MECHANISMS OF THE DEVELOPMENT OF IMPAIRED CONSCIOUSNESS IN PATIENTS WITH TRAUMATIC BRAIN INJURY AND MAXILLOFACIAL TRAUMA

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https://doi.org/10.5281/zenodo.10849806

Abstract. *The ineffectiveness of existing methods of treatment of impaired consciousness of traumatic etiology indicates that the mechanisms of development of impaired consciousness in patients with CCI have not yet been clarified. Purpose: to study the mechanisms of development of impaired consciousness in patients with CCI. Materials and methods: thorough clinical and neurological, laboratory (early screening markers of coma: leukocytosis, hyperglycemia and acidosis), ECG, chronographic, Echo ES, EEG, TCD and MSCT of the brain were performed in 124 patients (80 men, 54 women) with various form of CCI.*

Analysis of the data obtained shows that the molecular mechanism of impairment of consciousness is depression of intracellular energy synthesis. IIE synthesis, developed as a result of cerebral ischemia. And the severity of the oppression of consciousness is proportional to the intensity of the decrease in intracellular energy synthesis.

Keywords: *impaired consciousness, increased intracranial pressure, decreased cerebral blood flow, depression of intracellular energy synthesis.*

Relevance. It is known that wakefulness with the ability to know oneself and the surrounding world is called consciousness, which is the main component of the higher nervous (cognitive) functions of the brain [1,2,8,9,15,16].

It has been established that impairment (depression) of consciousness is one of the main symptoms of craniocerebral injuries (CCI). Assessment, impairment of consciousness and, especially, its dynamics in CCI are of great importance in diagnosis, selection of an adequate method and scope of treatment, as well as in establishing a prognosis.

First of all, the degree of impairment (depression) of consciousness in a patient with CCI needs to be assessed. Various degrees of impairment of consciousness are observed: from a short-term complete or partial shutdown of consciousness followed by stunning of varying durations to a severe comatose state.

According to many authors, disturbances of consciousness in CCI in 73% of cases manifested themselves in the form of stunning, and in 27% of cases sopore and coma were observed [2, 11].

Based on the results of a comprehensive study of victims of CCI with impaired consciousness, many scientists dealing with the problem of CCI have come to the conclusion that the basis of the disorder of consciousness is the blockade of the ascending activating influences of the reticular formation of the brainstem. Based on this, many methods of treating disorders of consciousness aimed at stimulating the functional activity of the reticular formation of the brainstem have been proposed [2, 5, 6, 11, 14].

However, the study of the results of the proposed methods of treatment of impaired consciousness in patients with CCI showed that the use of these methods does not lead to a noticeable clearing of consciousness. That is, the proposed methods of treating the disorder of consciousness turned out to be ineffective. [5, 6, 14].

The inefficacy of existing treatments for impaired consciousness in patients with CCI indicates that the mechanisms for the development of impaired consciousness in patients with CCI have not yet been elucidated. This means that the determination of the molecular mechanisms of the development of consciousness disorders in CCI is an urgent problem of modern medicine.
The aim of the study was to study the mechanisms of the development of impaired consciousness in patients with CCI.

Materials and methods of research. The study was conducted in 124 patients (80 men and 54 women) with various forms of CCI, including:

1) 25 (20%) patients had a concussion.

2) Brain contusion:

(a) Mild 17 (14%) patients;

b) moderate severity of 31 (25%) patients;

c) severe 53 (43%) patients

3) Cerebral compression – a total of 23 (19%) patients

a) depressed fractures of the cranial vault bones in 17 (14%) patients;

b) membrane hematomas – 4 (3%) patients;

c) intracerebral hematomas – 2 (1.6%) patients.

Patients aged 17 to 58 years (mean 43.6+2.0)

In order to determine somatic disorders, all patients underwent thorough clinical studies using the following laboratory and objective research methods: general blood and urine analysis; biochemical analyses; determination of blood and urine sugar concentration; ELECTROCARDIOGRAM; X-ray of the skull and internal organs; Ultrasound of internal organs. All patients underwent thorough neurological examinations using fundus examination, electroencephalography (EEG), echoencephaloscopy (Echo-ES), transcranial Doppler sonography (TDS) and multispiral computed tomography (MSCT) of the brain.

To determine the condition of the patients, 7-gradations of the state of consciousness were used: clear; moderate torpor; Deep stun soporous; moderate coma; deep coma; The coma is beyond measure. The degree of impairment of consciousness was determined using the Glasgow scale [11-14].

Intracranial pressure was determined by lumbar puncture, and in comatose patients, a queen's foramen was placed on Kocher's point on the right with drainage of the anterior horn to determine intracranial pressure. A catheter placed in the anterior horn is connected to a water monometer and intraventricular pressure was measured. That is, intracranial pressure was monitored and intravenous pressure was measured [14].

