УДК 616.33-089:616.71-007.234]-06-055.1-008.9



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Characteristics of Clinical Parameters and Hormonal and Metabolic Homeostasis in Men with Postgastric Resection Disease and Comorbid Osteoporosis

Introduction. Despite the optimistic predictions of gastroenterologists, the number of patients with peptic ulcer disease (PUD) continues to grow steadily. Despite the significant success of conservative treatment, gastric resection (GR) having a 150 years of history currently remains the surgery of choice for patients with complicated PUD. Since under the existing socio-economic conditions, more than 80.0 % of patients with PUC cannot afford proper dietary therapy, adequate medical and sanatorium treatment, the tendency towards a decrease in the number of such surgical interventions may change its vector towards growth. In five or more years after gastric surgery, 78.3 % of patients develop postgastric resection disease (PGRD), which is manifested by numerous clinical syndromes, including hormonal and metabolic, pancreatic-hepatobiliary, intestinal, immunological, etc., and, among the others, certain bone disorders (BD), including secondary osteoporosis (OP) [1].

Although in Ukraine as well as in the rest of the world OP reached a pandemic scale [3, 6, 7], most of the recent research in OP is dedicated to the investigations of OP syndrome in postmenopausal women [4], while studies of same problem in men is far from sufficient. In particular, published materials are related only to studies of some aspects of the assessment of the condition of bone tissues (BT) after surgery and are reduced to the statement of the fact that GR is recognized as one of the causes of secondary OP [2, 5]. No data concerns clinical indices, hormonal and metabolic homeostasis of bone tissue in male organism post GR due to complicated PUD and of long-term PGRD development them, though clarification of these aspects of the problem can be the basis for improving the diagnosis and pathogenetic treatment of BT mineral density disorders in this category of patients.

The aim of the study. To characterize clinical parameters, hormonal and metabolic homeostasis in men with postgastric resection disease and comorbid osteoporosis.

Materials and methods. The study began with obtaining written consent for the examination based on the principles of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, relevant laws of Ukraine and international acts. A total of 190 men with PGRD were examined with preliminary random stratification by the presence of a history of five or more years of GR resulting with complicated PUD (Order of the Ministry of Health of Ukraine N 1514 of 25.08 2023 "On Approval of the Unified Clinical Protocol of Primary and Specialized Medical Care in Peptic Ulcer of the Stomach and Duodenum in Adults and Children"), of whom 123 were diagnosed with PGRD I-st degree of severity, and 67 - with PGRD II-nd degree of severity [1]. Most of them at the time of the study were middleaged (65.8 %), somewhat less - elderly (23.7 %), and least of all - of mature age (10.5 %).

As a result of a comprehensive examination by "Guideline 00419. Osteoporosis" of the Ministry of Health of Ukraine dated 22.09.2017, OP was diagnosed in 164 men - they represented the study group (SG). The control group (CG) consisted of 31 practically healthy men of similar age.

The hormonal homeostasis was studied according to the effect of hormones on protein metabolism: anabolic (growth hormone (GH), parathormone (PH), gastrin (G) and testosterone (TS)) and catabolic (triiodothyronine (T_3), thyroxine (T_4), glucagon (GG) and cortisol (CS)) hormones, as well as cyclic nucleotides. The examinations were conducted in the radioisotope laboratory of the Lviv Regional Clinical Hospital.

Determination of GH in blood serum was performed using a commercial test kit GH by IRMA (Italy); determination of PH - using a commercial test kit RIA KIT-parathyroid hormone by International-CIS (France); G - by Sea-ire-Sorin (France). The TS content in the blood was determined using a commercial test kit RIA Testosterone Kit; T₃ TT₃ content by Lia Kit; T₄ - TT₄ Lia Kit, all from Immunotech

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(Czech Republic). GG was determined using a commercial test kit CNR-70-ki "Biodata" (Italy), and CS was studied with a kit using iodine¹²⁵ labeled CS and a precipitating reagent, Steron-K-¹²⁵J and M, according to the provided instructions. The basal concentration of cyclic nucleotides in the blood: cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) was determined using commercial test kits, respectively, Cyclic AMP (125j) RIA KIT and Cyclic GMP (125j) RIA KIT by Immunotech (Czech Republic), according to the provided instructions. The electrolyte balance (total and ionized calcium (Ca²⁺), magnesium, phosphorus) was also studied using the E-Lyte Plus blood electrolyte and gas analyzer and the main parameters of the proteinogram by serum protein electrophoresis.

