tampon was inserted into the vagina. The total blood loss was 100 ml. The urine through the catheter was light and clear.

After the operation, the patient received ceftriaxone 2.0 + 0.9% NaCl 200.0 IV No. 5, pentoxifylline 5.0 + 0.9% NaCl 200.0 IV No. 3, infulgan 100.0 IV No. 3, asparkam 10.0 + 5% glucose 200.0 IV No. 3, dexalgin 2.0 IV No. 4, analgin 2.0 + dimedrol 1.0 IV No. 3, unorm 5.0 + 0.9% NaCl 200.0 IV No. 3, flenox 0.4 p.c. No. 3, eufilin 2.4% 10.0 + 0.9% NaCl 200.0 IV No. 2.

Data of the patient's laboratory examination: HBC – hemoglobin – 130 g/l, erythrocytes – 4.82 x 1012/l, leukocytes – 7.20 x 109/l, platelet count – 252 x 109/л. CSF – light yellow, transparent, erythrocytes – 2-3 in the field of view, leukocytes – 3-4 in the field of view.

The early and late postoperative periods were uneventful. The gauze tampon was removed the next day after the surgery, slightly soaked with blood. The vaginal mucosa was treated with Ginodek gel No. 7 after the operation. The patient was discharged from the hospital on the 7th day in a satisfactory condition under the supervision of the district gynecologist.

The effectiveness of the result of surgical treatment was evaluated taking into account subjective and objective criteria for the restoration of anatomical parameters and functional parameters, as well as the patient's quality of life during dynamic follow-up for 2 years. We noted the high efficiency of surgical treatment of stress urinary incontinence using synthetic material. The woman is satisfied with the result of the operation and the improvement in quality of life, no relapse has been observed.

DISCUSSION

According to various authors, patients with stress urinary incontinence should undergo a comprehensive examination to clearly determine the type of incontinence and choose surgical treatment. The examination should include the following components: careful collection of complaints and anamnesis, detailed objective examination, general and bacteriological urinalysis, assessment of residual urine volume after urination, assessment of urinary frequency and volume of urine output, and urodynamic tests. The introduction of modern methods of combined urodynamic examination into medical practice makes it possible to comprehensively assess the urinary function, determine the cause and type of disorders, and determine the prospects for treatment [8-11].

During the objective examination, a general physical examination, neurological screening, with special attention to the lower extremities and perineum, and urogynecological examination are performed. Healthy 40-year-old women with moderate symptoms of urinary incontinence who lead an active lifestyle require different treatment approaches than 80-year-old patients with dementia and constant urinary leakage. Older patients have decreased physiological reserves and numerous pathological processes and may require only medical treatment. Neurological examination is indicated due to the possibility of numerous neurological causes of urinary incontinence. The presence of a cough reflex indicates the intactness of the spinal cord. The deep tendon reflexes, anal reflex, pelvic floor muscle reflexes, and contractility of the bulbocavernosus muscle are checked [4, 10, 11].

The goal of treating stress urinary incontinence is to provide support for the pelvic organs and restore the anatomical position of the urethrovesical junction. Surgical treatment is the most optimal way to correct it. The choice of surgery method is determined by the type of incontinence, primary or secondary procedure, and the degree of concomitant pelvic relaxation [12, 13].

In the world clinical practice, the installation of a synthetic suburethral sling is the most effective and safe surgical method of treating stress urinary incontinence. Its effectiveness is 80-95% [14,15]. The most commonly used surgical procedures for the treatment of age-related urinary incontinence in women are surgical operations with the use of synthetic tape – TVT and TVT-O. It is installed in place of damaged or weakened ligaments, maintaining the urethra in the correct position. The procedures are very similar. The difference lies in the location of the incisions through which the tapes are inserted. During TVT plastic surgery, the tape is passed through the paraurethral canals, and its ends are brought to the abdominal wall. During the TVT-O operation, the tape is passed through the locking holes located inside the pelvic bones.

The TVT-O technique was developed by the French doctor E. Delorm in 2001 as an alternative to the TVT operation. The main reason why the surgeon decided to improve the existing method was that it was associated with a high risk of damage to the intestines and bladder. The analysis of literature data comparing TVT and transobturator tape urethropexy (TOT) techniques showed that the TOT technique requires less time, the postoperative period is shorter and more comfortable, and there are fewer postoperative complications. Anatomical studies have shown that the transobturator sling technique is safe in terms of damage to the main pelvic vessels (occluding artery and vein) and bladder with proper perforation, since the latter does not penetrate the pelvic cavity but passes

under the sphincter muscle. The perforators in the outside-in technique are located much further from the occluding vessels than in the inside-out technique. However, when performing an operation using the outside-in technique, it is necessary to perform a much larger dissection of the paraurethral space for finger control of the perforator into the vaginal wound [13,16].

C.M. Gomes et al. (2017) conducted a study of the literature on complications of synthetic suburethral slings, including transobturator slings. The authors noted that bleeding during transobturator suburethral sling placement occurred in -02% of -cases, bladder damage – in 015%-, urethral damage – in 0.-12.-5%, urethral erosion – in 0.-030.8%, intestinal damage – in 0%, vaginal erosion – in -010.-9%, urinary tract infection – in 7.413%-, inguinal pain – in -09.-4%, *de novo* -detrusor hyperactivity – in 015.-6%, urethral obstruction – in 3.011.-0%, and urinary retention – in 2.711.-0% of patients [17].

In connection with the occurrence of pain in the inguinal area (thigh), the formation of inflammatory infiltrates and abscesses of the thigh (labia) after the installation of transobturator slings, scientists began to look for options to reduce (avoid) these complications. One of the options was to reduce the length of the polypropylene tape and avoid its placement on the thigh. In 2009, Johnson & Johnson introduced the Gynecare TVT Abbrevo set for practical use for performing transobturator sling using the inside-out technique. This is a modification of the previous Gynecare TVT-obturator system, in which the mesh is much shorter (by 38%), has a length of 12 cm and is fixed in the pelvic muscles to avoid inflammation and abscesses of the thigh [7].

CONCLUSIONS

The basis for the correct determination of stress urinary incontinence is the history taking and physical examination, followed by confirmation of the diagnosis by using urodynamic tests.

The most universal operation for the correction of stress urinary incontinence is the TVT-O sling operation.

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Short Communication

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THE FRAMEWORK OF THE PILOT PROJECT FOR TESTING A TELEMEDICINE MODEL IN THE FIELD OF GERIATRICS – HEALTH CHALLENGES AND JUSTIFICATION OF THE PROJECT IMPLEMENTATION

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ABSTRACT

Aim: To present the essentials of the pilot project for testing a telemedicine model in the field of geriatrics, along with a snapshot of the health challenges.

Materials and methods: This review paper use the synthetic method summarizing the main objectives of the telemedicine project in the field of geriatrics. The described project involving telemedical care of patients with geriatric complexes in the area of frailty syndrome, sarcopenia and malnutrition, according to the proposed model addresses the aforementioned problems. The project provides a holistic model of home and outpatient care, which will allow concerting on 3 groups of the above-mentioned geriatric syndromes. The project will have a pilot character and is aimed at clinical verification through the introduction (implementation) of the new method and accompanying organizational and technological solutions (platform, equipment) in an area where current models and schemes of therapeutic and diagnostic support were insufficient.

Conclusions: The implementation of telemedicine solutions creates an opportunity for geriatric patients and their families by improving access to specialized medical care. This project will support patients, but also caregivers, who (through training and telemedicine) will be better able to provide care services with the ability to reconcile them with their own work.

Key words: geriatrics, frailty syndrome, sarcopenia, malnutrition, telemedicine, Norway Founds

INTRODUCTION

Population aging creates the need for effective prevention, prompt identification, and appropriate treatment of significant geriatric syndromes. These include in particular, sarcopenia, malnutrition, and frailty syndrome (FS), which intertwine [1]. Malnutrition promotes the development of sarcopenia, i.e., loss of strength and muscle mass primary related to age or secondary to concomitant conditions, in turn, sarcopenia through deterioration of functional capacity is one of the factors in the development of malnutrition and FS, which is an important factor in their joint diagnosis and treatment [2].

According to estimates by the Marshal's Office of the Lower Silesian Voivodeship [3] malnutrition affects 28% of elderly inpatients in the province, 17.5% in inpatient care, and 8.5% of those in ASC care, especially those approaching 80 years of age with at least one comorbidity. In contrast, FS affects up to 27.3% of people, depending on the population and the diagnostic tools used [4], including 6.7% of people 60+, but as many as 30% of those aged 75-80 and 50% over 80 [5]. Sarcopenia is responsible for about 70% of FS cases [6]. Data from the PolSenior2 survey [7], clearly show that among about 8.5 million people, the prevalence of malnutrition is 3.2%, the risk of malnutrition 23.6%; sarcopenia 11.9%, FS 15.9% and the risk of developing full FS (so-called pre-frailty) 55.8%.

