BIOCHEMICAL MANIFESTATIONS OF STRESS REACTIONS IN THE BLOOD OF DENTAL PATIENTS WITH VARIOUS INDIVIDUAL AND PSYCHOLOGICAL CHARACTERISTICS DURING PLANNED SURGICAL INTERVENTIONS IN A MAXILLOFACIAL HOSPITAL

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Abstract

Introduction. Surgical interventions are accompanied by acute stress reactions, which are staged and cause functional changes, primarily in the nervous, cardiovascular, endocrine systems. The study of biochemical stress markers in blood provides valuable information about the state of patient's state under conditions of surgical aggression. **Aim:** To investigate the biochemical manifestations of stress reactions in blood of dental patients with different individual psychological characteristics during planned surgical treatments in the maxillofacial department. **Materials and methods.** The level of neuroticism was determined in 64 patients at the Department of Maxillofacial Surgery of Lviv Regional Clinical Hospital, by testing according to the well-known Eysenck method. The level of reactive anxiety and depressive manifestations in patients was determined using the Hospital Anxiety and Depression Scale (HADS). Before the surgery (before premedication) and five hours after its completion, the content of cortisol, prolactin and interleukin-1β was examined in the peripheral venous blood of the patients. **Results and discussion.** Before premedication, the highest levels of cortisol and prolactin in the peripheral venous blood of patients with high neuroticism and anxiety, which could not be eliminated by antistress therapy in the stage of preoperative preparation, were found. In the pre-surgery period, all patients, regardless of their level of neuroticism, had a low level of interleukin 1-β in blood - 8.5 ± 3.6 pg/ml ($p = 0.2547$). Despite the satisfactory anaesthetic support of the surgical interventions, all patients had increased cortisol in blood, due to the development of an acute inflammatory reaction induced by surgical trauma. In the postsurgical period, there was also a statistically significant increase of interleukin 1-β in the blood in all patients - up to 19.7 ± 4.6 pg/ml. There is a close relationship ($\chi^2 = 17.89$, $p < 0.01$) between the anxious state of the patients and the increase in the concentration of prolactin in their blood. **Conclusions.** Under conditions of surgical stress in dental patients before analgesia, similar changes occur at biochemical level - the blood cortisol and prolactin levels increase, the intensity of this process being more pronounced in emotionally labile patients (with a high level of neuroticism). There is a close relationship between the psycho-emotional state of patients (their level of anxiety) and the dynamics of prolactin concentration in blood, while the concentration of cortisol in blood is affected by phlogogenic factors caused by surgical trauma.

Keywords: *surgical stress, dental patients, neuroticism, anxiety, cortisol, prolactin premedication.*

1. INTRODUCTION

Surgical interventions are accompanied by acute stress reactions, which are staged and cause functional changes, primarily in the nervous, cardiovascular, respiratory, endocrine and immune systems [1-3]. Among the factors causing them there are: psycho-emotional stress (anxiety, fear), mechanical tissue damage during surgery, postoperative pain syndrome, and others [4-7]. The severity of stressful manifestations depends on the individual psychological characteristics of the patients, adequacy of their pre-surgical preparation, effectiveness of anaesthesia during the intraoperative period, duration and surgery trauma [8,9]. An excessive altering effect of surgical stress leads to tension in body's defence, intensification of metabolic processes, haemodynamic disorders and other adverse changes [4]. Therefore, the diagnosis of acute stress in surgical patients is of great importance.

Laboratory parameters allow an objective assessment of the state of patient's body before, during and after dental surgery. Cortisol traditionally serves as a marker of the severity of

body's stress response [10-13]. High efficiency and diagnostic sensitivity of cortisol levels for assessing the level of psychoemotional stress (fear, reactive anxiety) and stress in dental patients have been confirmed [14-16]. The level of adrenocorticotropic hormone, cortisol, thyroxine, thyroid-stimulating hormone, and prolactin in blood in patients of the maxillofacial hospital are also examined to identify the patterns of surgical stress in the stages of surgical treatment [17,18]. The release of prolactin from the pituitary gland is a very sensitive marker of surgical stress. The stress-induced release of this hormone into the blood is not just a side effect of the adrenergic activation of the central nervous system, but also a factor that reduces homeostatic disorders and is important in behavioural adaptation to adverse environmental conditions [17].