The results were statistically analyzed using standard Excel computer programs for a personal computer. The significance of the difference between the two parameters was assessed by the Student's t-test. The difference was considered significant at p < 0.05.

Results and discussion. It was revealed that out of 190 men who had undergone GR five or more years ago

and had PGRD, generalized OP was diagnosed in 164 (86.3 %; p < 0.001 compared to the CG). Among them, 127 (77.4 %; p < 0.01 compared to the CG) had clinical signs of calcium metabolism disorders. Almost half of the SG (80 patients who underwent surgery - 48.8 %, p < 0.001 compared to CG) had muscle cramps; every fourth one (41 men - 25.0 %, p < 0.01) noted rapid tooth decay; 96 patients (58.5, p < 0.01) complained of bone pain; 22 (13.4 %, p < 0.01) exhibited constant general weakness, 17 (10.4 %, p < 0.01) demonstrated severe paresthesias; 10 patients (6.1 %, p < 0.05) had a single low-traumatic bone fracture, and 4 (2.4 %, p < 0.05) exhibited multiple low-traumatic bone fractures. Only 37 (22.6 %) of patients who underwent surgical treatment of PUD had no clinical manifestations of calcium metabolism disorders.

Radioimmunoassay of the concentration of anabolic (tabl. 1) and catabolic (tabl. 2) hormones in the blood showed that in most patients who underwent the surgery the serum levels had significant deviations from control indexes.

Table 1

Anabolic hormones content in serum (n; %; M \pm m; p)

	CG, n = 31	SG, n = 164						
Name of hormones		Increased		Normal		Decreased		
		n (%)	$M\pm m$	n (%)	$M\pm m$	n (%)	$M\pm m$	
Growth hormone, ng/mL	1.12 ± 0.14	44 (26.8)	3.11 ± 0.31***	1 (0.6)	1.09 ± 0.00	119 (72.6)	0.18 ± 0.02**	
Parathormone, pg/mL	52.80 ± 4.65	84 (51.2)	147.08 ± 19.74***	0 (0.0)	0.00 ± 0.00	80 (48.8)	14.18 ± 1.47***	
Gastrin, pg/mL	58.67 ± 12.80	17 (10.4)	117.87 ± 1.77**	26 (15.9)	56.72 ± 1.12	121 (73.8)	22.76 ± 1.16*	
Testosterone, ng/mL	3.43 ± 0.58	113 (68.9)	21.07 ± 3.04***	1 (0.6)	3.40 ± 0.00	50 (30.5)	1.60 ± 0.11 *	

Notes: * - p < 0.05 between SG and CG; ** - p < 0.01 between SG and CG; *** - p < 0.001 between SG and CG.

The obtained results demonstrate, that 119 (72.6 %) patients of SG had a significant decrease in GH level (0.18 \pm 0.02 ng/ml, p < 0.001) compared to the same index in the CG, while 44 (26.8 %) patients who underwent surgical treatment demonstrated this hormon increased secretion (3.11 \pm 0.31 ng/ml, p < 0.001), and only one OP patient who underwent surgery (0.6 %) exposed GH level without deviation from that of the CG (1.09 \pm 0.00 ng/ml; p > 0.05).

84 (51.2 %) patients who underwent surgery had a significantly elevated PH level (147.08 \pm 19.74 pg/mL, p < 0.001), while the rest (80, 48.8 %) patients with OP had hypoparathyroidism (14.18 \pm 1.47 pg/mL; p < 0.001). In the SG were no patients who underwent surgical treatment with a PH index corresponding to the same of CG.