In elderly patients, malnutrition, sarcopenia and FS increase the risk of a complicated and more severe course of many acute conditions, exacerbations of chronic diseases, emergency and elective surgery and trauma, and thus prolong hospitalization, worsen prognosis and increase mortality. Conversely, the ability to effectively identify the aforementioned geriatric syndromes in a timely manner means that the prognosis of many comorbidities with them improves [8]. As sarcopenia, malnutrition and FS can largely be eliminated or reduced through effective prevention, the

role of access to a physician and comprehensive methods of diagnosis and management of the patient is particularly growing, but these cannot be done without the active involvement of the patient. These condition the maintenance of fitness, social activity and perceived quality of life (QOL) [9]. The risk of functional impairment, on the other hand, promote the development of disability and increase the risk of dependence on third-party assistance. Consequently, they significantly worsen the QOL of patients and their caregivers, also worsening the prognosis of comorbidities, reducing life expectancy and increasing the number of expensive and unnecessary hospitalizations [10].

AGING PROCESS

Age-related pathological changes, both structural and functional, affect the course of disease processes in the elderly, resulting in significant differences in the incidence and course of diseases at this age. These changes are observed in all organs and systems[11]. Organ changes in aging are associated with progressive deterioration of organ function making it difficult to maintain homeostasis begins between the ages of 30 and 40. Then begins their specific dimension, which undergoes significant intensification in the first phase during the age of 50, and then in the 7th and 8th decades of life. It mainly manifests itself in the aging of the cardiovascular system which means a decrease in the elasticity of the arterial vessels, a decrease in the relaxation capacity of the left ventricle in particular and its vulnerability, a weakening of the function of the sinus node and a decrease in the response to stimulation - adrenergic; as well as in the aging of the respiratory system, in which there is an increase in the size of the alveoli and terminal bronchi with a tendency to collapse air spaces, a decrease in the gas exchange surface area and a decrease in tidal volume [12].

The above-described changes are not in themselves pathological, they are normal (ordinary), however, they significantly complicate treatment and promote the development of senile ailments (a situation of pathological, pathological aging). These changes exacerbate or cause the onset of COPD, which is the most common comorbidity of geriatric syndromes (as are the aforementioned cardiac changes, leading to cardiovascular disease) [13]. Unfortunately, we can speak of ordinary positive aging for only 10% of the population. The remainder experience so-called pathological aging, i.e., aging in which changes in organs result from both the passage of time and ongoing disease processes in the body. In relation to the population of the Lower Silesian Voivodeship, this means a group of up to 380,000 people whose aging may be pathological in nature [3].

Socio-cultural changes that affect the perception of old age, work and social activity in old age. Old age is increasingly no longer associated with illness or infirmity, as a growing group of elderly people, despite the limitations of the physiological aging process, want to enjoy good health and fitness [14]. They do not accept the limitations of traditional ailments, expecting the health care system to provide the right thing - prompt diagnosis and treatment, efficient preferably community and outpatient services, which ideally should be provided in their immediate communities. They expect an outpatient clinic to be located in a place that provides transportation accessibility, functioning as part of an integrated transportation system and public services that are a coherent part of a coherent socioeconomic system that they understand, in which they find themselves, and that provides them with sufficient psychological comfort when they are ill (reinforcing the effects of treatment) [15].

Nowadays in medicine, the notion that disorders caused by aging are not a direct threat to life is increasingly winning, while the death of an old person is the result of diseases caused mainly by the impact of adverse environmental factors [16]. Being able to identify it in everyday life and direct rehabilitation and prevention, remotely, in the face of greater patient self-awareness is an important gain and opportunity that the project is trying to exploit.

Multi-morbidity along with atypical symptoms in the course of multiple diseases. Significantly complicates the diagnosis and treatment of elderly patients. It requires special knowledge of the consequences of the aging process, pathology and symptomatology of diseases of old age [17]. Often the goal of the work of specialists dealing with the elderly, is to assess the functional capacity of organs, to learn about the health, psychological and social needs of the elderly, and to establish a management plan to raise the level of health to an optimal degree relative to the capabilities of the elderly. This necessitates the cooperation of a number of specialists and the coordinating role of the PCP. It results in the need for an expanded multispecialty diagnostic base and involves a number of physicians sometimes distant (in subject matter) specialties such as diabetology, neurology, rehabilitation or primary care (internal medicine) in the treatment (management) of the same disease entity / ailment [18].

CONSEQUENCES OF AGING – DEMENTIA

Among the most common diseases with the progression of aging, which necessitate particularly widespread cooperation between specialists, can be included dementia, often a complication after cardiovascular or respiratory diseases, as well as in mental and neurological diseases. It is estimated that dementia mainly affects the elderly. 6% of people over 65 and 20% over 85 suffer from the disease. Moreover, the number of sufferers due to the aging of the population is expected to grow rapidly [19].

The treatment process is extremely complex, requiring in the diagnostic phase the use of both specialized psychological and neurological tests (clock test), hematological tests (ESR, blood count, platelets, hematocrit), performing biochemical tests (thyroid hormones, cholesterol levels, lipidogram, creatinine, urea, levels of vitamin B_{12}, folic acid, iron, sodium, potassium, calcium, chloride and liver enzymes), general urinalysis, serological tests (syphilis tests, antinuclear antibodies, HIV diagnosis), cerebrospinal fluid tests (in selected cases) as well as helpful imaging studies [20]. Magnetic resonance imaging (MR, MRI) is also increasingly being ordered. Doppler ultrasound of the blood vessels of the head is also sometimes useful [21].

In the case of dementia, two aspects of treatment are particularly important: the need to have a broad diagnostic base (due to the size of the potential patient group and repeated examinations - on site) that is, extensive screening, and in addition, it is necessary to have a significant range of care from psychological (dementia in the initial stages is illustrated by immediate memory loss), due to the significant inconvenience for the patient, to a neurologist, physiotherapist - who should be included in the rehabilitation process, which significantly reduces the impact of dementia on the emergence of other diseases. The participation of the primary care physician is also extremely important here due to the factors causing the disease, some (most!) of which are environmental and reversible [22]. These include:

- vitamin deficiencies: this is usually a lack of vitamin B_{12}. It is associated with an inadequate diet, hence the importance of a combination of dietary treatment, diabetic coordination and community care support. Of course, malnutrition is an important factor in the development of syndrome;
- depression, which in older people can present the same symptoms as dementia, examples of which include confusion, memory problems and mood swings. Often depression is an offshoot of chronic pain associated with sarcopenia or fragility syndrome. Depression can be treated and therefore it is important to be able to distinguish between the two conditions. On the other hand, untreated depression can lead to dementia;
- subdural bleeding dura very easily occurs in elderly people even after light blows to the head and may resemble the initial stages of dementia (which is associated with falls and mainly with sarcopenia as its complication);
- bladder infection or pneumonia can manifest as disorientation and memory problems, especially if the elderly person is also dehydrated. Dementia can also be caused by encephalitis and AIDS. Diseases passed pneumonia and COPD are almost textbook examples of lack of coordination and close supervision;
- misuse of drugs, especially those affecting the nervous system, can lead to symptoms of dementia. Hence the importance of an integrated system of information on prescribed medications and dosages, which almost forces coordination between Primary Health Care (PHC) and Ambulatory Specialized Care (ASC);
- alcohol, which can induce a state of disorientation and inertia that resembles dementia, but this subsides when the alcohol is no longer administered. However, it can also cause the development of true dementia (see further);
- low blood sugar: this and other metabolic problems, such as myxedema, can put the patient in a state of lethargy, similar to dementia;
- the presence of a brain tumor: again, the symptoms may resemble dementia; however, if the tumor can be removed, in many cases the patient's condition improves;
- other causes include thrombosis, Alzheimer's disease, Parkinson's disease, Wernicke-Korsakov syndrome (caused by alcohol) and Creutzfeldt-Jakob disease.

Importantly, the treatment modality, in addition to pharmacological elements, considers movement therapy, behavioral therapy, home care, support and care from relatives. As in the postulated model. All this is aimed at limiting the patient's loss of vital functions, as well as delaying the need to move the patient to a nursing home for as long as possible [23].