Based on the fact that the entire biology, physiology and morphology of our body are based on adequate intracellular energy synthesis of IIE synthesis [10], we decided to study the importance of energy exchange processes in the brain in the pathogenesis of impaired consciousness in patients with CCI.

The degree of expression of intracellular IIE synthesis was determined by studying the value of intracranial pressure, cerebral blood flow, acid-base equilibrium, and residual oxidation of cerebrospinal fluid [4,7,9,10,16].

The acid-base equilibrium of cerebrospinal fluid or ventricular fluid was determined using a portable PH meter (FRG), and the residual oxidation of cerebrospinal fluid was determined by the method of K.S. Kosyakov [7].

Static processing of the obtained data was carried out using descriptive methods and the ANOVA model. The change from baseline was assessed using the t-test.

Results and discussions. Concussion patients (25 patients) experienced instant loss of consciousness at the time of CCI. Due to the short duration of the loss of consciousness, some of the victims did not even notice that they had lost consciousness. The victims complained of headaches and nausea. In 4 (3%) patients, there was a single vomiting. All the victims had symptoms of mild damage to the autonomic nervous system in the form of brady- or tachycardia, pale skin and slight anizoroflexia, which lasted for the first day. Consciousness is clear - 15 points on the Glasgow scale. There were no signs of bone damage on craniograms. On lumbar puncture, signs of a moderate increase in cerebrospinal fluid pressure, and an increase in residual oxidation of cerebrospinal fluid was not noted in anyone, acid-base balance -7.2

17 (14%) patients with mild cerebral contusion experienced longer loss of consciousness, dizziness, nausea, and vomiting two or three times. Fourteen (11%) patients had moderate stunning, which progressed gradually after admission to the hospital, and the remaining patients had lucid consciousness. Craniograms in 14 (11%) patients revealed fractures of the bones of the cranial vault of the fracture type. On Echo-ES, there was no displacement of the median structures of the brain, Multiple different-amplitude additional echoes with distinct pulsations were detected, indicating the presence of moderate cerebral edema. MSCT showed a moderate increase in brain density with small-point hemorrhage. Lumbar cerebrospinal fluid pressure in the supine position averaged 200-10±water columns. The residual oxidation of cerebrospinal fluid averaged 20±5%. The acid-base equilibrium of cerebrospinal fluid was 6.5-7.0 (average 6.7).

There is a moderate decrease in cerebral blood flow on TCDH. 22 (18%) of the 31 (25%) patients with moderate cerebral contusion had deep stunning, and the remaining 9 (7%) patients had soporous consciousness. In all patients, in addition to cerebral symptoms, there were also pronounced meningeal symptoms developed as a result of subarachnoid hemorrhage. In 17 (14%) patients, craniograms showed fractures of the cranial vault of the fracture type of fissure, and in 9 (7%) patients, there was a clinical picture of a fracture of the base of the middle cranial fossa in the form of otohemologorrhea (of which 2 (1.6%) patients had a fracture of the base of the middle cranial fossa on both sides). On MSCT of the brain, all patients had subarachnoid hemorrhage, and 21 (17%) patients had intracerebral hemorrhage. EEG showed a decrease in the electrical activity of the brain. There was no echo-ES displacement of the median structures of the brain, there were multiple echoes of different amplitude with a decrease in cerebral pulsation, indicating the presence of cerebral edema. TCDH showed a decrease in cerebral blood flow, grade II angiospasm, and lumbar cerebrospinal fluid pressure was (on average) 25010 mm of water column. All patients had subarachnoid hemorrhage. The residual oxidation of cerebrospinal fluid is 35±5%. Acid-base balance -6.0-6.2.

In case of severe cerebral contusion, out of 53 (43%) patients, 12 (9%) had soporous consciousness (Glasgow scale 9-12 points), 21 (17%) patients had a moderate coma (7-8 points), and the remaining 20 (16%) patients had a deep coma (4-7 points).

In patients who were in a soporous state on the fundus of the eye, there were initial manifestations of edema of the optic nerve discs. There was no displacement of the median M-ECHO on the echo-ES, and there were multiple high-amplitude echoes with a slight decrease in their pulsation. EEG showed a significant decrease in the electrical activity of the cerebral cortex. TCDG showed grade I (100 cm/s) cerebral circulatory insufficiency. The residual oxidation of cerebrospinal fluid was 43±2.8% (average 45%). Acid-base balance 5.8±2 (average 5.9).

