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FEATURES OF CLINICAL MANIFESTATIONS, FREE RADICAL, COAGULATION AND AGGREGATION PROPERTIES OF BLOOD IN PATIENTS WITH CRANIOCEREBRAL TRAUMA

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ABSTRACT

Introduction: In recent years in Ukraine, as in the entire world, there has been an increase in cases of domestic injuries with a raise in the number of patients with craniocerebral trauma and its consequences.

The aim of our research was to study clinical symptoms, the state of free radical oxidation, aggregate and hemocoagulative properties of blood in patients with mild craniocerebral trauma.

Materials and methods: We conducted comprehensive clinical and laboratory examination of 34 patients with mild craniocerebral trauma and 20 apparently healthy patients (the control group). The diagnosis was made under ICD-10. The verification of the diagnosis was based on data from clinical examination, neurological status of neuroimaging (computer tomography and magnetic resonance imaging). The study group included 24 men and 10 women aged from 19 to 40. In addition, 20 apparently healthy individuals of the same age were examined, who comprised the control group (14 men and 6 women). In the blood parameters of all patients, we examined free radical oxidation, hemostasis and aggregation properties of platelets.

Results: The conducted study revealed clinical disturbances, changes in the parameters of free radical lipid oxidation, coagulation and microcirculatory hemostasis. **Conclusions:** All patients with mild craniocerebral trauma, develop disturbances in the form of symptoms of microorganic lesion of the central nervous system: convergence weakness in 100% of patients, Mann's symptom (76.4%), disruption of the function of the cranial nerves (58.8%), signs of pyramidal insufficiency (68.4%), vestibular disorders (94.1%), autonomic vascular dysfunction (100%). Mild craniocerebral trauma is accompanied by the activation of free radical lipid oxidation processes, decreased activity of antioxidant enzymes, hypercoagulation, and increased aggregation properties of platelets.

KEY WORDS: mild craniocerebral trauma, free radical oxidation, hemostasis

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INTRODUCTION

In recent years in Ukraine, as in the entire world, there has been an increase in cases of domestic injuries with a raise in the number of patients with craniocerebral trauma and its consequences [1,2]. Increasing urbanization and industrialization, a sharp increase in the number of vehicles, increased population migration, rising frequency of military conflicts, widespread engagement of young people in traumatic sports, and other circumstances, characteristic of the modern way of life, led to a progressive increase in injuries, especially craniocerebral traumas [3]. According to the World Health Organization, more than 10 million people are traumatized every year in the world, and the number of patients with craniocerebral trauma (CCT) increases by 2% every year. CCT annually constitutes from 2.3 to 6 cases in different regions of Ukraine (an average of 4-4.2 per 1000 of population) [4]. In Ukraine, from 10 to 11 thousand people die of craniocerebral injury every year, that is, the mortality rate is 2.4 per 10 thousand [3]. Over the past 10 years, the incidence of CCT in Ukraine has more than doubled, with the annual number of victims of up to 200.000.

The consequences of CCT lead to a reduction in working capacity and disability in patients depending on the severity of the injury and related injuries. Only 7% of survivors recover [5]. Within 2-10 years after the trauma, 90% of patients with CCT have neurological deficits and psychiatric disorders [6]. Therefore, neurotraumaticism remains a relevant social problem [1-6].

One of the main causes of brain function impairment is the disruption of blood flow as a result of increased local intracerebral pressure. Changes in the intracranial pressure are possible in the direction of its increase or decrease. In clinical practice, there is most often a stable, or short-term increase in pressure, the so-called hypertension syndrome. Less common, but with no less importance, one can observe pressure decrease (hypotension syndrome). The liquor-distension syndrome occurs in various diseases of the brain, including those with traumatic lesions [7].

In the pathogenesis of CCT, hydrodynamic forces and liquor wave affect the limbic-hypothalamic-reticular system, which leads to neurohumoral and vegetative-vascular disorders. Clinically, this is manifested by the development of cerebral symptoms, symptoms of cerebral dysfunction,

Table I. Clinical manifestations of liquor-distension syndrome

Complaints	Patients, % (n = 34)
Headache	100
Vertigo	89.5
Nausea	63.2
Vomiting	26.3
Head noises	21
Pain in the eyeballs	26.3
Grogginess	15.8
Loss of consciousness	21