CONSEQUENCES OF AGING – DEPRESSION

The World Health Organization (WHO) estimates that 7-10 percent of the world's population suffers from depression. According to the Polish Psychiatric Association, between 2% and 4% of people in the country currently suffer from it [24]. This means that in Poland about 1 million. Persons show clinical symptoms of the disease. It is estimated that for people over the age of 60, its various symptoms affect up to 20-25% of the population at different times. This means that, to varying degrees, depression can affect nearly 160,000 wasps of the Lower Silesian population. By 2035, the number of patients will increase by about 15%. The main types of depression in adulthood are endogenous depression, reactive depression or dysthymia, which is a chronic form of depression of unexplained origin.

A big problem for patients with depression is its effect on the patient's motivation to fight other illnesses and overall vitality. Even moderate depression is usually accompanied by loss of appetite. Often there is a 5-10% reduction in body weight from normal weight. What's more, in the elderly, depression is prone to frequent recurrences, for example, as a result of relatively harmless somatic illnesses (such as the flu or other diseases). Depression requires constant monitoring of the patient, cooperation of the patient's primary care physician, community nurse and day care, as well as comprehensive work with the patient, allowing him or her to rehabilitate - including physical therapy, psychological care [25].

Also here, the project responds to both the conditions implied by the model and the intentional problems with which sarcopenia, malnutrition, and FS may be associated (such as just depression or dementia changes). This implies the involvement of a geriatrician, internal medicine physician, and other specialists because of comorbidities such as strokes, heart failure, shortness of breath, nycturia, exercise intolerance and fatigue, accelerated or uneven heartbeat, edema, and weight loss [26].

NON-SPECIFICITY OF SYMPTOMS ASSOCIATED WITH AGING

The clinical variability of a geriatric patient's condition is becoming one of the elements causing diagnostic difficulties. Typical for the treatment of the elderly is the phenomenon when the appearance of lesions in one organ, entails the risk of extending the disease process to other organs. The multiorgan nature of the lesions is due to the poorer function of all organs, which is associated with the aging process. The situation is exacerbated by the typical multi-disease nature of old age and the associated multi-drug use [27].

In addition, geriatric ailments are characterized by a specific approach to treatment: the need for largely symptomatic treatment with a strong aspect of prevention and monitoring of the patient (often long before reaching senior status - even starting at 45-55 years of age, where the above-mentioned geriatric syndromes begin to give the first symptoms), also after treatment. Modern specialized - outpatient care for the elderly should therefore also take into account preventive and conservative measures in which the significant role of the primary care physician as coordinator of care and screening tests [28].

Among the most important elements of prevention, is proper rehabilitation and recovery from diseases, which significantly reduces the problem of recurrence or negative complications. This applies to the greatest extent to musculoskeletal, cardiac and pulmonary diseases. Rehabilitation also makes it possible to prolong professional activity. On the other hand, a significant proportion of diseases can also be prevented after the age of 60. Hence, preventive measures should be continuous, possibly involving the patient independently and facilitated with the help of technology. More importantly, they should be characterized by increasing intensity at a later age [29].

A critical aspect is also the mundane issue of recall. This involves memory problems. Memory disorders make it necessary to take into account that the patient will not be able to give all the information relevant to the diagnostic process and treatment, so he needs the constant care of the PCP and support in the form of community care, which must have both a directly therapeutic and preventive dimension [30].

CLINICAL EVALUATION OF AGING CHANGES

Due to the high prevalence of the problem, simple questionnaire tools are currently being used to identify sarcopenia, FS and malnutrition, which can be self-administered by the patient or caregiver and take little time to complete. Self-diagnosis allows, through cooperation with primary health care (PHC) facilities, to refer the patient to a specialist (geriatrician) in the situation of exacerbation of symptoms, complete assessment, early diagnosis and implementation of treatment, significantly faster and more effective [31]. Currently available solutions related to the possibility of providing some consultations and services through the PHC and remotely, can further facilitate access to the care and support in question, overcoming the pains of "queues to the specialist" as a bottleneck in the treatment process. Indeed, in the treatment of all three syndromes, the most important thing to do first of all is an appropriate dietary and rehabilitation intervention, including a complete diet containing an adequate amount of protein and regular physical activity including resistance exercises, i.e. rehabilitation performed with the involvement of the PHC or even a community nurse, which also relieves the burden on specialized entities, reducing the overall queue and speeding up access to highly specialized procedures.

The analyses described in the document: Reducing social inequalities in health through telemedicine and e-health solutions – geriatrics [32], indicate that the adopted solution should be: (a) easy to use, (b) freely available to the public, (c) free for users, (d) validated (providing reproducible valuable and reliable information), (e) accessible to people with disabilities including the visually impaired (compliant with current regulations on digital accessibility of websites and mobile applications of public entities), (f) secure (communication will be implemented via encrypted HTTPS protocol), and (g) efficient (allow simultaneous use by multiple users). In addition, it should offer the possibility, including legal, of integration with the existing and developing e-health system in Poland.

Finally, they should use recognized and simple scales (questionnaire tools): (a) MNA-SF (Mini-Nutritional Assessment, Short Form) regarding malnutrition and risk of malnutrition [33]; (b) (b) SARC-F (A Simple Questionnaire to Rapidly Diagnose Sarcopenia: Strength, Assistance with Walking, Rise from a Chair, Climb Stairs and Falls) regarding the study of sarcopenia [34]; or (c) FRAIL (Fatigue, Resistance, Ambulation, Illnesses, & Loss of Weight) regarding the study of FS and frailty risk) [35].

RESEARCH PERSPECTIVE

Currently, there is no similar tool "addressing the problem of FS, sarcopenia and malnutrition in a simple and at the same time comprehensive way - so there is no solution to be transferred directly to the Polish ground," which requires the development and research of a national model for screening and treatment of the aforementioned disease phenomena, by methods including telemedicine. The records of the documentation and model itself are therefore a significant justification for the project. Analysis of patient surveys (dated 06.2021, on a group of 197 PHC and 72 ASC patients) confirm the above analysis: 73% of PHC patients and 81% of ASCs point to the key barriers of excessive waiting times for specialists in accessing health services for treating geriatric syndromes; 91% of PHC patients and 95% of ASCs said that access to modern preventive care for seniors in their municipality is insufficient; according to 95% of ASCs, coordination of the work of PHCs and ASCs is particularly problematic (ordering treatment, setting joint plans and goals in therapy already by the PHC, analyzing the entire spectrum of the patient's health problems, exchanging information, one standard of service - most frequently indicated); the worst overall level of health care is rated by people: (a) the elderly-above 60 yrs. ż. (69% of negative ratings) who are affected by diseases of old age (so-called geriatric syndromes); b) people with chronic diseases (72% of negative ratings); c) people of working age expecting a quick return to work and requiring rehabilitation care (73% of negative ratings).

Most often the above-mentioned individuals indicated: Lack of adapted infrastructure, lack of possibility to carry out specialized rehabilitation in one place or at home with the support of a doctor, the need to "think" for doctors (medications, results, appointments) due to lack of coordination; quality of treatment due to equipment, waiting time); in other groups (people 18-24; 18-65, or 65+) who are not affected by a particular health problem, the number of negative evaluations was less than 50%, and the most common negative aspect

was the waiting time for an appointment; the largest group of respondents who indicated that their health condition makes it difficult or impossible to work were those with osteoarticular and muscular problems (63%), all of whom indicated difficulties in receiving rehabilitation support due to: length of waiting for consultation (72%), lack of the most suitable therapy for their condition (43%). According to the previous studies [36], elderly people experience "a decrease in the functional efficiency of cells, tissues, and organs, a progressive impairment of the efficiency of regulatory mechanisms, and a decrease in the body's ability to adapt to environmental changes as a consequence of the aging process," which affects the scope of care and determines the necessary resource of equipment in health care facilities that direct care for people aged 60+.

AIM

The overarching goal of the paper is to present the essentials of a pilot project to test a telemedicine model in the field of geriatrics, along with a snapshot of the health challenges and the rationale for the need for the project.

MATERIALS AND METHODS

This review paper summarizes the main objectives of the telemedicine pilot project in the field of geriatrics. The objectives of the pilot were presented, the pilot model was described, the recruitment scenarios and recruitment visits were described, the summary stage and the results of the pilot were characterized, and the feasibility of the project was analyzed.

