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Changes in cerebral haemodynamics in patients depending on the severity and catamnesis of combat traumatic brain injury

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Abstract

In our time, under the influence of the ATO in the East of Ukraine and the full-scale invasion of Ukraine by the Russian Federation, the incidence of combat injuries, particularly combat traumatic brain injuries (cTBI), has significantly increased. The traumatic factor initiates a series of pathological processes, including immune, hemodynamic, metabolic, etc. These processes further shape the long-term consequences of cTBI. The cerebral vascular system is highly sensitive to mechanical impacts. Over time, vascular processes become more aggressive, and cerebrovascular accidents that develop often have a pessimistic prognosis. **Purpose.** To determine the peculiarities of changes in cerebral hemodynamics in patients with cTBI depending on the severity and duration of the condition and to correlate these changes with clinical manifestations.

Materials and Methods. The study involved 350 male patients with cTBI, conducted at the Municipal Non-Profit Enterprise of the Kharkiv Regional Council "Regional Hospital for War Invalids." Patients were divided into groups based on the severity of their injury: 145

individuals with mild cTBI (mTBI), 125 with moderate cTBI(MT), and 80 with severe cTBI (sTBI). The duration of the condition (catamnesis) was also considered: from 6 months to 1 year, 1 to 3 years, and 4 to 7 years. The average age of the patients was 38.5 ± 1.5 years. A control group consisted of 30 relatively healthy individuals matched by sex and age, without a history of cTBI. Neurological status and primary syndromes were studied, along with laboratory and instrumental methods, including ultrasound dopplerography of the head and neck vessels (USDG). The study utilized the Versana Essential diagnostic ultrasound system, employing a linear transducer L6-12-RS with a frequency range of 4.0–13.0 MHz.

Results and Discussion. Measurements of the intima-media thickness of the carotid artery (IMT) were conducted. In the mTBI and TBI(MT) groups, mean IMT values were within normal ranges (0.78 mm and 0.8 mm, respectively). However, in the sTBI group, there was an increase of approximately 15.0%. In the mTBI group, normal Doppler signal spectra corresponding to the relevant arteries were observed. No pathological turbulence was detected. Interhemispheric asymmetry in the carotid basin was within acceptable limits. In contrast, the TBI(MT) and sTBI groups exhibited reduced curve amplitude, elevated incisura, and the absence of a "systolic window." Changes in the vertebrobasilar basin (VBB) included a decrease in blood flow velocity by 26.5%, an increase in pulsatility index (PI) by 42.6%, and an increase in resistance index (RI) by 22.5%. These changes were accompanied by significant decreases in blood flow in the middle cerebral artery (MCA).

Conclusions. Changes in cerebral hemodynamics are closely correlated with the severity of cTBI and the duration of the condition. The longer the time since the injury, the more pronounced the progressive deterioration in cerebral blood flow due to the exhaustion of vascular tone regulation mechanisms. In the sTBI group, there was a significant decrease in velocity characteristics and an increase in PI, RI, and resistance coefficients in both the carotid and vertebrobasilar basins. This emphasizes the need for continuous monitoring of patients with sTBI due to the high risk of vascular complications

Key words: combat traumatic brain injury; cerebrovascular disorders; ultrasound Doppler.

Introduction

In our time, under the influence of the ATO in the East of Ukraine and the full-scale invasion of Ukraine by the Russian Federation, the incidence of combat injuries, in particular, combat traumatic brain injury (cTBI), has become much more frequent. The traumatic factor triggers a number of pathological processes: immune, haemodynamic, metabolic, etc. These

processes will further shape the long-term consequences of TBI. The vascular system of the brain is very sensitive to mechanical stress. Over time, the vascular process manifests itself more aggressively and developing cerebrovascular accidents in most cases have a pessimistic prognosis [9, 14, 15].

Patients with cTBI can present both direct and indirect consequences. Direct consequences include: autonomic dystonia syndrome (60–65% of patients) [4, 5, 9]; psychopathological disorders, often combined with autonomic dystonia (up to 90% of patients); vestibular syndrome and cerebrospinal fluid dynamics disorders in the form of intracranial hypertension (up to 50% of patients); post-traumatic epilepsy in 20–25%; narcoleptic syndrome caused by dysfunction of the limbic-reticular formation in 12–14% of patients; and hypothalamic syndrome accompanied by neurotrophic disorders (more characteristic of the long-term period) [3, 4].

Cerebral focal syndrome, including pyramidal, coordination, and motor disorders, is observed in nearly 65% of patients. Conversely, extrapyramidal system disorders, such as parkinsonism, chorea, or athetosis, occur in only 2.0–3.5% of patients with cTBI. Indirect consequences may include vascular complications in 80% of patients and post-traumatic cerebral arachnoiditis (PTCA), which occurs in 20–25% of individuals with a history of moderate or severe cTBI [6, 9, 10].