And in patients in a mild fundus coma, there were initial manifestations of optic nerve disc edema. In all patients on the Echo-ES, there was no displacement of the median M-Echo, there were multiple high-amplitude echo signals with expansion of the base of the median M-Echo. EEG showed a diffuse decrease in the electrical activity of the brain. Early screening markers (hyperglycemia, leukocytosis, and acidosis) became positive. Grade II cerebral circulatory disorder was observed on TCDH. The residual oxidation of ventricular fluid ranged from 60 to 70% (mean 67%). And the values of intraventricular pressure averaged up to 300 mm of water column. The value of residual oxidation of ventricular fluid was 75±5%. Ventricular fluid acid-base balance 5.4±1.2 (mean 5.5).

In victims who were in a deep coma clinically and neurologically, extinction of all reflex acts, including vital ones, was noted. There is congestion in the fundus with hemorrhage. On Echo-ES, multiple high-amplitude Echo signals were noted, adjacent “to each other” with an expansion of the base and doubling of the top of the middle M-Echo; the pulsation of Echo pulses was not determined. There is electrical silence on the EEG. Cerebral blood flow was not detected on TCD. The value of intraventricular pressure is 350±25 mm water column. Residual oxidation of ventricular fluid from 70% to 87.1. acid-base balance from 4.7 to 5.0 (average 4.9).

Similar results were obtained when examining victims (23-18.9%) with compression of the brain. It should be noted here that when the brain was compressed in victims, the impairment of consciousness worsened gradually, which indicated the formation of intracranial hematomas.
After determining the degree of depression of consciousness, all patients underwent appropriate intensive pathogenetic treatment with the use of antihypoxants.

In patients who were in a moderately stunned state, clarity of consciousness occurred on days 3-4, and in victims who were in a deeply stunned state, clearing of consciousness occurred on days 5-6. In two of the 12 patients, soporous consciousness changed to superficial comatose consciousness. And in 10 (8%) patients, stuporous consciousness cleared up on days 6-7 after injury. In 17 (14%) of 21 patients with moderate coma, complete recovery of consciousness occurred on days 8-9, and in 4 patients, moderate coma turned into deep coma and ended in death. In 6 (5%) patients with deep coma, there was a death at the stage of a life-threatening coma, that is, the death developed within 3 days after receiving a severe head injury. And in 8 (6%) acute deep coma turned into chronic coma (apallic syndrome).

In 4 (1.5%) patients with deep coma, clearing of consciousness began in the subacute period, and in 2 patients, clearing of consciousness began during the period of restoration of autonomic functions.

The results of a comparative analysis of clinical and neurological data with data from additional research methods (state of the fundus, Echo-ES, EEG, TCD, MSCT of the brain and

determination of residual oxidation of cerebrospinal fluid) showed that the degree of depression of consciousness in CCI depends on the intensity of depression of intracellular energy synthesis (IIE synthesis). The intensity of the latter depends on the severity of anaerobic glycolysis, which develops as a result of hypoxia and cerebral ischemia. An increase in residual oxidation of cerebrospinal or ventricular fluid in patients with CCI confirms that there is a direct relationship between the intensity of depression of intracellular IIE synthesis and the degree of depression of consciousness. Thus, the values of residual oxidation of cerebrospinal or ventricular fluid in patients in moderate stupor ranged from 10 to 20%; with deep stunning ranged from 20 to 30%; with stupor from 40 to 50%; with superficial coma from 60 to 70%; with deep coma from 70 to 87%;

A study of the neurological status in patients with impaired consciousness showed that all victims had a violation of all five main interacting components (perception of information; processing and analysis of information; memorization and storage of information; exchange of information; construction, implementation of an action program) of the cognitive functions of the brain. This means that any degree of depression of consciousness is a violation of the higher nervous (cognitive) functions of the brain. A decrease or cessation of the substances of aerobic glycolysis (oxygen and glucose) due to the ischemic-hypoxic cascade leads to the development of anaerobic glycolysis with a decrease or cessation (depression) of intracellular IIE synthesis. After all, the energy that ensures the vital activity of any cells, including brain cells, is formed due to the removal of the phosphorus atom from IIE [10,15].

One IIE molecule contains 30.6 J⁄mol of free energy.

During anaerobic glycolysis, one molecule of glucose produces 2 molecules of lactic acid and 2 molecules of IIE. Energy produced by anaerobic glycolysis. (2ATP = 61.2 kJ⁄mol) satisfies only the relatively short-term needs of brain cells [4, 9, 10].

Under conditions of energy deficiency, some brain cells die (apoptosis), and some cells begin to exist due to exothermic energy formed as a result of the breakdown of macromolecules (proteins of the mucopolysaccharide complex) of brain tissue, first into protein and mucopolysaccharides, then gradually to deaminated amino acids and monosaccharides - catabolic (destructive) metabolism. Exothermic energy generated as a result of catabolic metabolism satisfies the very short-term needs of brain cells. Therefore, energy deficiency and catabolic metabolism in brain tissue are constantly progressing.