REVIEW AND DISCUSSION

PILOT ASSUMPTIONS

The project involving telemedicine care of patients with geriatric complexes in the area of FS, sarcopenia and malnutrition, according to the proposed model addresses the above-mentioned problems. It provides a holistic model of home and outpatient care, which will allow concerting on the 3 groups of the above-mentioned geriatric complexes, to overcome significantly the current barriers and realize the needs of patients diagnosed in the Applicant's analysis. First and foremost is increasing the availability of non-hospital health services for elderly patients. According to the Ombudsman [37]" the weakness of the public health system" is a significant barrier to the realization of constitutional rights - art. 68 as well, and manifests itself in long queues, inefficient forms of care, inadequate to the needs of the patient, and the capabilities of current medical technologies. According to the Watch Health Care Foundation (2021), the average waiting time to see a specialist in Poland is about 100 days- one of the longest in the OECD (same for women as men, no discrimination here). At the same time, for elderly patients, with sarcopenia, malnutrition, FS, and often another chronic accompanying disease (most often it's COPD), due to multiple complications, it is even 2 times longer (according to NHF, it's about 6 months), which causes that patients instead of going to ASC, go straight to the hospital in acute crisis situations, in worse condition, so that later they become dependent, worsen their prognosis, quality of life and the possibility of treating also other diseases.

According to the Center for Health Information Systems (pol. Centrum Systemów Informacyjnych Ochrony Zdrowia, CSIOZ), in 2020 (before the pandemic) there will be about 7.216 million hospitalized people in Poland (3.19 million men and 4.02million women), above the European Union (EU) average. Taking into account that age is an important factor in both morbidity and patient chances, the number of patients over 60 will increase by 31% in the province by 2035 (just due to the aging of the population). According to the National Health Fund (NHF), in 2017, the average indebtedness of hospitals was 8.3% of the NHF contract, which also corresponds to overcharges due to the lack of alternative care in ASCs. In addition, people 60+ with malnutrition, FS, and sarcopenia are accompanied by multiple conditions/at once, which involve multiple specialists. Hence the need for coordination and collaboration of physicians responsible for prevention, diagnosis, and therapy, in a consistent model of care, "close to home, without compromising daily activities, which improves outcomes and lowers treatment costs" with a strong role for PHCs [38].

Importantly, in 30 years Poles will be the 2nd oldest society in the EU, and already in 2020 "1/4 are over 60 years old." According to the Marshal's Office of the Lower Silesian Province (2019), there are 3 geriatric outpatient clinics in the province, including 1 outside of Wroclaw, and "there should be 24" (according to WHO standards), which is a barrier to accessing adequate health care. The system currently lacks an effective model of care for patients with frailty, malnutrition and sarcopenia, as well as an effective screening mechanism (despite the rationale indicated in the documentation and rationale for the model based on clinical studies and simple and accessible scales). What is available, however, is technology that could be used by a network of PHC facilities, which are required by the NHF to have computers, software, and which now often provide telemedicine services (e.g., teleconsultation, which has become particularly popular during the pandemic) [39].

PILOT OBJECTIVES

The main (primary) goal is to increase access of 520 people (including min. 260 women) meeting the inclusion criteria (including age ≥ 60, who have given written informed consent to participate in the project) including at least 52 people (min.10 %) coming from excluded areas (from counties with average income per capita below the national average, including those using PHC located in a rural area far from large cities), to health services mainly telemedicine in accordance with the assumptions of the "2 GERIATRIA" model, including enabling min. 520 individuals with screening tests, and among those in whom malnutrition, sarcopenia and FS will be detected, to improve (in 80% of them) the prognosis during the period of pilot coverage, to counteract the development of disability during this time and reduce the risk of dependence on the help of others in performing the duties of daily life, as well as to reduce the risk of hospitalization, exacerbation of chronic

comorbidities and reduce the risk of death, in the course of the Partners' activities in Lower Silesia province, from 01.06.2022 to 31.12.2023. The main goal will be achieved by achieving specific (secondary) goals, which include:

1. Increasing the independence and a sense of health security in the 60+ population, including patients with malnutrition, sarcopenia and FS - regardless of income and place of residence, as well as nearby access to an ASC (geriatric specialist);
2. Verification of the effectiveness of the investigated model as a tool to conduct effective screening in the population, including typing of patients with malnutrition, sarcopenia and FS and improvement of health status in these individuals, in cooperation of the Hospital, PHC, ASC and using the assumed telemedicine tools;
3. Optimization of health services targeting people over 60 years of age, which will increase the emphasis on screening activities, related to secondary prevention and health education, involving in patients diagnosed with malnutrition, sarcopenia, and FS first a PHC physician, and only in situations that require it a specialist (a geriatrician at an ASC or hospital), and more widely involve and engage the patient (and/or hypothetically their formal or informal caregiver) in taking care of their own health and the process of rehabilitation and treatment, through the use of telemedicine solutions.

The objective will be in accordance with the objectives of the Norwegian Financial Mechanism 2014-2021 and with the objectives of the planned results and objectives of the competition (including program documents and relevant provisions of national and EU law referred to in part 2 of the Rules of Recruitment: "2. LEGAL BASIS"). All project activities that will achieve the primary goal of the call and the program, i.e. improved prevention (within the services offered by the model) and reduced (due to this) health inequalities" (by making available services that are currently covered by specialized treatment with limited accessibility due to the need to travel, limited access to doctors and lack of tested and adequate diagnostic and treatment regimens along with the necessary ICT infrastructure) will also be in line with the provisions of the above-mentioned goals and documents.

The project will achieve the objective, with the program result: "Reduced social inequalities in health, including improved access to telemedicine and e-health care services", by covering 520 people with such services and creating the infrastructure and conditions for the provision of similar services after the end of the project, together with their scaling to the entire country.

PILOT MODEL

The project will have a pilot character and is aimed at clinical verification through the introduction (implementation) of a new method and accompanying organizational and technological solutions (platform, equipment) in an area where current models and schemes of therapeutic and diagnostic support were insufficient. The project will make it possible to check whether the planned measures are having the desired effect in terms of treating the effects in old age. It will also make it possible to reduce the risk of failure of hypothetical nationwide solutions and to obtain user feedback. The main activities in the implementation of the study (according to the model presented):

a. recruitment of patients over 60 years of age, considering the pathways: (a) telephone contact – information about the project; (b) appointment "0" from the PHC doctor's proposal; (c) appointment "0" from the patient's proposal (request). The patient/caregiver will be recruited within the PHC. It will not be required for the patient to be enrolled in a given PHC facility, and persons will also be admitted, from outside a given PHC facility, who, as a result of ongoing information and promotion activities, have received information about the possibility of joining the project.
b. patient examination (visit "0" – recruitment), during which there will be:
   - providing the patient and/or caregiver of the geriatric patient with detailed information about the project being conducted;
   - giving informed consent to participate in the project and consent to the processing of personal data of the project participant;
   - training in the use of the online platform (if necessary);
   - supervision and support of the physician during the patient's (and/or the patient's caregiver's) initial self-assessment using the platform;
   - providing feedback to the patient regarding the patient's current health status with respect to deficits (or lack thereof) in Sarcopenia, malnutrition and FS. There will also be follow-up information on further management.
c. Follow-up teleconsultation (hereafter visit "1") approximately 30 days (+/- 5 days) after the visit "0". This will be a standard physician teleconsultation with an assessment of the occurrence of the previously indicated adverse events, supervision, and support while the patient (and/or the patient's caregiver) performs a follow-up self-assessment using an online platform (if necessary). The physician will also identify patients who will require extended evaluation (it is assumed that this will apply to approximately 20% of patients participating in the pilot). The extended evaluation will be carried out on the basis of ordered additional laboratory tests (including blood count, assessment of kidney and liver function, as well as Albumin, Sodium, Potassium, Calcium, Vitamin D, and Vitamin B_{12} tests) with assessment of each case in consultation with a geriatrician (during the specialist teleconsultation). Teleconsultation "1" and "3" will include: (a) a discussion of dietary recommendations for the patient; (b) a discussion of exercise recommendations (optional, as needed), (c) referral for advice at a highly specialized – geriatric clinic. In the case of abnormal self-assessment results (MNA-SF <12 points or SARC-F ≥4 points or FRAIL ≥ 1 point), after prior teleconsultation of the PHC physician with a geriatrician, referral of patients for teleconsultation

with a geriatrician. It is assumed that for these patients, teleconsultation with the PHC will take place within 7 days and teleconsultation with the geriatrician within 28 days. In the case of abnormal (alarming) self-assessment results (MNA-SF <7 points or SARC-F >5 points or FRAIL ≥ 3 points), the patient will be fast-tracked for in-depth diagnostics and referral for teleconsultation with a geriatrician.

d. a final teleconsultation in the third month after patient inclusion (hereinafter: visit "3"). This will be a standard medical teleconsultation, along with an assessment of the occurrence of adverse events and endpoints indicated earlier, an assessment of satisfaction with the solution used (beneficiary and provider), and the formulation of final recommendations for the patient. If warranted, it will be possible to carry out additional specialized teleconsultations: (a) on the PHC physician-geriatrician line (for a minimum of 10% of participants), (b) on the patient-geriatrician line (for a minimum of 5% of participants).