Analysis of scientific professional publications has shown that, over the past decade, original psychological, functional, biochemical methods for diagnosing human stress reactions during surgical and dental interventions have been developed and implemented in clinical practice [19]. Study of biochemical stress markers in blood provides valuable information about patient's state under conditions of surgical aggression.

The aim of the study: To investigate the biochemical manifestations of stress reactions in the blood of dental patients with different individual psychological characteristics during planned surgical treatments in the maxillofacial department.

2. MATERIALS AND METHODS

The level of neuroticism was determined in 64 patients (18– 45 years old) from the Department of Maxillofacial Surgery of Lviv Regional Clinical Hospital, by testing according to the well-known Eysenck method. The level of reactive anxiety and depressive manifestations in patients was determined using the Hospital Anxiety and Depression Scale (HADS), where: 0-7 points - normal, 8-10 points - subclinically expressed symptoms, more than 11 points - clinically expressed symptoms. Before the surgery (before premedication) and five hours after its completion, the content of cortisol, prolactin and interleukin-1β was examined in the peripheral venous blood of the patients. The level of these hormones was calculated by radioimmunoassay using reagent kits from Beckman Coulter (Czech Republic). The level of interleukin-1β was determined by enzyme-linked immunosorbent assay using reagent kits from Elabscience (USA), according to the instructions.

In the stage of preoperative preparation, patients with clinical manifestations of psychological stress, detected by the HADS scale, were prescribed L-tryptophan (contained in the drug Antistress, Ukraine) - for 3 days before the planned surgeries - 220 mg 2 times a day, in the morning and in the evening, and a course of endonasal electrophoresis with Dalargin - 1 mg dissolved in 1.0 ml of 0.9% sodium chloride solution, once a day. Such a physiotherapeutic method of a synthetic analogue of Leu-enkephalin administration allows to overcome the blood-brain barrier and penetrate the central nervous system, where its stress-limiting effect is realised.

All patients were administered intramuscularly Nefopam 20 mg, 1% Dimedrol solution 1.0 ml, 0.5% Sibazon solution (Diazepam 10 mg) 2.0 ml, 0.1% Atropine solution 1.0 ml during premedication.

The surgical treatments were performed under potential local anaesthesia: atypical extraction of impacted mandible third molars (severe complexity according to Pederson's), cystectomy of large odontogenic cysts (diameter over 3.0 cm) in the maxilla and mandible jaws, radical maxillary sinusotomy.

Statistical analysis of the results was performed using Student's t-test with the help of the computer program "Statistica 8". The data was analyzed by means of Pearson's chi–square tests.

Scientific research was performed in compliance with the basic provisions of the "Rules for Ethical Principles for Scientific Medical Research Involving Human Subjects" approved by the Declaration of Helsinki (1964-2013), orders of the Ministry of Health of Ukraine No. 690 of 23.09.2009, No. 944 of 14.12.2009, No. 616 of 03.08.2012.

3. RESULTS AND DISCUSSION

As a result of psychological testing according to Eysenck's method, a high level of neuroticism (16.5 ± 2.4 points) was found in 19 patients, a moderate level of neuroticism - 10.3 ± 1.8 points in 21 people, and a low level of neuroticism (5.9 ± 1.4 points) was diagnosed in 24 patients. Before premedication, the highest levels of cortisol and prolactin in the peripheral venous blood of patients with high neuroticism and anxiety, which could not be eliminated by antistress therapy in the stage of preoperative preparation, were found. In particular, in 12 patients with a high level of neuroticism against the background of psychoemotional stress (9.8 ± 2.1 points on the HADS scale), the concentration of cortisol was 261.4 ± 17.3 nmol/l, prolactin - 8.5 ± 1.4 ng/ml (Table 1). At the same time, in 16 individuals with a low level of neuroticism, who did not have reactive anxiety (6.7 ± 1.5 points on the HADS scale), the content of cortisol and prolactin in blood was statistically and significantly lower - 189.5 ± 16.2 nmol/l (p = 0.0042) and 4.5 ± 0.8 ng/ml (p = 0.0149).

