

Clinical and biochemical parameters of blood in the acute period of concomitant severe traumatic brain injury

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Abstract

Timely blood transfusion therapy made it possible to maintain the parameters of erythrocytes, hemoglobin, hematocrit within the normative values. The tendency to an increase in glucose in the blood was revealed on day 4.5, which corresponds to the acrophase of the about-week rhythm of the inflammatory reaction. On the 5th day, an increase in stabs was noted up to $11\pm 4.8\%$ and up to $13\pm 2\%$ on the 6th day. Hyperglycemia in the acrophase of a weekly biorhythm on days 4-5 caused a decrease in immune tolerance and an exacerbation of the systemic inflammatory response on days 6. The tendency to an increase in AST throughout the observation period caused a tendency to hypercoagulability, decreasing APTT (-0.89). The synergism of the functional activity of the hematopoietic function and the immune response in the acute period of CSTBI was revealed.

Keywords: clinical and biochemical blood parameters, acute concomitant severe traumatic brain injury.

Relevance. The International Normalized Ratio (INR) is 0.8-1.2 in a healthy person. An increase in INR is caused by: hypofibrinogenemia (deficiency of factor I), dysfibrinogenemia (synthesis of a defective protein that is not able to participate in the cascade of biochemical reactions), hereditary or acquired deficiency of factors II, V, VII, deficiency of factor X (for example, purpura in amyloidosis), deficiency vitamin K, hemorrhagic disease of newborns, malabsorption with impaired fat absorption (due to celiac disease, chronic diarrhea), acute leukemia, congestive heart failure, liver pathology (hepatitis, cirrhosis, alcoholic liver disease). The reasons for the

decrease in INR are (indicate a tendency to form blood clots): DIC syndrome (period of hypercoagulation), deep vein thrombosis (initial stages), polycythemia, pregnancy (recent months), increased factor VII activity. APTT - activated partial thromboplastin time. Reflects the activity of the factors of the internal path. The test is sensitive to a deficiency of all factors, except for VII, to heparin, to specific and nonspecific inhibitors. Activated Partial Thromboplastin Time (APTT): 21.1 - 36.5 sec. Prolongation of APTT –DIC syndrome, liver disease, massive blood transfusions, administration of anticoagulants, deficiency of clotting factors, vitamin K deficiency, presence of clotting inhibitors, presence of VA, leukemia, hemophilia. Shortening of APTT - hypercoagulation, risk of thrombosis. With hypofibrinogenemia, anemia, low hematocrit, the clot is small and this leads to a false overestimation of the retraction index (even when the latter is reduced). On the other hand, with an excess of erythrocytes (polyglobulia, erythremia), an increase in hematocrit, hyperfibrinogenemia, the clot is large, which leads to a false decrease in the retraction index [1,2]. Due to the lack of sufficient information on changes in clinical and biochemical blood parameters in the acute period of CSTBI, we tried to present the results of the study of parameters in dynamics after CSTBI.

Purpose of work. To study and assess the dynamics of clinical and biochemical blood parameters in the acute period of combined severe traumatic brain injury.

Material and research methods. We studied the indicators of a comprehensive examination of 30 patients with concomitant severe traumatic brain injury (CSTBI) who were admitted to the ICU of the RSCEMA neurosurgical department in the first hours after an accident - 28, catatrauma in 2 patients. Continuous daily monitoring of the general blood test, hemostasiogram, biochemical parameters was carried out: alanintransferase - ALT, creatine - Cr, hematocrit - HMT, international normalized relation - INR, activated partial thromboplastin time - APTT, platelets - Pl, asparantransferase - AST, protrombin index - PI, diastase - Dias, retraction - R, urea, hemoglobin - HG, monocytes, fibrinogen, lymphocytes, palcoidal - plc, potassium, segmented - Segm, glucose - gl, general protein - GP, leukocyte, direct bilirubin - DB, general bilirubin - GB, fibrinolytic activity - FA, trombotest - TT, estimation of vegetative tone - EVT, the need of myocardium in oxygen - TNMO were performed for 25 days after CSTBI (daily in the first 8 days, average values on days 9-17 and 18-25 after CSTBI).