After analysing the literature on the long-term consequences of TBI, including BCI, it was found that organic neurological symptoms gradually smooth out and vegetative and emotional and mental disorders come to the fore [5, 10]. As a rule, 3 years after TBI, almost 70% of patients complain of deterioration in health: various clinical manifestations of TBI consequences are formed, which most researchers interpret as a consequence of chronic cerebrovascular disorders [6, 8, 7]. One of the causes of cerebrovascular disorders in such patients is functional insufficiency and depletion of mechanisms for regulating vascular tone [4, 5, 13, 16].

Spasm and/or dilation of blood vessels, as well as increased permeability of their walls, are manifestations of the main changes that occur in the vascular system in traumatic brain injury. Vascular spasm inevitably affects cerebral blood flow, which can be impaired for many years, which is consistent with the well-known provisions on the provocative role of traumatic brain injury in the development of early atherosclerotic lesions.

Even 10–15 years after TBI, patients associate their deterioration of health with it. Such late decompensation of traumatic illness differs from the early one by a longer duration of the exacerbation period and an increase in psychopathological symptoms [5, 8, 12, 14].

Angiodystonic disorders that were present at the time of TBI eventually become permanent, structurally defined syndromes of cerebrovascular disease. The more time has passed since the moment of TBI, the greater the likelihood of developing vascular disease. In other words, it takes time for nonspecific autonomic disorders to develop into a vascular disease as an independent nosological unit requires time [3, 5, 9, 11, 13].

The aim of the study was to determine the peculiarities of changes in cerebral haemodynamics in patients with cTBI depending on the severity and anamnesis, as well as to establish their correlation with clinical manifestations.

Materials and methods of research

The study, which was conducted on the basis of the Regional Hospital for War Disabled, a municipal non-profit enterprise of the Kharkiv Regional Council, involved 350 men with TBI aged 25 to 55 years. The patients were divided into groups depending on the severity of the injury and their medical history [8].

There were 145 patients with consequences of mTBI, with an average age of 36.3 ± 0.7 years. In 88 patients (60.68 %) there was a concussion, in 57 (39.31 %) - a mild brain contusion. In 45 (31.03 %) patients, repeated mTBI was documented.

The distribution of groups by the history of TBI: from 6 months to 1 year - 35 (24.13 %), from 1 to 3 years - 60 patients (41.37 %), from 4 to 7 years - 50 (34.48 %)

There were 125 people with consequences of cTBI(MT), the average age was 42.03 ± 0.7 years. Distribution by the nature of the injury: TBI was recorded in 100 (80 %) patients, and BBI(ST) in 25 (20 %) patients. In 9 (7.2 %) patients, a combination of moderate brain contusion with subarachnoid haemorrhage was diagnosed, and in 8 (6.4 %) patients, a combination of moderate brain contusion with intracerebral haematoma. The distribution of groups by the history of TBI (CT): from 6 months to 1 year - 30 (24.0 %), from 1 to 3 years - 45 patients (36 %), from 4 to 7 years - 50 (40 %)

There were 80 patients with consequences of TBI (22.85 %), the average age was 46.5 ± 0.85 years. Distribution of groups by history of TBI: from 6 months to 1 year - 20 (25.0 %), from 1 to 3 years - 30 patients (37.5 %), from 4 to 7 years - 30 (37.5 %).

The control group consisted of 30 people of representative gender and age without a history of TBI.

The research was conducted with the permission of the Bioethics Committee of the Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine, in compliance with the basic provisions of the GSP (1996), the Council of Europe Convention on Human Rights and Biomedicine (4 April 1997), the World Medical

Association Declaration of Helsinki on the Ethical Principles for Scientific Medical Research Involving Human Subjects (1964-2000) and Order of the Ministry of Health of Ukraine No. 281 of 01.11.2000, and the Ethical Code of Scientists of Ukraine (2009).

The pathology studied, according to -X, corresponded to code T90.5 -consequences of intracranial trauma. In the course of this work, the complaints, medical history, life history, social status (family situation, referral to the expert commissions), level of education, and neurological symptoms were studied in the studied patients.

Patients were included after assessment of their somatic and neurological status, neuropsychological testing, instrumental methods (electroencephalogram (EEG), ultrasound dopplerography of head and neck vessels (USDG)), neuroimaging methods (CT or MRI of the brain), laboratory methods and verification of the clinical diagnosis. The inclusion criteria were patients with TBI consequences of varying severity and history, aged 25 to 55 years, no chronic somatic pathology in the stage of decompensation, no reliable data on alcohol, precursor, narcotic and psychoactive substance abuse, and patients without a history of oncological pathology and neoplastic syndrome.