SUMMARY STAGE

The summary stage of the project will follow the telemedicine model for geriatrics and will include the following elements:

- evaluation of the proposed solution with analysis of feedback from beneficiaries and involved providers;
- evaluation of the implementation possibilities of the proposed e-health system in the Polish healthcare market (feasibility assessment);
- detailed evaluation of the consistency of individual stages and elements of the system with the option of Re-evaluation of the system structure after the pilot stage;
- assessment of the degree of satisfaction of beneficiaries (patient, patient caregiver) and providers involved in the implementation of the model (PHC doctor, PHC nurse, geriatric specialist) with the proposed solution;
- evaluation of selected health indicators in patients recruited for the pilot system (frequency of hospitalization, frequency of use of hospital emergency department and emergency room, institutionalization, falls, death).

As part of the evaluation of the proposed path of patient participation in the project, an analysis of the feasibility of a given form of support in Poland will be carried out, with particular emphasis on the effectiveness of the introduced solution, the satisfaction of doctors and patients. Conclusions will be drawn from the pilot study, which – in the form of an easily understandable report - can be presented to a wide audience, and the rationale from the experience will become the basis for possible correction of the proposed telemedicine solutions. The Local Pilot Conduct and Evaluation Team (5 geriatricians), selected by the project coordinator (PC) and assistant (APC) during the project implementation, will be responsible for supervising the substantive correctness of the conducted project, as well as the summary and evaluation stage. The responsibilities of the healthcare facility will include:

- training and supervision of PHC physicians and geriatricians on: conducting the pilot and principles of cooperation between PHC physicians and geriatricians, operation of the online platform, definition and diagnosis of malnutrition, sarcopenia and frailty syndrome, discussion of dietary and physical activity recommendations for malnutrition, sarcopenia and frailty syndrome;
- conducting a survey on user needs in relation to the designed solution;
- conducting a survey on user satisfaction with participation in the project;
- conducting a feasibility assessment of the implementation capabilities of the proposed e-health solution in the Polish health services market;
- conducting a detailed evaluation of the consistency of individual stages and elements of the system with an option to re-evaluate the structure of the system after the pilot stage;
- evaluation of selected health indicators in patients recruited for the pilot;
- disseminating to the public of preliminary results demonstrating the project, promoting the idea (development of publications, webinar, materials for the website);
- legal services;

consulting solutions with the foreign partner, exchanging experiences and transferring them to Poland;

- performing other activities necessary for the proper implementation of the project.

PILOT EFFECTS

The main (primary) outcome will be to bridge social inequalities in health by reducing the residence and income factor in access to screening and medical services through the use of telemedicine, which overcomes geographic limitations in access to outpatient specialized care (in centers far from the supply of specialists, among others. e.g., in villages and small towns far from large metropolitan areas) and incorporates the PHC clinic (along with a nurse) into care close to the patient - using remote contact with the specialist and in-person and remote contact with the PHC.

At the same time, the project will make it possible, by building on the FRA-MA-SARC model solutions already produced, to provide universal services without the need for additional costs and specialized purchases that are part of the current NHF benefit system (making it available regardless of income).

The project will be based on technologies that are easily scalable and IT-consistent with the solutions implemented by the Ministry of Health, which will facilitate its implementation at the national level. Partners and the Leader represent entities from different municipalities and districts with different sizes and characteristics of health services, strongly differentiated also in terms of income, which will ensure the representativeness of the target group and the effectiveness of the developed organizational solutions. The project, thanks to the applied solutions, will increase:

- opportunities for therapy and rehabilitation (through adequate care and health education focused on lifestyle changes), particularly for people with overlap-

ping conditions who, until now, have been deprived of multispecialty support and care in the ASC in the course of their illness. Consultation and the guiding role of the specialist will help ensure ongoing coordinated care reinforced by PHC physician involvement, which will improve the patient's prognosis;

- independence (according to the Barthel scale) and restore maximum possible well-being (as measured by standardized QOL tests, as recommended by the WHO, performed by PHC) by promoting solutions that involve the patient himself in treatment and make treatment outcomes independent of the need to commute and wait in line for appointments;
- the use of adapted software for people with disabilities which will increase mobility and enable greater social and professional activity;
- knowledge of the patient's disease and ways to minimize its negative effects by the patient himself, which will improve the prognosis of therapy and help increase the effectiveness also financially of the overall basket of services (in view of the globally growing needs of an aging and more frequently ill population);
- the use of e-health and telemedicine applications that create a network of services for a group of seniors with geriatric syndromes according to the described model, which will facilitate the wider inclusion of solutions related to deinstitutionalization in treatment processes (as an added value that will enable the preservation of care after the project).

CONCLUSIONS

The implementation of telemedicine solutions creates an opportunity for geriatric patients and their families by improving access to specialized medical care. The project under discussion will support patients, but also caregivers, who (through training and telemedicine) will be better able to provide care services with the ability to reconcile them with their own work. This will reduce discrimination against the economically disadvantaged, who suffer from multiple exclusions. The project will better utilize the potential of caregivers' knowledge and experience in the labor market and reduce the inheritance of poverty. It also contributes to overcoming the limitations of exclusion due to: (1) age and health (does not exclude people who cannot afford private care); (2) education (given the simplicity of the planned solutions, use of popular technologies); (3) mobility capabilities; (4) living with a caregiver (telecare monitoring, calling for help). The project will also respond to the frequent situations of avoidance of treatment by people 65+, due to motor ailments (will be held at home by means of telemedicine) that make it difficult to contact the doctor (travel to the clinic, especially the remote ASC). The project in the scopes presented will be implemented in accordance with the Guidelines in the area of social inclusion, the Guidelines in the area of health, the European-wide guidelines for the transition from institutional care to care provided at the level of local communities.

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Short Communication

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THE FRAMEWORK OF THE PILOT PROJECT FOR TESTING A TELEMEDICINE MODEL IN THE FIELD OF CHRONIC DISEASES – HEALTH CHALLENGES AND JUSTIFICATION OF THE PROJECT IMPLEMENTATION

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ABSTRACT

Aim: To present the essentials of the pilot project for testing a telemedicine model in the field of chronic diseases, along with a snapshot of the health challenges.

Materials and methods: This review paper use the synthetic method summarizing the main objectives of the telemedicine project in the field of chronic diseases with a focus on COPD. The described project will have a pilot character and is aimed at clinical verification through the implementation of a new method and accompanying organizational and technological solutions (platform, devices) in an area where current models and schemes of therapeutic and diagnostic support were insufficient. The main (primary) outcome will be the leveling of social inequalities in health by reducing the residence and income factor in access to screening and medical services through the use of telemedicine.

Conclusions: Implementation of telemedicine solutions creates an opportunity for patients diagnosed with COPD and their families by improving access to specialized medical care. With early detection of COPD exacerbation symptoms (deterioration of remotely monitored spirometric parameters), it will be possible to introduce appropriate preventive measures for these patients offsetting the adverse consequences.

KEY WORDS: chronic diseases, telemedicine, chronic obstructive pulmonary disease, lung diseases, pulmonology, Norway Founds

INTRODUCTION

Chronic diseases are a significant global health problem, being one of the biggest causes of burden on health care systems [1, 2]. They are characterized by a long-term course, causing long-lasting or permanent changes in the body, which affects patients' quality of life (QOL) and performance. The most common chronic diseases include cardiovascular diseases, chronic pulmonary diseases, diabetes, cancer, gastrointestinal diseases, and conditions related to the nervous system. The increase in the incidence of chronic diseases is often associated with unhealthy lifestyles, including excessive consumption of unhealthy foods, lack of physical activity, smoking or excessive stress. In addition, an aging population also contributes to the increase in chronic diseases, as age is a significant risk factor for many of these conditions [3, 4]. Successfully combating the problem of chronic diseases requires a comprehensive approach that includes not only symptomatic treatment, but also prevention, public education and promotion of healthy lifestyles. Awareness of the risks associated with chronic diseases and access to appropriate preventive screenings are key to early detection and prevention of the progression of these diseases [5]. Supporting medical research and innovation is also essential for developing more effective therapies and new diagnostic methods. One of the most common chronic diseases is chronic obstructive pulmonary disease (COPD).