The G index in 121 patients who underwent the surgery and had OP in the SG (73.8 %) was significantly decreased (22.76 \pm 1.16 pg/ml; p < 0.05), in 26 patients who un-

derwent the surgery of the SG (15.9 %) its values did not differ significantly from the values of the CG, and only 17 patients who underwent the surgery and had OP in the SG (10.4 %) were diagnosed with hypergastrinemia (117.87 \pm 1.77 pg/ml; p < 0.01).

In the SG, 113 (68.9 %) men had hypertestosteronemia $(21.07 \pm 3.04 \text{ ng/mL}; p < 0.001)$, 50 patients who underwent the surgery (30.5 %) had hypoestosteronemia $(1.60 \pm 0.11 \text{ ng/mL}; p < 0.01)$, and only one patient who underwent the surgery (0.6 %) had TS levels that did not differ from those of the CG.

In the SG, OP prevailed both in conditions of increased and decreased T₃ levels: 73 (44.5 %) had hypersecretion (2.45 \pm 0.16 nmol/mL; p < 0.05), the same number was diagnosed with hypothyroidism (0.96 \pm 0.12 nmol/mL; p < 0.05), and only 11.0 % of men had T3 levels that did not differ significantly from those of CG (1.60 \pm 0.07 nmol/mL; p > 0.05).

Table 2

The content of catabolic hormones and cyclic nucleotides in the serum (n; %; M \pm m; p)

Name of hormones	CG, n = 31	SG, n = 164						
		Increased		Normal		Decreased		
		n (%)	$M \pm m$	n (%)	$M \pm m$	n (%)	$M \pm m$	
Triiodothyronine, nmole/L	1.67 ± 0.25	73 (44.5)	2.45 ± 0.16*	18 (11.0)	1.60 ± 0.07	73 (44.5)	0.96 ±0.12*	
Thyroxine, nmole/L	87.80 ± 13.86	92 (56.1)	128.75 ± 6.10*	40 (24.4)	86.00 ± 5.79	32 (19.5)	53.72 ±3.36*	
Glucagon, pr/mL	122.70 ± 6.81	27 (16.5)	186.37 ± 11.43***	(0.0)	0.00 ± 0.00	(83.5)	56.93 ± 3.23***	
Cortisol, nmole/L	490.70 ± 32.30	116 (70.7)	898,00 ± 58.59***	(0.0)	0.00 ± 0.00	48 (29.3)	410.54 ± 22.87°	
cAMP, nmole/L	12.06 ± 0.31	0 (0.0)	0.00 ± 0.00	(0.0)	0.00 ± 0.00	164 (100)	2.02 ± 0.37***	
cGMP, nmole/L	5.2 ± 0.04	(0.0)	0.00 ± 0.00	(4.9)	4.9 ± 0.07	156 (95.1)	1.58 ± 0.20***	

Notes: * - p < 0.05 between SG and CG; *** - p < 0.001 between SG and CG; • - p < 0.05 between SG and CG.

In the SG, OP prevailed both in conditions of increased and decreased T $_3$ levels: 73 (44.5 %) had hypersecretion (2.45 \pm 0.16 nmol/mL; p < 0.05), the same number was diagnosed with hypothyroidism (0.96 \pm 0.12 nmol/mL; p < 0.05), and only 11.0 % of men had T3 levels that did not differ significantly from those of CG (1.60 \pm 0.07 nmol/mL; p > 0.05).

The T₄ level among men in the SG was increased $(128.75 \pm 6.10 \text{ nmol/L}; p < 0.05)$ in 92 patients (56.1 %), hypothyroxinemia was observed in 32 (19.5 %) $(53.72 \pm 3.36 \text{ nmol/L}; p < 0.05)$, and in 40 men (24.4 %) it did not differ significantly from the CG.

In the SG, 137 patients who underwent the surgery (83.5 %) had hypoglucagonemia (56.93 \pm 3.23 pg/ml; p<0.001), 27 patients who underwent the surgery (16.5 %) had an elevated GG (186.37 \pm 11.43 pg/ml; p<0.001), and there was no patient who underwent the surgery with indicators similar to the CG (122.70 \pm 6.81 pg/ml; p>0.05).

