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OPTIMIZATION OF INTENSIVE THERAPY IN PATIENTS IN THE ACUTE PERIOD OF COMA

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ABSTRACT

When prescribing intensive care to an unconscious patient, it is important to determine the etiological factor of the critical condition. The distribution of patients by neurotropic or vasotropic mechanism of disturbance of consciousness is extremely important for successful treatment and prevention of complications. Determination of autoantibodies to brain tissue is an important diagnostic criterion for the adequacy of intensive care. Administration of substances with succinic acid and D-fructose-1,6-diphosphate sodium salt hydrate is pathogenetically determined in this category of patients.

Introduction. Coma is one of the most common disorders of consciousness. It was found that about 3% of visits to intensive care units of city hospitals are states accompanied by loss of consciousness. The importance of this class of neurological disorders determines the need for a systematic approach to their diagnosis and treatment [1, 2].

The increased capabilities of computed tomography led to a not entirely justified turn of diagnostic measures in coma towards lesions detected by computed tomography (for example, hemorrhages, tumors, hydrocephalus). This approach, at times advisable, is sometimes unreasonable, since in most cases the coma is of toxic or metabolic origin [3].

The tactics of patient management should be conditioned by the knowledge of the pathological nature of the diseases that cause coma. The normal level of consciousness (wakefulness) depends on the activating effect on the cerebral hemispheres from the groups of neurons located in the reticular formation of the brain stem. To ensure a normal level of consciousness, the integrity of the cerebral hemispheres, the reticular formation and their connections is necessary [4, 5]. Consequently, the main causes of coma are bilateral lesions of the cerebral hemispheres or inhibition of their activity by drugs and other drugs or toxins; brain stem lesions or metabolic disorders that damage or inhibit the reticular formation [6].

There are observations that large unilateral lesions of the cerebral hemispheres, especially the left, can cause drowsiness (but not to whom) even in the absence of damage to the opposite hemisphere and reticular formation [7].

The pathophysiological bases of coma are either mechanical destruction of vital parts of the brain stem or cerebral cortex (organic coma), or a global violation of metabolic processes in the brain (metabolic coma). A coma of metabolic origin can occur due to the cessation of delivery of energy substances (hypoxia, ischemia, hypoglycemia) or damage to the neurophysiological reactions of neuronal membranes (drug or alcohol intoxication, epilepsy, or acute traumatic brain injury) [8].

Brain activity depends on the continuity of blood flow and delivery of oxygen and glucose, which are consumed at a rate of 3.5 ml / 100 g per minute and 5 ml / 100 g per minute, respectively. The stores of

glucose in the brain are able to provide energy metabolism for about 2 minutes after stopping the blood flow, although loss of consciousness occurs within 8-10 seconds. When hypoxia occurs simultaneously with ischemia, the available glucose supply is depleted even faster. Normal cerebral blood flow at rest is approximately 75 ml / 100 g per minute in gray matter and 30 ml / 100 g per minute in white matter (average 55 ml / 100 g per minute). This level of blood flow provides an adequate metabolism with a moderate safety factor to accommodate most physiological changes. With a decrease in cerebral blood flow to 25 ml / 100 g per minute, a slow rhythm appears on the electroencephalogram (typical for metabolic encephalopathy), and at 15 ml / 100 g per minute, the electrical activity of the brain stops [9].

Even if all other functions, such as temperature and blood oxygen saturation, remain within normal limits, a decrease in cerebral blood flow below 10 ml / 100 g per minute causes irreversible changes in the brain.

Electroencephalography provides important data on the general electrophysiological state of the cerebral cortex, and the presence of asymmetry may indicate a unilateral lesion that is not visualized by CT examination [10].

In most cases, coma is part of a known pathological process, such as hypoxia, stroke, trauma, hepatic or renal failure, and reactions to various medications and other medications. In this case, the main attention should be paid to the primary disease.

It is important to remember some general rules: the causes of acute sudden coma are most often the intake of various drugs or traumatic brain damage - hemorrhage, trauma or hypoxia; subacute development is usually due to previous therapeutic or neurological conditions, including secondary cerebral edema, occurring around a pre-existing lesion [11, 12]. Thus, it can be concluded that the existing etiological classifications of coma are not convenient for use in an intensive care situation and only complicate the choice of the optimal tactics for conducting intensive therapy.

By the method of advancing the results of the treatment of ailments in the state of the comatose period, with the help of preventive measures, the accelerated methods of intensive therapy will be improved.

Materials and methods.

There are 122 patients, who were on the basis of the intensive therapy of the Kharkiv hospital of non-removable benches during the period from 2017 to 2020. Among them there are 40 patients, group I, bully spilled according to the protocol adopted by the protocol of the ill person at the state period comatose. There were also 82 patients: 40 - of them with the so-called neurotropic start (toxic accent, yes, the primary accent - the primary toxicity of the cells of the central nervous system) - group II, 42 patients - with the vasotropic start (primary in the brain) - group III.