Importantly, in 30 years (by 2050), Polish patients will be the second oldest population in the EU, and already in 2020, about 25% are over 60. According to the Marshal's Office of the Lower Silesian Voivodeship (2019), there are only 3 geriatric outpatient clinics in the voivodeship, including 1 outside Wrocław, a dozen pulmonology clinics treating COPD, and according to WHO standards, there should be 24. The above is a barrier to access to adequate health care (as evidenced by queues to the pulmonologist, often over 200 days!). Currently, the system lacks an effective model of COPD care (despite the rationale indicated in

the documentation and rationale for the model based on clinical studies). However, technology is available to develop and implement such a model. According to the survey – 91% of households have access to high-speed Internet, 97% of households have a device with Internet access, of which 84% of households have a computer/laptop. 89% of seniors say they use a smartphone [6].

Given the above, it should be concluded that the barrier is therefore not technology, but organization and the lack of appropriate system solutions. In addition, among COPD patients in the hospital, as many as 76% (! out of about 200 respondents) do not see any barriers for themselves in terms of joining the projects, and the only barriers indicated by 24% of patients are access to a tablet / computer (which at home they have to share with, for example, a grandchild and thus is not fully accessible) – here the lack of access to a device with the Internet is declared by between 5% and 10% of respondents. Some problem may be (according to 16%) their insufficient competence (although by far the majority indicates, the possibility of obtaining help from actual caregivers). More than 90% of respondents would be interested in the project according to the assumptions indicated in the application [7].

PROBLEMATICS OF COPD

According to the definition in the Recommendations of the Polish Respiratory Society (pol. Polskie Towarzystw Chorób Płuc) – COPD is a common, chronic, and persistent restriction of airflow through the lower airways, with the restriction usually progressive and associated with an excessive inflammatory response. According to the aforementioned recommendations, COPD is a disease (among fatal and chronic diseases) that lends itself relatively well to prevention and treatment. This is because it develops as a result of two groups of factors: environmental (including ambient air pollution and occupational exposure to dust and pollutants, as well as smoking) and personal (genetic factors). It most often affects people over the age of 40 who smoke and/or have been exposed to other risk factors, and who have symptoms: shortness of breath, shortness of breath, and coughing (often with expectoration of sputum) [8, 9].

The number of patients with COPD in Poland ranges from 1.3 million to as many as 2.8 million people (in Lower Silesia Province, from 98.3 thousand to 211.7 thousand people). According to the data, about 10% of the population over the age of 40 suffers from COPD in Poland, and the disease more often affects men [10]. According to the WHO, COPD is the 5th cause of death worldwide, and will be the 3rd most common cause of death by 2050 [11]. As a pulmonary disease, it more often and severely affects patients from regions with highly developed industries – especially mining, heavy industry, where employees work hard in a heavily dusty environment. In addition, the disease is a problem especially for the elderly, causing severe complications or co-occurring with most of the most fatal disease entities [12]. A major impediment to taking appropriate therapy or prevention is the relatively low level of diagnosis of the disease (it is estimated that there may be about 2 million patients in Poland, of whom about 600,000 people, or 30%, have a diagnosis). This means that the patient is diagnosed already during hospitalization. Nevertheless, up to a third of patients diagnosed and treated for COPD in the hospital may be inaccurately diagnosed as COPD on the basis of a confirmatory spirometry test. Factors contributing to inaccurate diagnosis include less frequent history of smoking, high BMI and associated comorbidities [13].

The mortality rate due to COPD alone in the general European population is estimated at 18 per 100,000 inhabitants per year (age-standardized rate). However, there is considerable fluctuation in values between countries, with Eastern European countries having an approximate 10-15% higher rate. Overall, on average in the European Union (EU), COPD is responsible for the deaths *per* year of about 4.1% of men and 2.4% of women (which is a rather underestimated value, since in many cases in severely ill patients coronary artery disease, hypertension, lung cancer etc. are reported as the cause of death – i.e., key comorbidities and complications after COPD) [14]. About 65 million people in the world population suffer from COPD, and the disease is becoming the third most common cause of death (behind ischemic heart disease: 13.2% and strokes: 11.9%) (Szalontai et al., 2021). COPD is also a disease that significantly affects a patient's daily life. A 2017 survey by the Social Research Institute (pol. Pracownia Badań Społecznych, PBS) shows that the most commonly experienced and most annoying complaint for patients is exertional dyspnea and cough, in the face of which it becomes problematic to perform daily activities, such as going to the store, walking, cleaning, *etc.* [15].

MANAGEMENT OF COPD

There is no freedom in the diagnostic and treatment management of COPD, as there are guidelines and recommendations from international scientific societies as well as national ones, which form the basis for physicians at various levels of medical care. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [16] are one of the key documents that are regularly updated to incorporate the latest scientific findings and advances in disease management. In the latest edition of GOLD 2020, a more precise definition of a COPD exacerbation was made and issues related to disease prevention, treatment of exacerbations, and non-pharmacological therapy were highlighted. The guidelines are based on a wide range of clinical studies and current literature data, providing a reliable and comprehensive approach to the management of the disease. The definition of COPD emphasizes its complex nature as a disease syndrome associated with persistent respiratory symptoms, airflow limitation and/or abnormalities in bronchial and alveolar structure [17].

It was pointed out that lesions result from exposure to harmful external agents, and that comorbidities, including emphysema without airway obstruction, can have a significant impact on COPD morbidity and mortality. In addition, the importance of Pseudomonas aeruginosa colonization in patients with COPD as a risk factor for exacerbations and

mortality was noted [18]. Particular attention was paid to the association of COPD incidence with increased levels of particulate matter in the air, which underscores the importance of improving the quality of indoor fuel used in the prevention of the disease, especially in developing countries, where COPD incidence may be linked to indoor air pollution from biomass burning. The GOLD guidelines are updated annually, which is extremely valuable because they are based on observations and clinical studies, allowing treatment and disease management principles to be adapted to the latest information. A prerequisite for the diagnosis of COPD is a spirometric test, and exacerbations are an important part of the natural course of the disease. The guidelines are therefore an indispensable tool for physicians, both primary care and specialists, to effectively diagnose, treat and manage patients with chronic obstructive pulmonary disease (COPD). They support physicians in delivering comprehensive medical care, optimizing both pharmacological and non-medical approaches to the disease, helping to improve patients' QOL, and reduce the risk of exacerbations [19].

The diagnosis of COPD is established on the basis of history, physical examination, functional tests (such as spirometry), imaging (chest X-ray, etc.), laboratory tests (peripheral blood count, etc.) and others (such as ECG) in connection with the study of numerous complications. In never-smokers, COPD accounts for 10-20% of cases, more often in women. Untreated COPD tends to exacerbate symptoms as assessed, for example, by the modified dyspnea scale (mMRC) or the CORD Assessment Test (CAT) COPD impact on the patient's life [20]. The current classification also allows assessment of the risk scale for exacerbation of the disease, which significantly worsens the prognosis. Other factors that worsen prognosis are comorbid heart disease, low body weight, resting tachycardia, hypercapnia and hypoxemia. Additional risk factors include advanced patient age, higher PaCO2 values and the need to take oral corticosteroids [21].

The risk of dying from COPD decreases in patients who stop smoking, eat healthier, restore healthy exercise, monitor their health, and take prescribed medications regularly. Conversely, a report by the Agency for Health Technology Assessment and Tariff System (pol. Agencja Oceny Technologii Medycznych i Taryfikacji, AOTMiT) cites the following as statistically more frequent sequelae in patients who do not adhere to the above recommendations: premature death, inability to live independently, inability to work (permanent or temporary, total or partial), chronic suffering or chronic illness, reduced QOL (permanent or temporary). The developed form of COPD cannot be permanently cured and it is necessary to apply chronic treatment for the rest of life, which, established on the basis of the classification, includes: observation of the patient, education, and rehabilitation, as well as chronic treatment, including pharmacological, oxygen, ventilatory support and surgical treatment (which relieves the symptoms of the disease, improves bronchial patency, reduces the number and severity of exacerbations and improves QOL and prognosis (also reducing negative complications) [22].

CONSEQUENCES OF COPD

COPD is an extremely costly disease (in social terms) – direct costs from COPD in 2019 amounted to about PLN 450 million (analyzing the basic variants of the disease – excluding the cost of complications), of which as much as PLN 297.1 million is the cost of drugs, and more than PLN 100 million is the cost of hospitalization. The rest is the cost of ambulaotory specialist care (ASC) visits. In turn, the indirect costs of COPD amounted to about PLN 6.4 billion (mainly due to inability to work, work absenteeism of formal and actual caregivers, as well as premature deaths of patients). To the aforementioned costs should be added the costs of treating comorbidities and complications. It is also necessary to consider the costs generated by undiagnosed patients, as well as the costs associated with the need to increase places of care.