Hypercortisolemia ($898.00 \pm 58.59 \text{ nmol/l}$; p < 0.001) prevailed among the patients who underwent the surgery and had OP, which was detected in 116 men (70.7 %), in 48 (29.3 %) patients who underwent the surgery, the index of CS was slightly reduced, but did not statistically significantly differ from the indexes in the CG ($410.54 \pm 22.87 \text{ nmol/l}$; $p > 0.05 (490.70 \pm 32.30 \text{ nmol/l})$.

Thus, in patients who underwent the surgery and had OP, there was a significant decrease in all studied anabolic hormones, except TS, and an increase in all studied catabolic hormones, except GG.

The study of cyclic nucleotides in the blood revealed that their concentration was significantly reduced: cAMP $(2.02 \pm 0.37 \text{ nmol/L}; p < 0.001)$ - in all subjects with OP (100.0 %), and cGMP $(1.58 \pm 0.20 \text{ nmol/L}; p < 0.001)$ - in 95.1 %.

The results of the study of metabolic homeostasis are shown in tabl. 3.

Table 3

Indicators of metabolic homeostasis (n; %; M ± m; p)

Name of hormones	CG, n = 31	SG, n = 164						
		Increased		Normal		Reduced		
		n (%)	$M\pm m$	n (%)	$M\pm m$	n (%)	$M\pm m$	
Plasma electrolytes								
Total calcium, mmol/L	2.32 ± 0.20	7 (4.3)	2.90 ± 0.36	111 (67.7)	2.30 ± 0.09	46 (28.0)	1.91 ± 0.02*	
Ca ²⁺ , mmol/L	1.09 ± 0.01	0 (0.0)	0.00	0 (0.0)	0.00	164(100%)	$0.900 \pm 0.008***$	
Maglesium, mmol/L	1.20 ± 0.50	0 (0.0)	0.00	85 (51.8)	1.11 ± 0.09	79 (48.2)	$0.03 \pm 0.1*$	
Phosphorus, mmol/L	1.18 ± 0.38	0 (0.0)	0.00	21 (12.8)	1.12 ± 0.31	143 (87.2)	$0.58 \pm 0.09*$	
Protein metabolism								
Total protein, g/L	75.0 ± 10.0	16 (9.8)	88.01 ± 0.96	142 (86.6)	73.84 ± 0.39	6 (3.7)	62.40 ± 0.54	
Albumins, %	61.0 ± 5.1	1 (0.6)	69.1 ± 0.0	31 (18.8)	59.2 ± 0.4	132 0.5)	50.2 ± 0.5***	
α ₁ -globulins, %	4.8 ± 1.29	115 (70.1)	$7.5 \pm 0.1*$	47 (28.7)	5.30 ± 0.10	2 (1.22)	2.93 ± 0.37	
α ₂ - globulins, %	8.89 ± 1.99	55 (33.5)	12.5 ± 0.4**	107 (65.2)	9.35 ± 0.11	2 (1.2)	6.65 ± 0.15	
β-globulins, %	9.89 ± 2.50	89 (54.3)	14.0 ± 0.1*	74 (45.1)	11.17 ± 0.12	1 (0.6)	7.10 ± 0.00	
γ-globulins, %	15.60 ± 3.40	58 (35.4)	21.6 ± 0.5*	103 (62.8)	16.56 ± 0.17	3 (1.8)	11.26 ± 0.39	

Notes: * - p < 0.05 between SG and CG; ** - p < 0.01 between SG and CG; *** - p < 0.001 between SG and CG.

Studying the indicators of electrolyte balance, shown in tabl. 3, it was found that in men with PGRD and comorbid OP, who underwent the surgery, there is a pronounced dyselectrolytemia manifested by a significant decrease in ionized calcium (0.900 \pm 0.008 mmol/L p < 0.001) in 100.0 % of patients who underwent the surgery, 87.2 % of patients of SG had a steady decrease in phosphorus concentration $(0.58 \pm 0.09 \text{ mmol/L}; p < 0.05)$, and 48.2 % of patients who underwent the surgery had a significant decrease in magnesium (0.3 \pm 0.1 mmol/L; p < 0.05). However, the study of total calcium in the blood of men in the SG with OP showed that in 72.0 % it did not differ significantly from the CG, and only in 28.0 % of the patients who underwent the surgery and had OP it was significantly reduced (1.91 \pm 0.02 mmol/L; p < 0.05).