Lactic acidosis developing as a result of anaerobic glycolysis leads to depression of consciousness. The results of a study of ASR, residual oxidation of cerebrospinal fluid and EEG data over time showed that the degree of depression of consciousness in patients with CCI is proportional to the severity of lactic acidosis. As a result, a decrease in the production of neuropeptides due to energy deficiency, the brain will lose controller functions, which leads to the development of multiple organ failure [9-10].

In addition, depression of intracellular IIE synthesis is always accompanied by activation of the release of highly active “free radicals” and oxygen intermediates, which destroy the body from the inside. This means that “free radicals” formed as a result of hypometabolism destroy the brain.

Moreover, as a result of depression of intracellular IIE synthesis, the adaptive abilities of all other systems for maintaining homeostasis are disrupted [9, 10].

A decrease or cessation of the supply of aerobic glycolysis substrates (glucose and oxygen) to the brain due to the ischemic-hypoxic cascade (hypoperfusion) leads to a decrease or cessation (depression) of intracellular energy synthesis (IIE synthesis).

The development of acidosis and an increase in residual oxidation of the cerebrospinal fluid in our patients with impaired consciousness show that pronounced anaerobic glycolysis with depression of intracellular energy synthesis (IIE synthesis) has developed in their brain.

Depression of intracellular energy synthesis leads to a decrease in the functional activity of the brain in the form of disruption (suppression) of the higher nervous (cognitive) functions of the brain, ranging from short-term loss of consciousness to deep or extreme coma. Stopping the supply of aerobic glycolysis substrates for more than six minutes leads to brain death [9, 10, 15, 16].

It has been established that all cells of the human body synthesize IIE molecules equal to their own weight per day. The reduction of which in any organ leads to disruption of specific functions, and then to the destruction of the structures of this organ. Thus, to maintain the vital activity of some cells, a small volume of substrates (glucose and oxygen) is enough, while other cells require a large amount of energy. Naturally, the higher the functional load of a tissue, the more energy it needs, and therefore more substrates. Thus, the brain, which feeds only on carbohydrates at rest, consumes 60% of glucose and 20% of oxygen brought by blood into the body, because to maintain higher nervous (cognitive) functions of the brain (consciousness) a very large amount of IIE is required [4, 8, 9, 10, 15, 16].

That is, maintaining higher nervous (cognitive) functions of the brain is considered the most energy-consuming process in the human body. The brain does not make any reserves of energy substrates; incoming substrates (glucose and oxygen) are immediately spent on active work. Therefore, stopping intracellular IIE synthesis for six minutes leads to the death of brain cells. And the decrease in intracellular energy synthesis (IIE synthesis), which has developed as a result of a decrease in the supply of aerobic glycolysis substrates to the brain, leads to inhibition of the functional activity of the brain. That is, a decrease in intracellular IIE synthesis in neurons of the brain leads to inhibition of higher nervous (cognitive) functions of the brain, ranging from short-term complete or partial switching off of consciousness, followed by stupor of varying durations to a severe coma [8, 9, 10, 15, 16].

Thus, the results of our study showed that the degree of depression (impairment) of consciousness depends on the severity of depression of intracellular energy synthesis (IIE synthesis).

The above shows that timely and rational stimulation of intracellular (energy synthesis) IIE synthesis in brain cells, by switching anaerobic glycolysis to the aerobic pathway, using dihydration, vasoactive, alkalizing, antihypoxic and antioxidant drugs is a pathogenetic method of treating impaired consciousness in patients with various form of CCI. Thus, as a result of switching anaerobic glycolysis to the aerobic pathway, 38 molecules of IIE -1162.8 kJ/mol of energy are synthesized in brain cells, which are quite sufficient to meet all the needs of the cells. Therefore, increased intracellular energy synthesis (IIE) as a result of switching anaerobic glycolysis to the aerobic pathway accelerates the natural restoration of consciousness (natural awakening of patients), stops the formation of “free radicals,” and restores the production of neuropeptides and other compensatory processes.

A comparative analysis of the results of our study with the listed literature data allows us to draw the following conclusions:

- the main molecular mechanism for the development of impaired consciousness during CCI is the depression of intracellular IIE synthesis in neurons of the brain, which occurs due to insufficient supply of substrates of aerobic glycolysis (glucose and oxygen).

-the degree of depression of consciousness is directly proportional to the depth of depression of intracellular IIE synthesis in brain neurons.

- timely and rational stimulation of intracellular IIE synthesis is a pathogenetic method of treating impaired consciousness.

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