Mechanical respiratory support (MRS) was initiated by mechanical lung ventilation (ALV) for a short time and then switched to SIMV. Mechanical ventilation was performed in the mode of normoventilation or moderate hyperventilation (pCO₂— 30—35 mmHg) with an air-oxygen

mixture of 30—50%. The assessment of the severity of the condition was carried out using scoring methods according to the scales for assessing the severity of concomitant injuries - the CRAMS scale, the assessment of the severity of injuries according to the ISS scale. On admission, impaired consciousness in 29 injured patients was assessed on the Glasgow Coma Scale (GS) 8 points or less. The above parameters of patients aged 19 to 84 years were studied.

Results and its discussion.

Table 1

Dynamics of blood analysis in the acute period of CSTBI

Days	1	2	3	4	5	6	7	8	9-17.	18-25.
Age, years	45.3± 16.8	49.5± 17.3	26.1± 3.6	47.7± 16.1	49.9± 17.9	43.2± 19.2	48.0± 18.6	49.9± 17.5	52.6± 15.6	52.2± 17.0
Erythrocytes*10 ⁹ /l	3.5± 0.9	3.4± 0.4	4.1± 0.2	3.6± 0.4	4.0± 0.4	3.8± 0.4	3.7± 0.1	3.7± 0.6	3.5± 0.4	3.6± 0.4
Hemoglobin, g/l	115.6± 21.7	112.4± 9.7	113.7± 13.6	101.9± 14.1	103.5± 17.4	115.8± 12.2	102.5± 10.3	106.5± 18.5	100.4± 13.4	108.9± 14.1
Platelets.10 ⁹ /l		201.3± 0.2			246.0± 0.03	312.4± 0.05*	220.0± 0.06		178.8± 31.8	210± 0.3
Hematocrit,%	36.9± 6.7	37.3± 3.3	39.3± 0.8	32.0± 4.2	32.2± 4.2	39.7± 0.9	32.8± 3.4	34.5± 5.5	32.3± 3.9	35.6± 4.0
Leukocytes, 10 ⁹ /l	11.3± 3.5	9.2± 1.5	10.3± 1.9	8.9± 2.4	7.9± 1.7	9.8± 1.9	8.3± 1.3	7.6± 1.3	9.2± 1.9	7.8± 2.1
Metamyelocytes,%	3.0± 1.0	4.0± 0.02				5.0± 0.03			2.3± 1.1	1.0± 0.01
Stab,%	3.1± 1.7	6.6± 3.3	4.3± 1.8	6.3± 1.6	2.5± 1.5	11.0± 4.8	2.0± 0.01	5.8± 4.8	3.5± 1.7	4.0± 1.6
Segmented,%	72.6± 5.3	73.8± 3.4	76.3± 1.1	74.3± 3.8	76.0± 7.5	73.0± 11.1	70± 0.02	72± 6.5	75.2± 4.8	70± 12.0
Eosinophils,%	1.7± 0.4	1.0± 0.01	1.0± 0.02	1.0± 0.01	2.0± 0.01	2.5± 1.5	1.0± 0.01	2.0± 0.7	2.5± 1.8	18.6± 26.2
Lymphocytes,%	18.0± 7.3	14.8± 3.8	15.3± 3.1	15.5± 4.0	16.0± 6.0	13.1± 4.2	26.0± 0.03	16.3± 5.3	17.5± 6.1	15.3± 4.4
Monocytes,%	4.5± 1.9	3.2± 1.8	3.7± 1.6	3.8± 1.6	5.0± 1.0	4.6± 1.6	1.0± 0.01	2.0± 0.5	3.8± 1.6	3.5± 1.4

As shown in tab. 1, timely blood transfusion corrective therapy for the identified deviations made it possible to maintain the parameters of erythrocytes, hemoglobin, hematocrit within the standard values. An increase in the number of platelets in the peripheral blood was revealed up to 312±0.05 on the 6th day. The appearance of metamyelocytes on days 1,2,6 indicated the significance of the stress reaction, and on the 9-17 and 18-25 days of the systemic inflammatory response of the injured patients.

Table 2

Changes in blood biochemical parameters

Days	1	2	3	4	5	6	7	8	9-17.	18-25.
Glucose, mmol/l	8±2	8±1	7±1	11±5	13±2*	7±1	8±0.2	7±1	7±1	7±1
Total protein, g/l	58±10	57±2	51±3	51±7	56±4	56±6	59±10	48±6	56±5	60±7
Urea, mmol/l	8±2	7±2	9±2	12±6	12±4	8±2	9±3	9±2	10±4	8±3
Creatinine, mmol/l	0.1±0.02	0.1±0.02	0.1±0.04	0.14±0.03	0.15±0.02	0.09±0.02	0.09±0.05	0.12±0.02	0.13±0.04	0.10±0.02
Total bilirubin, μmol/l	16±3	37±30	33±17	23±8	20±2	18±3	18±0.3	20±0.4	18±3	15±2