USG of the head and neck vessels was performed according to the generally accepted methodology on the Versana Essential ultrasound diagnostic system, China, using a linear transducer L6-12-RS with a frequency range of 4.0-13.0 MHz, a frequency in the centre of the image of 7.7520% and a slice thickness of ≤ 15.0 mm. The following parameters were studied: maximal systolic (MSV) and end-diastolic blood flow velocity (EDV), average blood flow velocity per cardiac cycle, pulsatility index (PI), systolic-diastolic index (SDI), arterial stenosis index (ASI), circulatory resistance index (CRI), asymmetry coefficient of linear blood flow velocity displayed as a percentage and carotid intima-media thickness (CMT) [10, 13, 14, 15].

The measurement of the CMT is performed in fractions of a millimetre, which is equal to the maximum resolution of even the best ultrasound equipment (0.1 -0.2 mm spatial resolution). Therefore, when measuring such a small structure, there is a significant probability of making an error in the measurement of percentiles. The discrepancies in the data obtained by all the scientists involved regarding Spearman's correlation coefficients ranged from 0.75 to 0.86. The discrepancies in the data obtained by each researcher in the course of the personal survey are also significant and ranged from 0.69 to 0.73. This makes it difficult to determine risk because there is very little difference between the categories. Functional tests were used for additional information.

The statistical processing of the data was performed using Statistica for Windows 13.0

(StatSoft Inc., USA; licence No. JPZ804I382130ARCN10-J) and the methods of correlation and regression analysis. The reliability of differences and changes between comparative values was assessed using the Student's t-test (t).

Results and discussion

USDG of the head and neck vessels was performed in 243 patients (69.4% of the total number of patients): 110 out of 145 patients with mTBI (75.9%), 88 out of 125 patients with TBI(MT) (70.4%) and 45 out of 80 patients with sTBI (56.25%).

CIMT were conducted to assess its changes. In the groups with mTBI and cTBI(MT), the mean CIMT was within normal limits in nearly all patients, averaging 0.78 mm and 0.8 mm, respectively (range 0.6–1.15 mm). However, in the group with sTBI, a 15.0% increase in mean CIMT thickness was observed.

In the mTBI group, normal Doppler signal spectra corresponding to the relevant arteries were recorded in almost all cases. Blood flow direction was physiological relative to the transducer, and no unphysiological turbulence was detected. Interhemispheric asymmetry in the carotid basin did not exceed acceptable values, remaining within 3.6 ± 1.0 . For functional test evaluations, the PI in the control group was 0.851 ± 0.032 .

The obtained hemodynamic indicators, both at rest and after functional tests, did not significantly deviate from age-appropriate norms. Pathological deformities of the right internal carotid artery (ICA), such as S-shaped tortuosity, were identified in 2 patients (1.8%). In 1 patient (0.9%), kinking of the left ICA was detected, and spiral deformities (coiling) of the left and right ICA were found in 2 patients (1.8%). Additionally, vertebral artery (VA) hypoplasia was noted in 4 patients (3.63%), and atherosclerotic changes in the form of plaques in the bifurcation area of the common carotid artery (CCA) were found in 3 patients (2.72%).

In the cTBI(MT) and sTBI groups, several specific features were observed, including:

- Decreased curve amplitude
- Upward displacement of the incisura
- Reduction and/or disappearance of the «systolic window»

These features reflected varying degrees of hemodynamic disturbances in vascular pools. In the cTBI(MT) group, significant changes in cerebral hemodynamics were observed, such as a 26.5% reduction in blood flow velocity, a 42.6% increase in PI, and a nearly 22.5% rise in SDC within the vertebrobasilar basin (VBB). In the carotid basin, significant reductions in cerebral blood flow (CBF) in the ICA ($p < 0.01$) were accompanied by decreased blood flow in the middle cerebral artery (MCA).

In 12.7% of CBF patients, systolic blood flow velocity in the MCA matched that of the mTBI group, likely due to compensatory vasospasm mechanisms that maintained normal cerebral blood flow levels despite reduced flow in the ICA [11, 12, 13]. Prolonged compensatory spasm in the MCA, confirmed by a significant 16.5% increase in PI ($p < 0.01$), led to increased peripheral vascular resistance in the ICA, further slowing ICA blood flow.

This was supported by a nearly 30.0% increase in the circulatory resistance index (CRI) in the ICA among MT patients, although interhemispheric asymmetry remained minor and within age-appropriate norms (3.4 ± 0.6). Significant blood flow disturbances, complete absence of flow, or changes in ICA direction relative to physiological norms were not identified in the cTBI(MT) group. However, Dopplergrams revealed signs of impaired cerebral circulation, particularly in the VBB.

