

## CHANGES IN THE THYROID HORMONE STATUS OF THE WOUNDED DEPENDING ON THE VOLUME OF WOUND DAMAGE\*

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The armed aggression of the Russian Federation against Ukraine, which began in February 2022, led to a significant increase in the number of both civilians and combatants who received physical and psychological injuries as a result of hostilities, bombing, rocket or mortar attacks [1-4]. The speed of healing of combat injuries and the actual course of the wound process depend on many factors, one of which is the thyroid hormone status of the wounded [5-7]. It should be noted that during the entire period of the armed conflict in Ukraine, studies of the influence of thyroid hormones on the speed and features of healing combat injuries were not conducted. The data representing research by foreign authors are quite contradictory, which determines the relevance of this re-

search among Ukrainian servicemen who were injured while performing combat missions.

According to the classification, all combat surgical injuries can be divided according to the following characteristics:

- type of ammunition that caused the injury (firearms, explosives);
- type of wound channel (blind, through, tangential);
- relation to the cavity (impermeable, penetrating);
- localization of the lesion (head, neck, chest, abdomen, pelvis, limbs) [8].

To understand this problem, it is important to clearly define some concepts that are important for a comprehensive assessment of the obtained results. Thus, a traumatic disease

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is a clinical concept that establishes the main patterns of cause-and-effect relationships between the nature of the injury and the features of its acute period (traumatic shock), on the one hand, and the features of the clinical course after recovery from shock, on the other hand. The term «traumatic disease» refers only to severe shockogenic, mostly multiple and combined trauma. Traumatic disease is a complex of local and general changes, a chain of pathological processes and adaptive reactions of the body from the moment of injury to its result. Traumatic disease is the life of an organism from the moment of injury to recovery or death. Traumatic shock is considered as the first period of traumatic illness [9, 10].

A separate case of traumatic is wound disease, which is characterized by the presence of an open wound with a violation of the integrity of the skin and adjacent internal organs. The wound process is the body's response to trauma, consisting of successive stages or phases that have their own anatomical, pathohistological, biochemical, and clinical features. Its essence lies in the mobilization of general and local protective reactions aimed at wound healing.

As for the clinical manifestations of gunshot wounds, they largely depend on the caliber and configuration of the projectile that caused the injury [9]. Localization, multiplicity, concomitant damage to vessels, nerves, internal organs and other important anatomical formations, the general condition and hormonal status of the wounded, as well as the stage of the wound process — all this significantly affects the course of the wound disease [11].

## MATERIALS AND METHODS

The set of studies was carried out in accordance with the ethical and moral and legal requirements of the Statute of the Ukrainian Association for Bioethics and Norms GCP (1992), GLP (2002), principles of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine and approved by the Ethics and Bioethics Commission of the Emergency Medical Care Clinic, Military Medical Clinical Center of the Northern District of the Medical Forces Command, Kharkiv, Ukraine. Our study included 30 men who received soft tis-

During the wound process, the following phases (stages) of development are distinguished:

- I — the inflammatory phase, which combines the processes of alteration, exudation, necrosis — cleaning the wound from necrotic tissues;
- II — proliferation phase — formation and maturation of granulation tissue;
- III — healing phase — maturation of scar tissue and epithelization of the wound.

Reparative regeneration is a biological phenomenon, the essence of which is reduced to the restoration of tissues lost as a result of external influences. The basis of reparative regeneration is physiological processes that determine the ability of tissues to recover. Changes in the wound are influenced by two main components. The first of them is the direct impact of the traumatic agent on tissues. The second is the indirect effect of trauma, which is manifested by the effect of tissue damage on the central nervous system, which is reflected in the activity of other organs and systems and, accordingly, negatively affects the development, course and consequences of the wound process [12, 13].

Thus, taking into account all of the above, it is possible to formulate the following statement: the research, the results of which are analyzed in this work, aims to determine **the main** regularities between the volume of wound damage and changes in the levels of thyroid hormones in blood serum at different stages of wound disease that developed as a result of combat trauma.

sue injuries and differed from each other in the size of the lesion, and 10 people of the control group. The wounded were divided into 3 groups of 10 people each, depending on the extent of the injury. The first group — injuries of a light degree (small volume); the second — injury of medium degree (medium volume); the third — injury of a severe degree (large volume) [14].

The age of the wounded is  $34.2 \pm 4.3$  years. The average body weight was  $78 \pm 3.5$  kg. The levels of the following hormones were studied: free T3, free T4 and thyrotropic hormone (TTH).

The concentrations of the studied hormones were determined using enzyme immunoassay kits of KhEMA LLC (Kyiv, Ukraine) in accordance with the manufacturer's instructions. Reference values of hormones: free T3 — 2.6–5.7 pmol/L; free T4 — 9–22 pmol/L; TTH — 0.4–4.0 mU/L.