Bil.direct, $\mu\text{mol/l}$	4 \pm 3	27 \pm 23	4 \pm 0.2	8 \pm 6	7 \pm 3	3 \pm 2	6 \pm 0.2	8 \pm 0.1	5 \pm 4	3 \pm 3
Diastase, mg.ml/hour	57 \pm 46	179 \pm 84	28 \pm 0.6	178 \pm 18	23 \pm 3	28 \pm 0.5	25 \pm 0.8	30 \pm 0.6	66 \pm 16	82 \pm 28
Ast, u/l	115 \pm 71	92 \pm 28	97 \pm 5	95 \pm 5	69 \pm 7	75 \pm 22	77 \pm 8	70 \pm 10	81 \pm 38	67 \pm 18
Alt, u/l	66 \pm 29	46 \pm 15	75 \pm 12	48 \pm 22	82 \pm 26	69 \pm 13	61 \pm 15	43 \pm 21	78 \pm 49	49 \pm 20

The tendency to an increase in glucose in the blood was revealed on the 4.5th day in conditions of complete exclusion of parenteral administration of carbohydrates, which corresponds to the acrophase of the circadian rhythm of the inflammatory reaction (tab. 2). After that, on the 5th day, an increase in stabs was noted up to 11 \pm 4.8 on the 6th day. Stress hyperglycemia on days 4-5 caused a decrease in immune tolerance and, most likely, caused an exacerbation of the systemic inflammatory response on days 6.

The tendency to an increase in total bilirubin in the blood on day 2 was due to a tendency to an increase in the direct fraction to 27 \pm 23 $\mu\text{mol/l}$, associated with the cytolytic effect of severe trauma on hepatocytes, also to an increase in ALT to 66 \pm 29 u/l on day 1, a tendency to increase in diastasis to 179 \pm 84 mg ml/hour on day 2. It should be noted that the tendency to an increase in indicators persisted throughout the observation period against the background of corrective infusion and detoxification therapy. Damage to the cellular structure of tissues by trauma caused an increase in AST in 1 day to 115 \pm 71 u/l. The average INR and APTT indices were within 1.5 \pm 0.2 and 23 \pm 6.2 seconds, that is, during the first 25 days after injury, the tendency to hypercoagulability persisted.

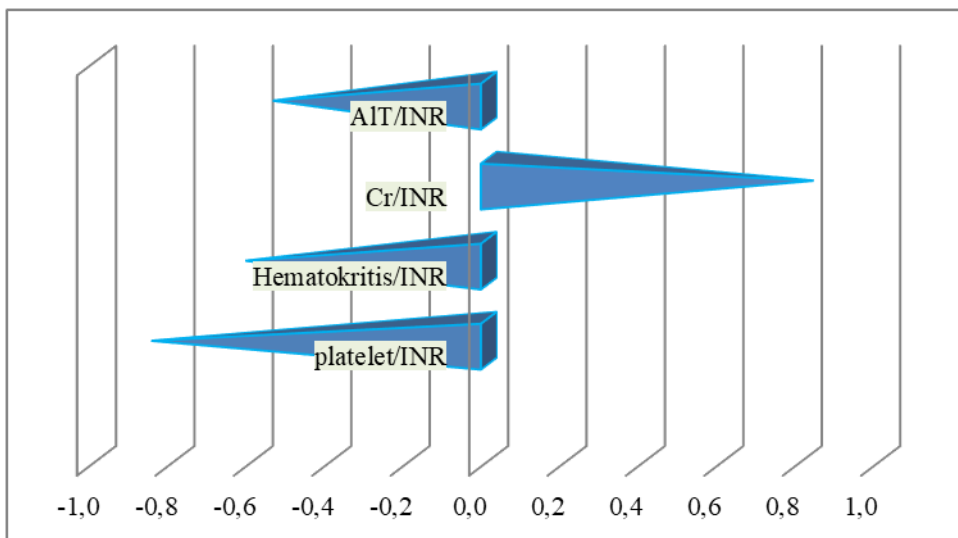


Fig. 1. Correlation links INR

A pronounced tendency to increase INR was facilitated by an increase in the blood creatinine index of age (0.79). A negative correlation between platelets and INR (-0.86), apparently, characterizes the compensatory response of internal coagulation factors to a possible loss of platelets.