At present, a major problem in the treatment of the sequelae of COPD is the lack of existing comprehensive health care procedures dedicated to patients, which would involve specialists, primary health care (PHC) practitioners and community nurses, so as to limit expensive hospitalizations and counteract the deterioration of the condition (which implies expensive and risky drug therapies for the patient). It is also necessary to be more active within the currently neglected health education, in order to be able to effectively influence the improvement of patient prognosis (reducing the negative impact of environmental and patient-dependent variables).

The guidelines are therefore an indispensable tool for physicians, both primary care and specialists, to effectively diagnose, treat and manage patients with COPD. They support physicians in delivering comprehensive medical care, optimizing both pharmacological and non-medical approaches to the disease, helping to improve patients' QOL and reduce the risk of exacerbations.

INNOVATIVE SOLUTIONS

There is a need for solutions to respond to the growing number of dependents with COPD (requiring support in daily functioning), most often aged over 60 (due to the declining number of actual caregivers), who are additionally affected by geriatric syndromes (as many as 20% of people with, for example, sarcopenia, frailty syndrome and malnutrition have COPD) [23]. According to the Health Needs Maps (HNMs), the Lower Silesian province is inhabited by hard-working people (agro-industrial economy, only in the last 20 years with a predominance of services) with a high risk of so-called geriatric syndromes (according to the 2015 HNMs – above the national average), particularly exposed to respiratory diseases due to developed industry and centuries-old mining traditions (more frequent exposure to dust) and generally long-term unhealthy lifestyles (more frequent smoking). In addition, in the COPD population, there is often a risk of multiple diseases coexisting at the same time in the patient (known as multimorbidity) [24].

Many municipalities in the province, compared to the national average, are characterized by a high number of

PHC dispensaries per person (4.7), compared to the national average of about 4 dispensaries per person. The relatively high number of tips given, while at the same time there are fewer PHC clinics in the province, further limits access to health services and lengthens queues to see a specialist (which have been lengthened anyway as a result of the pandemic), which is a significant barrier to treatment. Another significant health problem in the province (and more broadly in the country) is the inadequate quality of health care. According to the Bank of Local Data (pol. Bank Danych Lokalnych, BDL), the Lower Silesian Voivodeship is characterized by low access to multispecialty treatment, which is confirmed by socio-economic indicators, i.e., among other things, a higher overall mortality rate than the national average, as well as lower employment rates, which are caused by the health of the population. Moreover, a significant portion of hospital treatment is located in Wroclaw, with which regional and local centers cooperate.

RESEARCH PERSPECTIVE

The project, which consists of telemedicine patient care according to the proposed model, responds to the above-mentioned problems, overcomes current barriers and realizes patients' needs: greater availability of non-hospital health services for patients with COPD. According to the WHO Director General: "access to health care overcomes social inequalities, especially for those most in need" – i.e. younger people from smaller centers for whom the disease is a problem of normal existence, older people, those aged 65+ and those with chronic diseases – regardless in principle of their place of residence due to their broad health needs [25]. According to the patient ombudsman (Report, 2020), "the weakness of the public health care system" is a significant barrier to the realization of rights, including constitutional rights – Article 68, and manifests itself in long queues, inefficient forms of care, inadequate to the needs of the patient and the capabilities of current medical technologies [26].

According to the Watch Health Care Foundation (2021), the average waiting time to see a specialist in Poland is about 100 days, and is one of the longest in the OECD (the same for both men and women), with up to twice as long for people with COPD, due to multiple complications (according to the National Health Service, it's about 6 months), resulting in patients going straight to the hospital instead of the ASC. They are in worse condition, making the patient dependent, worsening prognosis, QOL, and the possibility of treating other diseases [27].

According to data from the Center for Health Information Systems (pol. Centrum Systemów Informacyjnych Ochrony Zdrowia, CSIOZ) for 2020, about 7.216 million people were hospitalized in Poland (including 3.19 million men and 4.02 million women), which is above the average for EU countries. In the Lower Silesian province, COPD patients are hospitalized for cardiovascular diseases (14.5%) or cancer (9.1%) together at the same time. Taking into account that age is an important factor in both morbidity and patient chances, the number of patients over 65 will increase by 31% in the province by 2035 [28].

According to the Supreme Audit Office (pol. Naczelnej Izby Kontroli, NIK) (2019), the average indebtedness of hospitals amounted to 8.3% of the contract with the National Health Fund (NHF), which also corresponds to overcharges due to the lack of alternative care in ASCs [29]. In addition, people 60+ with COPD with multiple comorbidities at the same time, involve multiple specialists, hence the need for coordination of treatment and collaboration of physicians responsible for prevention, diagnosis and therapy – in a consistent model of care, close to home, without compromising daily activities, which improves outcomes and reduces treatment costs [30]. In practice, this means involving telemedicine and PHC

AIM

The overarching goal of the paper is to present the essentials of the pilot project for testing a telemedicine model in the field of chronic diseases, along with a snapshot of the health challenges and the rationale for the need for the project.

MATERIALS AND METHODS

This paper summarizes the main objectives of the telemedicine pilot project in the area of chronic diseases with a focus on COPD. The objectives of the pilot were presented, the pilot model was described, the recruitment scenarios and recruitment visits were described, the summary stage and the effects of the pilot were characterized, and the feasibility of the project was analyzed.

REVIEW AND DISCUSSION

PILOT ASSUMPTIONS

The target group of the project and will be people qualified for health support, i.e. people over 18 years of age who have submitted informed consent (signed) to participate in the project (and other recruitment documents) with diagnosed COPD. In addition to patients, the activities will be directed to other groups that will participate, according to the assumptions of the model, in the results of project activities: PHC physicians, nurses, pulmonology specialists, and to some extent, also caregivers of the sick (legal or actual).

While patients will be the group that will receive health and health education support, medical personnel will gain additional knowledge and qualifications in how to manage a patient with COPD and use telemedicine solutions for this purpose. Caregivers of patients, on the other hand, will gain knowledge in the operation of the telemedicine platform used as a basis for the services provided, as well as knowledge resulting from health education aimed directly at them and the patients. It is estimated that the number of sick people will be 520, including about 50% women (according to the approximate distribution in the population, no gender inequality in access to health services in the province has been found). The number of caregivers of sick people is difficult to estimate (the participation of about 20% of them, i.e. about 100 people, is assumed). The number of doctors is 10 specialists, 9 PHC doctors and 9 community nurses.

The project does not assume a preference for any of the groups (which will allow the model to be tested as a target solution used in the universal health system, where there is no access censorship). Nevertheless, given the goals of the program, priority in participation will be assigned to people from municipalities in excluded areas, i.e. areas with per capita income below the national average. This will make it possible to ensure that the assumed indicator is achieved, and that support will be directed first to those who, due to living in places where it is difficult to access private care or NHF providers (i.e., places far from large agglomerations or in areas that do not provide an efficient market for health services), receive appropriate support. Such an approach will also make it possible to analyze the impact of telemedicine solutions on increasing access to services, the possibility of equalizing social security levels in the area of health, and therefore on the perceived level of life independence. At the same time, guaranteeing a certain group of people from such areas will make it possible to verify the technological effectiveness of the model (based on the operation of the wireless Internet) in areas remote from the centers of activity in the region, and thus test the effectiveness of the entire model as a mechanism for improving the prognosis and preventing the appearance of acute phases of the disease and/or mechanisms to respond more quickly in such a situation. The analysis of project costs relative to the therapeutic outcomes achieved will be a measure of the achievement of the assumed optimization of services, which, in view of the anticipated increase in the number of patients, requires significant pro-efficiency and cost-containment changes, through better scheduling of specialist involvement and greater involvement of PHC and nursing care.

PILOT OBJECTIVES

The main (primary) goal is to test the project so that its results could be implemented on a large scale (e.g., nationwide) in monitoring COPD disease progression and predicting disease exacerbation through continuous monitoring of health and performance parameters through a self-administered spirometry test.

Given the sometimes-limited perception and ability to use information and communication technologies (ICT) among the recipients, it will be permissible to support a guardian (son/daughter/wife/husband, etc.) in the use and during training (on the use of the platform and educational), with the informed consent of the study participant (In the Declaration of Participation). In order to minimize the risk of "technical exclusion", there will be the possibility of renting a tablet with Internet access (for about 50 people, in case of greater needs-additional purchases), so that the spirometry and saturation tests performed regularly (which the patient will learn about at the hospital or clinic) will go straight to the platform automatically, and provide interpretation to the patient himself (in order to max reduce the risk of COPD exacerbation between visits). From there, the platform will include materials to help the patient assess his or her health, understand individual test results and project milestones, and encourage healthy lifestyles (which will increase the patient's involvement in treatment, improving the prognosis itself), and in his or her personal account he or she will also find medical recommendations, or dedicated education and test results.