The analysis of protein metabolism parameters shown in tabl. 3 revealed that in 86.6 % of the patients who underwent the surgery, the blood content of total protein did not differ significantly from that of the CG. At the same time, attention was drawn to the pronounced dysproteinemia manifested in 80.5% in hypoalbuminemia (50.2 \pm 0.5 %; p < 0.001), in 70.1 % - hyper- α_1 -globulinemia (7.5 \pm 0.1 %; p < 0.05), in 54.3 % hyper- β -globulinemia (14.0 \pm 0.1 %; p < 0.05), less often (35.4 %) - hyper- γ -globulinemia (21.6 \pm 0.5 %; p < 0.05) and hyper- α_2 -globulinemia (12.5 \pm 0.4%; p < 0.01) were detected in 33.5 %. Also, in all (100.0 %) men of the SG,

a significant decrease in blood glycoproteins (14.15 \pm 0.06 units; p < 0.001) was detected.

The detected deviations in clinical parameters and hormonal and metabolic homeostasis in men with PGRD and comorbid OP were significantly different from those in healthy individuals. In our opinion, this indicates the undoubted importance of the abnormalities in the pathogenesis of secondary OP in this category of patients and will be the basis for optimizing their treatment and prevention measures.

Conclusions. Clinical parameters, hormonal and metabolic homeostasis indices in men with postgastric resection disease and comorbid osteoporosis have significant deviations manifested by: signs of calcium metabolism disorders with a predominance of bone pain and muscle stiffness; dyshormonemia: a significant decrease in the levels of all studied anabolic hormones, except testosterone, accompanied with an increase in the levels of all studied catabolic hormones, except glucagon, and a decrease in the concentration of cyclic nucleotides; dyselectrolytemia: persistent hypophosphatemia, hypomagnesemia, significant decrease in ionized calcium, while the total calcium level was normal or decreased in the majority of patients; dysproteinemia: hypoalbuminemia, hyper-α,-globulinemia, hyper-β-globulinemia, and rarely hyper-γ-globulinemia, hyper-α,-globulinemia and hyper-β-lipoproteinemia, sharply reduced glycoprotein levels, total protein being normal in most patients.

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The article was submitted to the editorial board on March 19, 2024.

Conflict of interest

The authors declare no conflicts of interest.

Characteristics of Clinical Parameters and Hormonal and Metabolic Homeostasis in Men with Postgastric Resection Disease and Comorbid Osteoporosis

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Introduction. The problem of osteoporosis (OP) has become an epidemic unprecedented in its scale. Numerous studies of various aspects of OP leave out men with a history of gastric resection (GR) as a result of complicated peptic ulcer disease (PUD). Therefore, a detailed characteristics of clinical parameters and hormonal and metabolic

homeostasis in men with postgastric resection disease (PGRD) and comorbid OP will allow the improvement of the treatment and prevention of osteodeficiency conditions in this category of patients.

The aim of the study. To characterize clinical parameters and hormonal and metabolic homeostasis in men with postgastric resection disease and comorbid osteoporosis.

Materials and methods. 164 men with PGRD and comorbid OP were examined with preliminary random stratification by the presence of a history of five or more years of GR surgery as a result of complicated PUD. In addition to routine examinations, hormonal homeostasis was studied by the effect of hormones on protein metabolism: anabolic (growth hormone, parathyroid hormone, gastrin, and testosterone) and catabolic (triiodothyronine, thyroxine, glucagon, and cortisol) hormones and cyclic nucleotides. Plasma electrolytes and protein profile were also analyzed.

Results. It was established that the vast majority of patients who underwent the surgery with PGRD and comorbid OP have clinical signs of calcium metabolism disorders. They had significant abnormalities in hormonal and metabolic homeostasis manifested by dyshormonemia, dyselectrolytemia and dysproteinemia. We believe that these scientific facts will help to improve the treatment and prevention of secondary osteoporosis complications in this category of patients.