Table II. Indicators of the prooxidant-antioxidant system and lipid metabolism

Indicators	Healthy people n=20	CCT patients n=34
PRE, %	1.88 ± 0.17	1.33 ± 0.11; $p_1 < 0.05$
MDA before incubation, mmol/ l	5.26 ± 0.57	8.2 ± 0.6; $p_1 < 0.05$
MDA after incubation, mmol/ l	9.8 ± 0.4	14.56 ± 0.73; $p_1 < 0.05$
DC, mmol/ l	49.79 ± 0.55	56.23 ± 1.21; $p_1 < 0.05$
Atherogenic lipoproteids, g/l	4.21 ± 0.19	6.12 ± 0.78; $p_1 < 0.05$
SOD, c.u.	1.17 ± 0.04	0.94± 0.05; $p_1 < 0.05$
Catalytic index, c.u.	3.25 ± 0.14	2.43 ± 0.25; $p_1 < 0.05$
Ceruloplasmin, mg/l	163.2 ± 4.23	142.15 ± 8.21; $p_1 < 0.05$

Note: p_1 – comparison of the indicators of the main group with the indicators of the control group

neurasthenic and psychopathic syndromes [8]. There are generalized vascular disorders due to changes in homeostasis, antioxidant defense with the development of hypertension syndrome [9].

Despite numerous studies conducted, many issues in this direction remain understudied. Among the mechanisms of the development of liquor-distension syndrome, the relationship between processes of lipid peroxidation, antioxidant enzymes, coagulation and microcirculatory hemostasis is becoming increasingly important and relevant.

THE AIM

The aim of the research: to study the clinical symptoms, the state of free radical oxidation, aggregation and hemocoagulative properties of blood in patients with mild craniocerebral trauma.

MATERIALS AND METHODS

A comprehensive clinical and laboratory examination of 34 patients with mild craniocerebral trauma was conducted. The diagnosis was made in accordance with ICD-10. The verification of the diagnosis was based on the data of clinical examination, neurological status of neuroimaging (computer tomography and magnetic resonance imaging). The main group included 24 men and 10 women aged from 19 to 40 years. In addition, we examined 20 apparently healthy persons of the same age (14 males and 6 females), who constituted the control group.

Indicators of free radical blood oxidation, hemostasis and platelet aggregation properties were studied in the blood of all patients. In conducting research, we defined the methods that characterize platelet aggregation, lipid peroxidation, antioxidant enzymes activity, blood coagulation. We conducted statistical processing of the results of the study. The basis for choosing research methods was the manual in experimental and clinical studies in biology and medicine [10].

RESULTS

When conducting a comprehensive clinical examination, the main complaints of patients with mild CCT were as follows: diffuse headache, which intensified in the morning, accompanied by nausea, vomiting, dizziness, grogginess, pain when moving the eyeballs; in some cases there was an asymmetry of the face, diplopia. In addition, patients complained of marked general weakness, fast fatigability, absent-mindedness, worsening of sleep, decreased working ability, and sometimes attacks of loss of consciousness (short-term, without seizures). Characteristics of clinical manifestations of liquor-distension syndrome are presented in Table I.

Table III. Indicators of blood coagulation and microcirculatory hemostasis

Indicators	Healthy people n=20	CCT patients n=34
Fibrinolysis,sec	200 ± 3	235 ± 9; $p_1 < 0.05$
Recalcification time, sec	128.5 ± 1.8	117.5 ± 4.1; $p_1 < 0.05$
Thrombin time, sec	12.82±1.07	10.31 ± 0.68; $p_1 < 0.05$
Prothrombin time, sec	17.18 ± 0.9	17.11 ± 0.7; $p_1 > 0.05$
AT-III, sec	19.82 ± 0.78	19.23 ± 0.64; $p_1 > 0.05$
Fibrinogen, g/l	2.11±0.19	3.14 ± 0.21; $p_1 < 0.05$
Platelets, x 10^9	215.8 ± 4.2	200.1 ± 4.3; $p_1 > 0.05$
Aggregation height, cm	3.9 ± 0.13	4.32 ± 0.19; $p_1 > 0.05$
Aggregation time, min	11.6 ± 0.96	4.58 ± 0.28; $p_1 < 0.05$
Aggregation angle (degree)	30.85 ±0.98	45.7 ± 0.94; $p_1 < 0.05$
TAI, %	51.78 ±1.65	53.35 ±1.15; $p_1 > 0.05$

Note: p_1 – comparison of the indicators of the main group with the indicators of the control group

During the objective neurological examination, the symptoms of microorganic lesion of the central nervous system were revealed: weakness of convergence in 100% of patients, Mann's symptom (76.4%), craniocerebral nerve function disorder (58.8%), signs of pyramidal insufficiency (68.4%), vestibular disorders (94.1%), vegetovascular dysfunction (100%).