Table 1. Cortisol and prolactin content in the blood of dental patients (state before premedication)

Biochemical stress markers	Patients with low level of neuroticism		Patients with moderate level of neuroticism		Patients with high level of neuroticism	
	Without anxiety manifestations (n = 16)	Anxious (n = 8)	Without anxiety manifestations (n = 11)	Anxious (n = 10)	Without anxiety manifestations (n = 7)	Anxious (n = 12)
Cortisol (nmol/l)	189.5 ± 16.2	234.8 ±15.9 p=0.0516	193.2 ± 14.5 p=0.8654	247.1 ±18.3 p=0.0220	206.4 ±15.1 p=0.4492	261.4 ±17.3 p=0.0042
Prolactin (ng/ml)	4.5 ± 0.8	7.6 ± 1.3 p=0.0478	4.8 ± 0.9 p=0.8040	8.1 ± 1.5 p=0.0387	4.9 ± 1.2 p=0.7827	8.5 ± 1.4 p =0.0149

In the pre-surgery period, all patients, regardless of their level of neuroticism, had a low level of interleukin 1-β in blood - 8.5 ± 3.6 pg/ml (p = 0.2547). Despite the satisfactory anaesthetic support of the surgical interventions, all patients had increased cortisol in blood, due to the development of an acute inflammatory reaction induced by surgical trauma. 34 patients who did not have reactive anxiety before surgery had lower blood cortisol levels after surgery than those with psychoemotional stress before surgery. At the same time, the obtained indicators differed little among low-anxiety patients, regardless of their level of neuroticism: in patients with a low level of neuroticism - 217.4 ± 16.3 nmol/l, in patients with a moderate level of neuroticism - 221.8 ± 15.4 nmol/l (p = 0.8451), in patients with a high level of neuroticism - 230.6 ± 17.2 nmol/l (p = 0.5803). In the postsurgical period, there was also a statistically significant increase of interleukin 1-β in the blood in all patients - up to 19.7 ± 4.6 pg/ml (p = 0.0121).

In individuals with a high level of neuroticism, the blood cortisol content increased to 294.3 ± 15.7 nmol/l (p = 0.1165), in individuals with a moderate level of neuroticism, the concentration of this biochemical marker increased to 278.6 ± 16.3 nmol/l (p = 0.2032), and in individuals with a low level of neuroticism - to 265.9 ± 14.8 nmol/l, p = 0.1669. (Fig. 1)

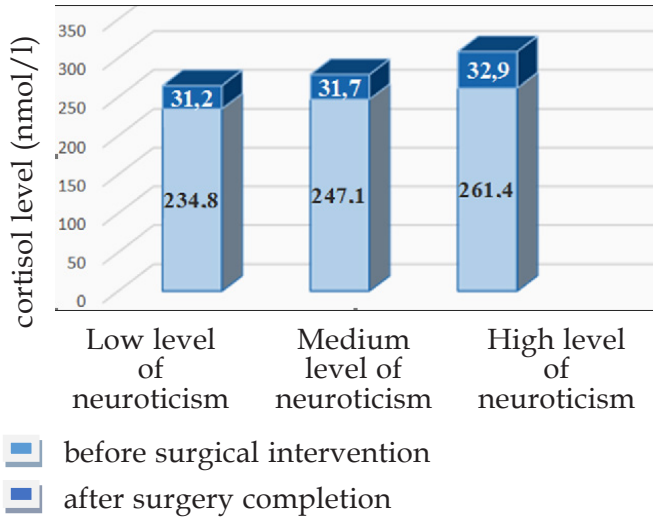

Fig. 1. Dynamics of cortisol content in blood of patients diagnosed with anxiety before surgery