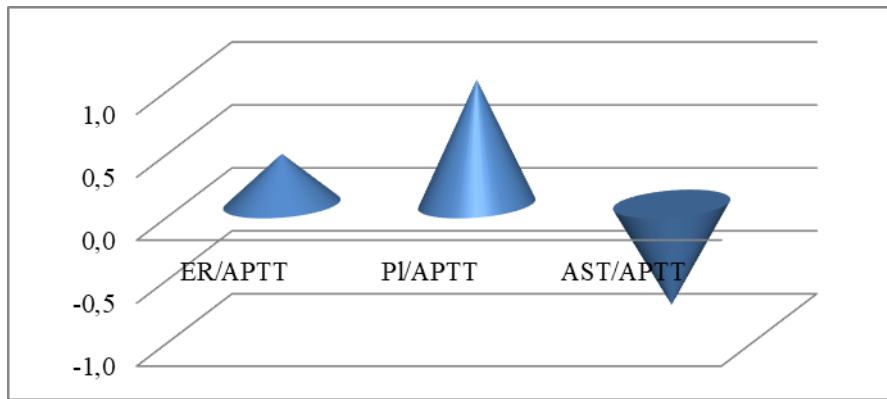


Fig. 2. correlations APTT

An increase in the number of erythrocytes above $3.5 \cdot 10^9/l$ (0.4), platelets above $300 \cdot 10^9/l$ (0.95), causing a tendency to increase APTT can negatively affect the blood coagulation activity, contributing to hypocoagulation (fig. 2). Perhaps, under these conditions, mechanisms are activated that prevent thrombus formation. The trend towards an increase in AST throughout the observation period caused a trend towards hypercoagulability, decreasing APTT (-0.89) (fig. 2).

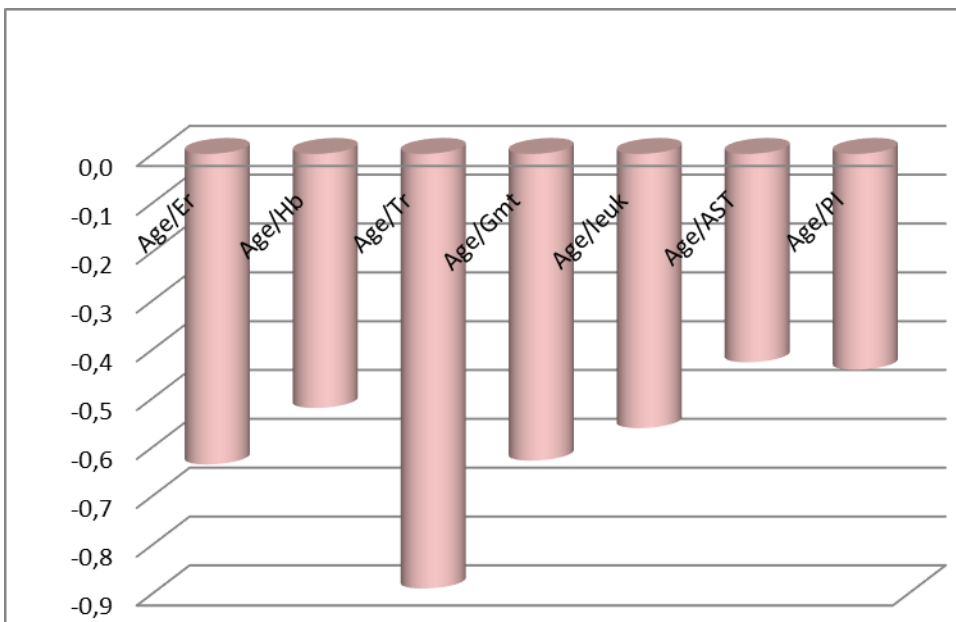


Fig. 3. Effect of age on blood counts

A negative effect of increasing age on the parameters of erythrocytes (-0.63), hemoglobin (-0.52), platelets (-0.89), HMT (-0.63), leukocytes (-0.56), AST (-0.42) and PI (-0.44), with a strong direct correlation with INR (0.79) (fig. 3.1). Thus, in response to the age-related decrease in hematopoiesis under conditions of severe stress - CSTBI, there was a compensatory increase in the factors involved in INR (PI).