In analyzing the parameters of free radical lipid oxidation, the following changes were found in patients: the level of malondialdehyde accumulation increased reliably by 55.8% as compared with the control group, the level of diene conjugates – by 12.9%, peroxide resistance of erythrocytes was reliably reduced by 29.6%. At the same time, there was a significant decrease in the activity of superoxide dismutase (24.5%), catalase (33.7%) and ceruloplasmin (14.8%). In patients of the main group, we observed disrupted lipid metabolism, in particular, increased level of atherogenic lipoproteins by 45.4% as compared with the control group (Table II).

As our studies have shown, the main group of patients develops a tendency to hypercoagulation and a decrease in the process of fibrinolysis. This is indicated by the reduction of recalcification time by 8.6%, thrombin time – by 24.3%, reduction of fibrinolytic activity by 17.5%, increased amount of fibrinogen by 48.8%. We did not detect reliable changes in prothrombin time and antithrombin III (Table III).

When studying the indicators of microcirculatory hemostasis, we found that in the main group, the time of platelet aggregation reduced by 2.5 times, and the aggregation angle increased by 48.1%. The obtained results allowed us to establish the fact of increased platelets pro-aggregation activity. However, the total index of platelet aggregation did not significantly differ in patients of the main and control groups. This suggests that the percentage of platelets that formed aggregates was virtually unchanged in the examined groups.

DISCUSSION

It is known that pathogenesis of structural and functional changes in the brain due to craniocerebral trauma is associated with a mechanical factor. Under the influence of trauma, hydrodynamic forces and liquor wave affect the limbic-hypothalamic-reticular region, which leads to various neurohumoral metabolic and endocrine, vegetative and vascular disorders. After the injury, patients report varying degrees of cerebrospinal symptoms: cerebral dysfunction, intellectual and mnestic impairment, changes in the psycho-emotional sphere, which include a wide range of disorders within neurasthenic and psychopathic syndromes.

Injury directly affects membranes, ion channels of axons, neurons and astrocytes, as well as cerebral blood flow and brain metabolism, which can be clinically manifested by various neurological disorders, including complete disintegration of brain activity.

In the process of injury, there is a disruption of both oxygenation and perfusion of the brain. In direct damage to neurons at the time of injury, there is a massive ion output and neurotransmitters into the extracellular space.

At the moment of injury, there is an excessive intake of glutamate, which launches the excitotoxicity mechanisms. Excessive stimulation of the NMDA receptors leads to active intake of calcium into the cell, followed by edema of the organelles and membranes, to necrosis or apoptosis, leading to death of the nerve cells.

All this leads to the fact that the sustained craniocerebral trauma, even at its easy degree, is far from always passing without a trace. Various consequences of the injury can appear both during the acute period and many years after the sustained craniocerebral trauma.

The consequences of craniocerebral trauma are extremely diverse, they include neurological pathology, which is manifested in the form of individual residual effects of trauma. The process can last from several months to several years and is accompanied by the emergence of new neurological

and neuropsychological symptoms, including cognitive impairment. Significant activation of lipid peroxidation and depletion of the antioxidant enzyme system, associated structural and functional changes characterize the post-traumatic stage of traumatic brain damage of moderate severity.

Our research using the experimental model (emotional-pain stress) in other diseases, such as generalized periodontitis and galvanosis, revealed disorders as a state of free radical oxidation, activity of antioxidant enzymes and hemostasis [11-16]. The above-mentioned studies prove the interrelation between the processes of free radical oxidation and hemocoagulative properties of blood. It has been established that the high level of free radical reactions against the background of reduced level of antioxidant defense can lead to significant disorders of the hemostasis and fibrinolysis system up to the development of local disseminated intravascular blood coagulation. Similar data were obtained in patients with mild craniocerebral trauma, indicating the need for correction of these processes in patients.

CONCLUSIONS

1. All patients with mild CCT develop disturbances in the form of symptoms of microorganic lesion of the central nervous system: weakness of convergence in 100% of patients, Mann's symptom (76.4%), dysfunction of cranial nerves (58.8%), signs of pyramidal insufficiency (68.4%), vestibular disorders (94.1%), vegetovascular dysfunction (100%).
2. Craniocerebral trauma of a mild degree is accompanied by activation of processes of free radical oxidation of lipids, decreased activity of antioxidant enzymes, hypercoagulation, increase in the aggregation properties of platelets.

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Authors' contributions:
According to the order of the Authorship.

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