We used a certain periodization depending on the processes that occur in the body in a certain period after receiving an injury:

- 1–3 days, during this period there is acute stress / acute (shock) period / catabolic phase of the wound process.
- 4–5 days, immunotoxicosis occurs / a period of unstable adaptation / anabolic phase of the wound process.

- 14 days — development of dystrophic and sclerotic processes / period of stable adaptation of wound disease / regeneration and wound healing.

Statistica 10.0 software (StatSoft, Inc., USA) was used for statistical analysis. Descriptive statistics were performed with the calculation of the mean value and its standard error. Sample means were compared using analysis of variance (ANOVA), values of  $p < 0.05$  were considered significant.

## RESULTS AND THEIR DISCUSSION

We observed the main patterns of hormonal changes in thyroid status. Namely, in all examined persons the level of free T3 did not undergo statistically significant changes during the entire period of the study in comparison with its level in the period of 1–3 days and was in the range of 3.4–5.2 pmol/L.

The level of free T4 in subjects with mild and moderate injuries probably did not change throughout the study. The levels of free T4 did not differ in persons with mild and moderate injuries. Free T4 levels in persons with severe injury were significantly ( $p < 0.05$ ) higher at all stages of the study compared to subjects with moderate and mild injury.

The level of TTH in persons with light injuries did not change during the entire period of the study. In case of injuries of medium and severe degree, a probable ( $p < 0.05$ ) increase was recorded in comparison with light injuries in the period of 1–5 days. But on the 14th day of the study, the value of this indicator probably decreased ( $p < 0.05$ ) in both groups to the same level as the group of people who suffered minor injuries.

Thus, it can be concluded that there was a probable increase in TTH levels 1–5 days after the injury in the examined persons with severe and moderate injuries, which was also accompanied by an increase in the level of free T4. The levels of free T3 did not undergo any significant changes.

The issue of changes in the levels of thyroid hormones and their regulator — TTH in

disabling diseases and injuries of various etiologies and topographies is being studied quite actively in the world [15].

Based on the analysis of literature data, it can be concluded that in acute conditions that arise as a result of an external traumatic factor, in the first 5–7 days (sometimes up to 10 days), there is usually an increase in TTH levels. The levels of T4 during this period can both increase and decrease, and the content of T3 in severe systemic disorders usually decreases [16]. The degree of decline in T3 and T4 levels is a marker of the severity of systemic wound or other pathological processes and a negative prognosis for the patient's recovery. An increase in T4 levels is an indicator of a better prognosis and characterizes to some extent the degree of ability to adapt to the existing conditions, the period when a decrease in these parameters is registered can be prolonged — and this prolongation is proportional to the severity of the injury [17]. There are reports of the possibility of a fall and TTH immediately after the occurrence of a serious injury or illness, but such a case is registered in fatal cases in the near future [7].

Thyroid hormones increase tissue demand for oxygen; increase systemic arterial pressure, frequency and strength of heart contractions. Increases mental energy and activity, accelerates the course of mental associations, motor activity, body temperature and level of basic metabolism, blood glucose level, enhances gluconeogenesis in the liver, inhibits glycogen syn-

thesis in the liver and skeletal muscles. They also intensify the capture and utilization of glucose by cells, increasing the activity of key enzymes of glycolysis. Thyroid hormones increase lipolysis [18, 19].

It is also necessary to note the stimulating effect of thyroid hormones on reparative processes in the case of injury to soft tissues in humans. Under the influence of thyroid hormones, the development and functional activity of mesenchymal cells takes place. This largely explains the beneficial effect of thyroid hormones on reparative regeneration. When the level of basic metabolism in the body is increased by thyroidization, favorable conditions are created for the trophic interaction of connective tissue elements with the newly formed epithelium. Thyroid hormones increase oxidative processes, contributing to the reproduction and differentiation of various cells [20]. Studies have shown

that a thyroid transplant or thyroxine administration accelerates wound healing by 2 to 11 days. On the contrary, with hypothyroidism, healing is delayed by 4–40 days [21].

A lack of thyroid hormone leads to a delay in the formation of granulation tissue and suppression of the activity of elements of the macrophage system. In the case of experimental thyroidization, the function of various cells increases, they form granulation tissue, which collectively promotes wound healing [7].

As for the apparent stability of T3 levels at the same time as T4 increases in subjects with moderate and severe injuries, it is possible that the reason for this lies in the inhibition of the peripheral conversion of T4 into T3. This is facilitated by metabolic disorders in various tissues of the body in various pathologies (acidosis, hypoxia, oxidative stress, etc.) [7, 22].

## CONCLUSIONS

Analyzing the obtained results, it is possible to conclude that it is advisable to continue the research on determining the levels of thyroid hormones, TTH with the involvement of a larger number of injured people, detailing the localization of the wound, the «endocrinological» history of patients, neurological and mental status, parameters of hemodynamics and the homeostasis system.