Conclusions. Among the clinical parameters in men with PGRD and comorbid OP, bone pain and muscle cramps prevailed. Hormonal homeostasis was characterized by dyshormonemia with a significant decrease in almost all studied anabolic hormones and an increase in almost all studied catabolic hormones. Deviations in metabolic homeostasis were manifested by dyselectrolytemia (hypophosphatemia, hypomagnesemia, decreased ionized calcium) and dysproteinemia (hypoalbuminemia, hyper- α_1 -globulinemia, hyper- β_2 -globulinemia, sharply reduced glycoproteins).

Keywords: osteoporosis, postgastric resection disease, peptic ulcer disease, hormonal and metabolic homeostasis.

Характеристика клінічних показників і гормонально-метаболічного гомеостазу у чоловіків із постгастрорезекційною хворобою та коморбідним остеопорозом

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Вступ. Остеопороз (ОП) в Україні та світі набув характеру непередбачуваної за масштабами епідемії, що вимагає створення адекватних профілактично-лікувальних заходів. Зв'язок між ураженнями органів травлення й опорно-рухового апарату є загальновідомим. Проте численні дослідження різних аспектів ОП залишають поза увагою чоловіків, які мають у анамнезі резекцію шлунка (РШ) через ускладнену виразкову хворобу (ВХ), зокрема, вивчення гормонально-метаболічного гомеостазу. Тому докладна характеристика клінічних показників і гормонально-метаболічного гомеостазу у чоловіків із постгастрорезекційною хворобою (ПГРХ) та коморбідним ОП, на нашу думку, стане основою для патогенетичного лікування й уможливить удосконалити лікувально-профілактичний комплекс остеодефіцитних станів.

Мета. Охарактеризувати клінічні показники та гормонально-метаболічний гомеостаз у чоловіків із постгастрорезекційною хворобою і коморбідним остеопорозом.

Матеріяли й методи. У рандомізований спосіб із попередньою стратифікацією за наявністю в анамнезі п'ять років і більше після РШ через ускладнення ВХ обстежено 164 чоловіків із ПГРХ та коморбідним ОП. Виконали рутинні обстеження, а також вивчили гормональний гомеостаз відповідно до впливу гормонів на білковий обмін: анаболічні (гормон росту, паратгормон, гастрин, тестостерон) і катаболічні (трийодтиронін, тироксин, глюкагон, кортизол) гормони й циклічні нуклеотиди. Здійснили аналіз електролітів плазми крови та показників протеїнограми.

Результати. У більшости оперованих чоловіків у віддалені терміни після РШ через ускладнення ВХ є клінічні ознаки порушення кальцієвого обміну. Суттєві відхилення в гормонально-метаболічному гомеостазі виявлялися дисгормонемією, диселектролітемією і диспротеїнемією. На нашу думку, такі наукові факти допоможуть удосконалити лікування і профілактику ускладнень вторинного остеопорозу у цієї категорії хворих.

Висновки. Клінічні показники у чоловіків із ПГРХ та коморбідним ОП мають суттєві відхилення, які виявляються ознаками порушення кальцієвого обміну з домінуванням болю у кістках і судом м'язів. Для гормонального гомеостазу характерна дисгормонемія, яка виявлялася достовірним зниженням показників майже всіх досліджених гормонів анаболічної дії та підвищенням показників майже всіх досліджених катаболічних гормонів. Відхилення у метаболічному гомеостазі виявлялися диселектролітемією (гіпофосфа-

темія, гіпомагніємія, істотне зниження показника йонізованого кальцію) та диспротеїнемією (гіпоальбумінемія, гіпер- α_1 -глобулінемія, гіпер- β -глобулінемія, гіпер- α_2 -глобулінемія та гіпер- β -ліпопротеїдемія, різко знижений показник глікопротеїдів).

Ключові слова: остеопороз, постгастрорезекційна хвороба, виразкова хвороба, гормонально-метаболічний гомеостаз.

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