PILOT MODEL

The project will have a pilot character and is aimed at clinical verification through the introduction (implementation) of a new method and accompanying organizational and technological solutions (platform, devices, spirometers) in an area where current models and schemes of therapeutic and diagnostic support were insufficient. This will also reduce the risk of failure of hypothetical nationwide solutions and obtain user feedback.

Recruitment of patients will take place both at the hospital, ASC and PHC partners, through Local Government Units (LGU; City of Wroclaw, Walbrzych County and City of Walbrzych-representing individuals from excluded areas) among a group of individuals diagnosed with COPD. The planned population is 500 patients (hence screening of 1500 people was planned to include those not interested in the project) from the Lower Silesia province (hence the choice of Leader-Hospital serving patients from the entire province, which will facilitate recruitment) who meet the inclusion criteria: (1) age ≥ 18 years; (2) obtaining a signed informed consent to participate (along with other documents); (3) diagnosis of COPD; (4) belonging to one of two groups: residents of areas with an average income above the national average (max 90% of patients) or areas with an average income below the national average for the municipality (min 10% of patients).

In support of face-to-face recruitment, meetings will be held (1 every 3 months) for interested patients to explain the scope of support. Meetings will also be held with centers caring for patients (1 every 4 months for each center separately) to mobilize them to recruit, prepare them to provide services, sustain the quality of care once patients are admitted, analyze and respond to the problems identified (including patients' expectations and perceptions-better considering their needs).

Recruitment scenarios:

- during hospitalization or ASC visit (in case of diagnosed COPD or de novo diagnosis), the attending physician will suggest the patient to participate or;
- the PHC, knowing the patient with COPD will make a telephone contact or provide information at the visit, also after the patient self-reports as a result of an information campaign or action by partners, e.g., the LGU.

Each of the scenarios requires:

- to provide information on the pilot, benefits and risks, collect relevant consents/documents;
- brief training on how to use the platform (based on a developed scheme verified among a group of people 65+);
- guidance on how to use the tutorial and where to seek technical assistance;
- supervision of the patient during the first spirometry and saturation tests;

- obtaining information about the patient's needs (according to a developed questionnaire) and incorporating them into the care plan (e.g., personal and professional issues). The above approach is a challenge on the scale of the described application. It is certainly not an easy task, but putting the patient at the center of the entire process is one of the main objectives of the entire project;
- information to the patient about his current health status, prospects and treatment plans.

Recruitment visit ("0" – is held according to the above scenarios with a pulmonologist or PHC and then with a specialist). In the course of it: after a month ± 5 days, visit 1 at the PHC will take place (teleconsultation with assessment of vital parameters with a note of the visit and recommendations for the patient on the platform). If there are worrisome symptoms, the patient will be referred for an expedited pulmonology consultation or to the hospital. To make it possible to achieve the objectives (cooperation of specialists and focus on the patient), on the platform provided:

- a consistent pattern of care will be maintained (control of benefits and possible change of plans by the pulmonologist as the attending physician);
- the patient will have access to recommendations through his/her account on the platform;
- there will be created and defined roles: patient, nurse, PHC physician, pulmonologist (both outpatient and inpatient) with assigned responsibilities (reflected in staff contract records), mapped processes and procedures. Each person will have specific tasks and capabilities within the platform for the treatment process.

The role of the pulmonologist at the hospital and or ASC is to stabilize the patient's condition and set the course for the treatment and diagnostic process (continued at the ASC and PHC). Contact with the ASC in two ways: through teleconsultation and in-person visit (spirometry and saturation measurements taken on-site and mobile, will be transmitted to the platform). In the event of alerts from the system or self-monitoring, the pulmonologist will initiate contact and change recommendations (e.g., intensify pharmacotherapy, report for an in-person visit or hospitalization). At the doctor's designated interval, the patient will come in for in-person visits for patient examination and reassessment), from which (like remote services) notes will be posted in the system (indicating the patient's current condition, short-term recommendations, plans and indications for respiratory rehabilitation, for example). Recommendations will be available to the patient and the PHC, which will monitor their implementation on a daily basis. A message will be sent to the PHC physician with a summary of treatment and diagnostic and therapeutic plans.

For patients with a diagnosis in the ASC (without hospitalization), the starting point will be the first visit to a pulmonologist in the ASC. The remaining stages of care will be the same. The pulmonologist will furthermore: (1) will develop the patient's management plan and intervals, as well as ranges of follow-up tests; (2) will consult with patients referred by the PHC and consult with the PHC about changing drug doses, test results or ranges of therapy; (3) will decide on the form of consultation g (teleconsultation or in-person consultation).

PHC physician will follow up on pulmonologist's recommendations after hospital discharge/ ASC visit, monitor and take care of patient's health (periodic teleconsultations, analysis of spirometry results) change/add dosage/new medications, support patient's prescriptions, refer for expedited visit or hospitalization-with a maximum of 48h to determine such necessity, coordinate holistic treatment with other specialists (e.g. cardiologists, oncologists, gastrointestinal specialists, etc. posting information about other parallel treatment processes, also on the platform). After participation, the PHC doctor will continue care in cooperation with the AOS/hospital (based on the therapy plan).

The nursing consultation will take place 2 months after the start of the pilot (through a telephone interview on a prepared form) and will allow the:

- assess whether the patient requires urgent contact at AOS/hospital (e.g., whether he/she is taking medication, what symptoms he/she has);
- provide health education (tailored to concomitant diseases), including an entry on the platform regarding the subject of the consultation/education and any conclusions (e.g., regarding an expedited visit to AOS/hospital);
- remind you of the ways to solve technical problems (by the IT department).

Finally, teleconsultation at PHC doctor (visit 3) after 3 months from the start of the pilot (with assessment of reported parameters and patient's health status, providing recommendations for further management, assessment of the impact of the proj. on QOL, prognosis, frequency. of unplanned hospitalizations etc.-according to the questionnaire, assessment of satisfaction with participation in the project).

SUMMARY STAGE

The care proposal implemented in the project is based on cooperation between PHC units, specialty offices and hospitals. Currently, these relationships also exist, but they are much looser and less organized. Practice shows that patients are simply redirected between different levels of care. When implementing a telemedicine solution, there will be a need to establish defined relationships on which cooperation will be based. In particular, the project will resolve issues of motivation for this type of cooperation, as both PHC units and specialist offices are overburdened and do not want to commit to more tasks. Taking this into account, the project will propose solutions for incentive mechanisms to encourage this cooperation (training, seminars, constant exchange of experience between PHCs and ASCs and the hospital).

Finally, the effectiveness of such tools to overcome the

aforementioned limitations will be examined and applied in the project:

- an extensive information and promotion campaign signed by the MZ and/or NHF, which will target health care units;
- conscientious pricing of benefits;
- incentives for the use of new technologies by seniors, so that all individuals want to use new solutions, along with a mechanism for overcoming identified problems;
- an extensive information and promotion campaign signed by the Ministries of Health (MH) and/or NHF to target potential patients;
- an extensive information and promotion campaign signed by the MH and/or NHF, which will be carried out in PHCs, so that the information conveyed gains credibility.

CONCLUSIONS

Implementation of telemedicine solutions creates an opportunity for patients diagnosed with COPD and their families by improving access to specialized medical care. With early detection of COPD exacerbation symptoms (deterioration of remotely monitored spirometric parameters), it will be possible to introduce appropriate preventive measures for these patients offsetting the adverse consequences. Importantly, early detection of an impending COPD exacerbation results in gaining time to organize contact with the doctor and implement more planned management needed for the patient. Ultimately, a study will be conducted on the feasibility of this solution on a large, nationwide scale, subject to the positive results of previous studies. Assistance will be requested from the Norwegian partner in the established cooperation. The Norwegian partner will be asked to look at the topic from a different perspective and identify potential strengths and weaknesses of the implemented project based on their own experience. Then, based on the developed results, it will propose a scheme for implementing the pilot model solution on a large scale. If necessary, the project may need to be analyzed for possible changes depending on the progress of the project and considering the possibility of changes specified by the regulations of the Norwegian Financial Mechanism 2014-2021. The project in the scopes presented will be implemented in accordance with the Guidelines in the area of social inclusion, the Guidelines in the area of health, the European guidelines for the transition from institutional care to care provided at the level of local communities.

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CONFLICT OF INTEREST

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