When divided into groups, we used the primary cause of the pathological condition - the absence of consciousness - in order to introduce in its acute period of additional substances with a fundamentally pathogenetically directed action.

Therefore, patients of group II were considered to be those in whom the primary was a toxic lesion of cells of the central nervous system with global metabolic disorders in the brain, in which there was a chemical inhibitory effect on the central nervous system with inhibition of metabolic and electrical activity of cell membranes. and in the bark. In addition to these patients, neurotropic drugs (nootropics) and antihypoxants (succinic acid) were added to the intensive care unit.

In turn, patients of group III were considered those in whom the process of primary destruction of brain structures was caused by blood spilled, or lack of its receipt, transmineralization or "sick cell syndrome", when the cells are rapidly excreted K, impaired excretion of Na (requiring energy expenditure that becomes deficient due to lack of oxygen.) Decreased intracellular ATP concentration enhances the normal function of the K-Na pump. These patients in the acute period of coma were additionally prescribed vasotron drugs (vascular wall protectors / disaggregants) – D-fructose-1,6-diphosphate sodium salt hydrate.

Material and methods. To confirm the adequacy of randomization of patients in group I, groups I and II, we used rating scales and instrumental methods.

Therefore, to assess the most important physiological systems in patients of the department, we used the method of Tarasov DG et al. (2017): in all patients, blood was taken daily to assess the severity to determine the indicators of the general blood test, including the calculation of the leukocyte formula, from the peripheral vein to the blood collection system with anticoagulant K2 EDTA. 30 minutes after blood collection, a peripheral blood smear was prepared and stained according to

Romanovsky. After staining blood smears by immersion microscopy, the leukocyte formula was determined. When detecting normoblasts in a blood smear, their number per 100 leukocytes was counted: when their number ranged from 1 to 6 per 100 leukocytes, the severity of the condition was assessed as moderate; when the number of normoblasts in the range from 7 to 20 per 100 leukocytes evaluated the severity of the condition as severe; with an increase in the number of normoblasts more than 21 per 100 leukocytes evaluated the severity of the condition as extremely severe.

To study the autoimmune response, the levels of autoantibodies to brain antigens in the serum were determined by ELISA on the day of admission, on the 3rd, 7th and 14th day of treatment.

Preparation of the studied biological material: blood for the study was taken from peripheral or central veins. Blood was centrifuged for 10 minutes at 2000 g. 1.5 ml of serum was frozen at -20°C and stored until the study. A total of 590 serum samples from patients with surgical aortic pathology were prepared for the study. To perform the study, the serum was thawed once at room temperature.

The determination of autoimmune antibodies was performed to assess the severity of brain tissue damage as the leading markers of disease prognosis.

Methods of parametric statistics were used to process the obtained data. Statistical processing of data that were entered into Excel spreadsheets was performed. The significance of the obtained data was checked using Student's t-test (for n <100) at a given level of reliability $p = 0.95$. To be able to use the Student's t test, the Fischer-Snedekor test was calculated − the ratio of the larger variance to the smaller. All mathematical operations and graphical constructions were performed using the software packages "Microsoft Office XP": "Microsoft XP Home" and "Microsoft Excel XP" on a personal computer.

Results of the research.

For the assessment of the young inflow of ailments on the prognosis of illnesses at all points of control - appropriate, 3rd, 7th and 14th, and for the addition - the method of Tarasov D.G. was used, de criteria of the severity of the patients of blood problems in the norm (table 1).

Table 1. The severity of the condition of patients in groups I, II and III (according to the method of Tarasov D.G., 2017)

Point of control	Group I n = 40	Group II n = 40	Group III n = 42
	Number of normoblasts		
Admission to the clinic	2,7±1,1	2,9±1,2	2,9±1,4
3rd day	4,2±1,7	3,9±1,9	4,1±1,6
7th day	2,9±1,2	2,7±1,9	2,9±1,4
14th day	1,8±0,6	1,6±0,9	1,8±0,7

Note: $p > 0,05$

From table 1 it can be seen that in all studied patients at all stages of the study − control points − the general condition was regarded as moderate, which confirmed the finding of the total number of normoblasts in a blood smear per 100 leukocytes in the range from 1 to 6. Which was evaluated clinically, depended in all patients solely on the functional state of brain tissue. In this case, an important point was the determination of autoimmune antibodies.

First, we determined autoimmune antibodies in all patients at the time of admission (table 2). Given the absence of probable differences between the groups in terms of autoantibody numbers to brain antigens, we calculated their average score between the groups and took it as the starting level of comparison.