Therefore, the analysis of modern scientific data and own research indicates the presence of a correlation between the hormonal status of the thyroid gland and the volume of wound

damage, and also showed that this problem is not fully resolved, is very relevant and requires further in-depth study.

Currently, research is being continued on the basis of the Emergency Medical Care Clinic, the Military Medical Clinical Center of the Northern District of the Kharkiv Medical Forces Command with the involvement of the National Academy of Medical Sciences headed by the president, academician V. I. Tsybalyuk, and the SI «V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine».

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The wound process is considered to be the local and general organism's responses which are developed to damaged tissues. The number of individuals with combat trauma was extremely increased due to Russia's armed aggression against Ukraine started in February 2022. The wound healing and the course of wound process depend on large number of factors one of them is thyroid status. The impact of thyroid hormones on the particularities of combat traumas' healing is the background of this investigation. The purpose of this research was to determine the link between wound sizes and thyroid hormones serum level at different period of the wound process.

**Material and methods.** 30 militaries with wounds of soft tissues of different sizes have taken part in this study. The average age of wounded men was  $34.2 \pm 4.3$ . The average body mass was  $78 \pm 3.5$  kg. Free T3 and T4, thyrotropic hormone (TTH) concentrations have been determined.

**Results.** During investigation free T3 concentration was at level 3.4–5.2 pmol/L and hasn't statistically changed in all the participants comparing to its concentration within 1–3 days. The concentration of free T4 did not differ in militaries with minimal as well as with mild injuries. The levels of free T4 hormones were significantly ( $p < 0.05$ ) higher in severely wounded men during the entire duration of the investigation. TTH levels considerably ( $p < 0.05$ ) increased in wounded men with severe and mild wounds in compare with participants with minimal wounds on 1–5 days. However, the concentration of TTH significantly ( $p < 0.05$ ) declined in the all groups of wounded on 14<sup>th</sup> day of the investigation.

**Conclusions.** The concentrations of free T4 and thyrotropic hormone significantly increased in wounded men with severe and mild wounds on 1–5 days after wounding. The concentrations of free T3 haven't considerably changed.

**Key words:** thyroid hormones, thyroid gland, combat trauma, wound process, reparation.

## ЗМІНИ В ТИРЕОЇДНОМУ ГОРМОНАЛЬНОМУ СТАТУСІ ПОРАНЕНИХ В ЗАЛЕЖНОСТІ ВІД ОБ'ЄМУ РАНОВОГО УШКОДЖЕННЯ

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Рановий процес — це складний комплекс місцевих та загальних реакцій організму, що розвиваються у відповідь на пошкодження тканин. Внаслідок розпочатої у лютому 2022 року збройної агресії росії проти України значно зросла кількість осіб, які отримали бойову травму. Швидкість загоєння цих травм та перебіг ранового процесу залежать від багатьох факторів, одним з яких є тиреоїдний гормональний статус. Вплив гормонів щитоподібної залози на швидкість та особливості загоєння бойових травм не вивчались, що й обумовлює актуальність цього дослідження. **Мета** дослідження: визначення основних закономірностей між об'ємом ранового ушкодження та змінами рівнів гормонів щитоподібної залози у сироватці крові на різних етапах ранової хвороби.

**Матеріали та методи.** У дослідженні брали участь 30 чоловіків, які отримали поранення м'яких тканин різного об'єму ураження. Вік поранених —  $34,2 \pm 4,3$  роки. Середня маса тіла становила  $78 \pm 3,5$  кг. Визначались рівні вільного Т3, вільного Т4 та тиреотропного гормону (ТТГ).

**Результати.** У всіх обстежених осіб рівень вільного Т3 не зазнав статистично значущих змін впродовж усього терміну дослідження у порівнянні із його рівнем у термін на 1–3 добу і знаходився в діапазоні 3,4–5,2 пмоль/л. У осіб із пораненнями легкого та середнього ступеня важкості рівні вільного Т4 не відрізнялись. Рівні вільного Т4 у осіб із важким пораненням були вірогідно ( $p < 0,05$ ) вищими на усіх етапах дослідження у порівнянні із особами з середнім та легким пораненням. Рівень ТТГ при пораненнях середнього та важкого ступеня зростав ( $p < 0,05$ ) у порівнянні із легкими пораненнями у термін 1–5 день. Але на 14 добу дослідження значення даного показника вірогідно зменшувалося ( $p < 0,05$ ) у обох групах до рівня, однакового із групою осіб, які зазнали поранення легкого ступеня.

**Висновки.** У обстежених осіб із пораненням важкого та середнього ступеня мало місце вірогідне зростання рівнів тиреотропного гормону у термін 1–5 діб від поранення, яке супроводжувалось також зростанням рівня вільного Т4. Рівні Т3 вірогідних змін не зазнали.

Ключові слова: тиреоїдні гормони, щитоподібна залоза, бойова травма, ранова хвороба, репарація.