In the group with severe cTBI (sTBI), significant reductions in blood flow velocity and increases in pulsatility index (PI), circulatory resistance index (CRI), and systolic-diastolic coefficient (SDC) ($p < 0.01$) were observed in both the carotid and vertebrobasilar basins (VBB). Changes in the middle cerebral artery (MCA) were marked by a significant 26.8% decrease in velocity characteristics ($p < 0.01$) compared not only to the mTBI group but also to the moderate cTBI (MT) group. These findings occurred against a background of existing vasospasm, as evidenced by an 8.65% increase in PI ($p < 0.01$).

The observed changes in cerebral hemodynamics in the sTBI group indicate the development of cerebral dyscirculation, which also extended to the carotid basin. The mean group PI in the sTBI group was 1.45 ± 0.05 , which was significantly higher than in the mTBI and MT groups.

Among sTBI patients, pathological deformities of the ICA were observed in 3 cases (6.66%) as S-shaped tortuosity. Vertebral artery hypoplasia was identified in 5 patients (11.11%). Atherosclerotic changes in the form of plaques were detected in 8 patients (17.7%).

In the group of patients with sTBI, signs of cerebral discirculation were detected in all vascular pools. The results of ultrasonography of the cerebral circulation in these patients corresponded to discirculatory encephalopathy of the third stage. Clinically, it was marked by the appearance or intensification of psycho-organic, cortical-subcortical syndromes, signs of damage to the pyramidal and sensory pathways. In the group of patients with sTBI, in AB and MCA, an increase in IP and vascular tone was accompanied by a slowing of cerebral blood flow, which may indicate the pathogenetic role of vasospasm in the development of haemodynamic disorders. In the group of patients with cTBI(MT) in the MCA, a direct correlation between IP and SBF was found.

According to the literature [11, 12, 14, 15], the authors believe that IP reflects the state of intracerebral vascular tone. In this regard, there was a certain interest in studying the correlation between IP and SBF in the groups with cTBI(MT) and sTBI. A correlation analysis was performed, which showed that in the group of patients with cTBI(MT) there was a significant negative linear relationship between the indicators in the VBB (AB) ($r = 2.4 \pm 0.16$), where r is the correlation coefficient. In the group of patients with sTBI, a negative correlation was found both in the carotid basin (CB) and in the VBB ($r = -0.68$ and $r = -0.71$).

Thus, it can be said that almost all patients with cTBI(MT) and sTBI in AB and in MCA in the group with sTBI showed an increase in the IP index and, consequently, intracerebral vascular tone, accompanied by a slowdown in cerebral blood flow.

These data prove the pathogenetic role of vasospasm in the further development of haemodynamic disorders in the examined patients [5, 7, 12, 13, 14]. In the group of patients with cTBI(MT) in the SMA, a direct correlation between IP and SBF was found. In our opinion and according to other authors, the positive relationship between these indicators may indicate the compensatory nature of the detected vasospasm, which arose to maintain intracerebral blood flow at the same level in the event of deterioration of blood circulation in the extracerebral regions. In the group of patients with sTBI, the detected slowing of cerebral blood flow indicated the transition of vasospasm from compensatory to pathological, with the development of discirculation in the carotid basin [12, 14, 15, 16].

Conclusions

Changes in cerebral hemodynamics closely correlate with the severity of cTBI and the duration of post-injury history. The more time that has passed since the injury, the more progressive deterioration in cerebral blood flow is observed, driven by the exhaustion of vascular tone regulation mechanisms. In the sTBI group, significant reductions in velocity characteristics and increases in PI, CRI, and SDC ($p < 0.01$) were found in both the carotid and vertebrobasilar basins. Changes in the MCA included a 26.8% reduction in velocity characteristics ($p < 0.01$) compared to both the mTBI and MT groups. Patients with sTBI require continuous monitoring due to the high likelihood of vascular complications. The use of USDG enables early tracking of chronic cerebral blood flow disorders from the initial stages, from compensatory arterial spasm to the development of cerebral discirculation.

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Prospects for further research consist in the further study of the modern model of providing qualified medical care and further rehabilitation to combatants with the consequences of a combat craniocerebral injury and finding ways of improvement and improvement.

Conflict of interest

The author state no conflict of interest.

Relationship with academic programs, plans and themes

The article is a fragment of the planned research work of the Department of Neurology, Psychiatry, Narcology and Medical Psychology of the Faculty of Medicine of V.N. Karazin Kharkiv National University of Ministry of Education and Science of Ukraine “Peculiarities of cognitive functions in young and middle-aged persons with neurotic and mental illnesses in the conditions of modern life challenges (martial law in Ukraine,

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