Table 2. Indicators of neurospecific proteins in groups I, II and III in patients in the acute period of coma

Autoantibodies to brain antigens	Group I n = 40	Group II n = 40	Group III n = 42	Average starting level
The main protein is myelin	32,1±2,2	32,9±2,1	33,1±1,9	32,7±2,06
Calcium-binding protein S-100	11,4±0,6	12,1±0,9	11,9±0,7	11,8±0,7
Neurospecific enolase	26,1±2,2	27,2±1,9	26,2±2,1	26,5±2,06
Total human brain antigen	32,1±1,7	32,2±1,8	32,4±1,9	32,2±1,8

Note: $p > 0,05$

It is known that the destruction of myelin is a universal mechanism of response of nervous tissue to damage. When the central nervous system is damaged, the function of the blood-brain barrier is disturbed, which is accompanied by an increase in the concentration of neurospecific proteins in the serum. The dynamics of their numbers in the blood has a proportional effect on the prognosis of the disease. Given the principle of grouping patients, it is important to observe the dynamics of neurospecific antibodies in all studied patients (table 3).

Table 3. Indicators of neurospecific proteins in groups I, II and III in patients in the acute period of coma

Autoantibodies to brain antigens	Group I $n = 40$	Group II $n = 40$	Group III $n = 42$
To the main protein of myelin, average starting level: 32,7±1,06			
3rd day	37,4±2,2$^\times$	32,9±0,1*	33,1±1,9**
7th day	36,1±1,6$^\times$	33,1±0,4*	33,4±0,7**
14th day	34,8±1,1	32,7±0,2*	32,9±0,4**
To the S-100 protein, average starting level: 11,8±0,4			
3rd day	15,6±1,2$^\times$	12,4±0,7*	12,6±0,6**
7th day	14,4±1,1$^\times$	12,2±0,8*	12,4±0,2**
14th day	13,7±1,2$^\times$	12,2±0,8	12,2±0,8
To neurospecific enolase, average starting level: 26,5±2,06			
3rd day	36,4±2,4$^\times$	29,2±1,9*	29,2±2,1**
7th day	34,7±1,6$^\times$	27,4±0,8*	28,2±1,1**
14th day	32,9±1,2$^\times$	26,8±0,68	26,9±0,9**
To the total human brain antigen, average starting level: 32,2±1,8			
3rd day	37,4±2,6$^\times$	34,2±2,7	32,4±1,9**
7th day	41,2±2,9$^\times$	35,6±0,8*	35,2±1,4**
14th day	38,1±1,8$^\times$	34,7±0,4*	34,8±0,9**

Note: * $p < 0,05$ − indicator between groups I and II; ** $p < 0,05$ − indicator between groups I and III; $\times$ $p < 0,05$ − the indicator between group I and the average starting level of the indicator.

During the statistical analysis of the dynamics of autoantibodies to brain antigens, a significant positive effect of the therapy prescribed in groups II and III pathogenetically aimed at the primary etiological factor was determined. Thus, the main protein of myelin on the 3rd day of treatment in patients of group I was probably $p < 0.05$, higher than the average starting level and was 37.2 ± 2.2. It was also probably $p < 0.05$, higher than its figures in patients of groups II and III, where it was 32.9 ± 0.1 and 33.1 ± 1.0, respectively. On the 7th day of observation, the dynamics of this indicator was identical. After 2 weeks of treatment in patients of group I the level of autoantibodies to the main protein of myelin was not likely to exceed the average starting level, was 34.8 ± 1.1, but was probably $p < 0.05$, higher than in groups II and III, 32.7 ± 0.2 and 32.9 ± 0.4, respectively.

When determining the dynamics in the blood of autoantibodies to the protein S-100 it was found that on the 3rd day of treatment in patients of group I their level was 15.6 ± 1.2, probably $p < 0,05$, exceeded the average starting level, and also figures in groups II and III, where it was 12.4 ± 0.7 and 12.6 ± 0.6, respectively. In the future, this trend was maintained and only on the 14th day of treatment, the probable difference between the groups disappeared. However, the level of this indicator after 2 weeks of hospital stay in patients of group I remained probably $p < 0.05$, higher than at the start, which indicated the possibility of long-term consequences in these patients.

The same dynamics was observed in the analysis of autoantibodies to neurospecific enolase and total human brain antigen, which can be seen in table 2.

Given the above results, it can be argued that the distribution of patients with coma at the stage of screening by etiological factor in order to assign the appropriate pathogenetically oriented component to the existing protocol of intensive care is an important mechanism for preventing long-term consequences and disease in general.

Conclusions. Being the triggering mechanism of the pathogenesis of coma development, the etiological factor is not always decisive in mortality

Therefore, the features of pathogenetic disorders and the level of control of their changes acquire a major role in the outcome of the disease.

One of the decisive moments in the prognosis of coma as a pathological condition is its acute period, which requires the identification of an integrative indicator in the priority prescription of drugs with one or another pharmacodynamics in addition to the main protocol.

The key point of the possibility of improving the prognosis in coma of any genesis is the achievement of the perfusion-metabolic balance, which depends on the timely determination of the dominant disorders (perfusion - metabolic) and the appointment of specific therapy from the first minutes of contact with the patient, even at the diagnostic stage.

Conflict of interest. The authors do not declare a conflict of interest.

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