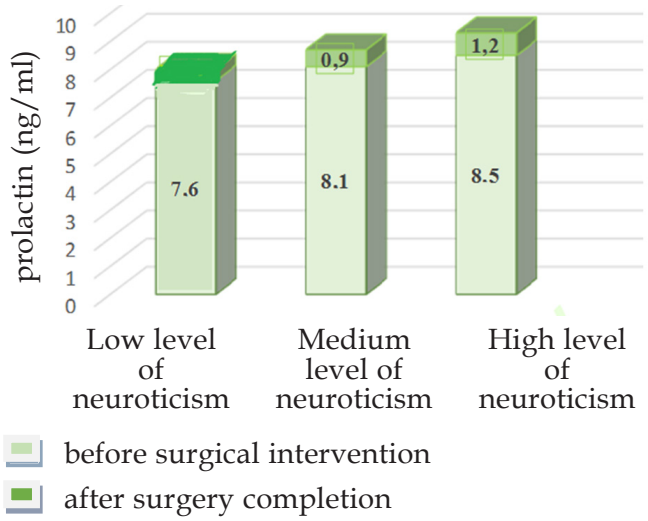

Fig. 2. Dynamics of prolactin content in the blood of patients with reactive anxiety before surgery

In patients having received sedatives, the influence of the psychoemotional factor on the development of acute stress is minimised, but the role of endocrine mechanisms (pituitary-adrenal axis) remains significant in the implementation of adaptive processes in the setting of acute inflammation of the maxillofacial tissues caused by surgical aggression. Interleukin 1-β of the inflammation focus haematogenously affects the hypothalamus, enhances the synthesis of corticoliberin, which in turn increases the production of the adrenocorticotropic hormone [20,21].

The normalisation of the psychoemotional state of anxious patients under premedication affected the content of prolactin in their blood in the postsurgical period. In such patients, a slow (not statistically significant) increase in the level of this hormone was observed. In patients with a high level of neuroticism, this indicator increased from 8.5 ± 1.4 ng/ml to 9.7 ± 1.3 ng/ml (p = 0.5345), in patients with a moderate level of neuroticism - from 8, 1 ± 1.5 ng/ml to 9.0 ± 1.4 ng/ml (p = 0.6624). 5 hours after the end of operations, in 8 patients with a low level of neuroticism, against the background of reduction of clinical manifestations of anxiety, no increase in the blood concentration of this hormone was determined - 7.6 ± 1.8 ng/ml, p = 0.9532 (Fig. 2).

In patients with no preoperative anxiety, the psychoemotional state remained stable, accompanied by no increase in blood prolactin levels. Only in 7 people with a high level of neuroticism, in whom recovery of psycho-emotional discomfort was observed, its concentration slightly increased - up to 6.2 ± 0.8 ng/ml, p = 0.497439. There is a close relationship (χ^2 = 17.89, p < 0.01) between the anxious state of the patients and the increase in the concentration of prolactin in their blood (Table 2).

Table 2. Dynamics of the prolactin content in the blood of patients during the post-surgical period depending on their level of anxiety (state 5 hours after the surgery)

Dynamics of the prolactin content in the blood of patients in the post-surgical period	Patients without clinical manifestations of anxiety (n = 34)	Patients with clinical manifestation of anxiety (n = 30)
An increase of prolactin concentration in the blood	7 cases	22 cases
Absence of prolactin concentration in the blood	27 cases	8 cases
Pearsons congruence criteria χ^2	χ^2 – 17,89 (p < 0,01)	

A number of researchers believe that this hormone can be considered a sensitive marker of psychological stress [22-25]. The results of our biochemical studies are consistent with the literature. It is known that the production of prolactin in the pituitary gland is inhibited by dopamine which, as a neurotransmitter in brain, plays an important role in the realisation of positive emotions, feelings of happiness, satisfaction and euphoria [26]. Under stress, the functional activity of the dopaminergic system decreases [26,27], resulting in prolactin hypersecretion [22,23]. At psychoemotional level, this is manifested by depressive disorders and anxiety [28,29]. Therefore, clinicians' understanding of these stress mechanisms allows them to monitor the development of this pathological process at biochemical level and to carry out adequate drug correction.

4. CONCLUSIONS

Under conditions of surgical stress in dental patients before analgesia, similar changes occur at biochemical level - the blood cortisol and prolactin levels increase, the intensity of this process being more pronounced in emotionally labile patients (with a high level of neuroticism). There is a close relationship between the psycho-emotional state of patients (their level of anxiety) and the dynamics of prolactin concentration in blood, while the concentration of cortisol in blood is affected by the phlogogenic factor caused by surgical trauma.

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