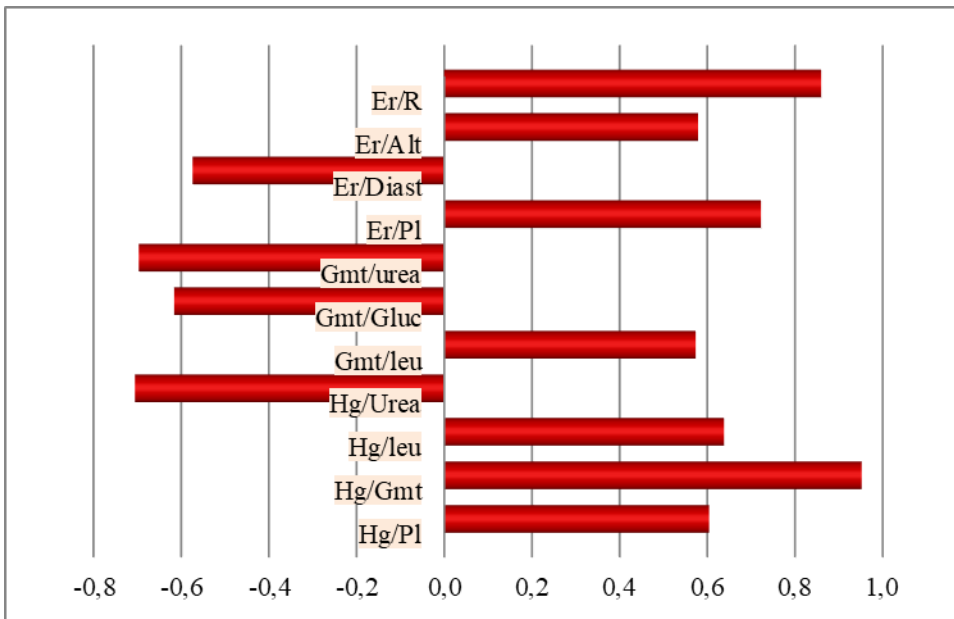


Fig. 4. Correlation links of the red part of blood

A direct strong correlation (fig. 4) was found between the number of erythrocytes and the index of blood clot retraction (0.84) and less pronounced with the ALT index (0.6). As well as the level of hemoglobin and HMT (0.87). A negative correlation was observed between HMT and the concentration of glucose (-0.6) and blood urea (-0.65). Attention is drawn to the direct relationship between HMT and leukocytes (0.6), hemoglobin and the number of leukocytes (0.6), the level of hemoglobin and the number of platelets (0.6). The revealed correlations, apparently, reflect the synergism of the functional activity of the hematopoietic function and the immune response in the acute period of CSTBI.

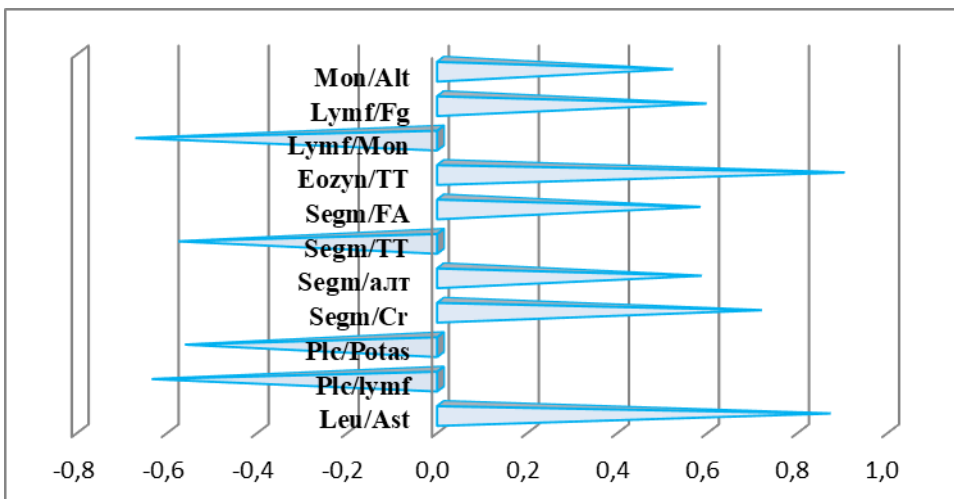


Fig. 5. Correlation connections of the white part of blood

Fig. 5 shows the correlations of the components of the white part of the blood, where a strong direct correlation was found between the number of eosinophils and TT (0.84), leukocytes and

AST (0.82). The revealed features characterize a close relationship between the integrity of cellular structures (AST), hemocoagulation and the severity of an acute systemic inflammatory response to severe trauma.

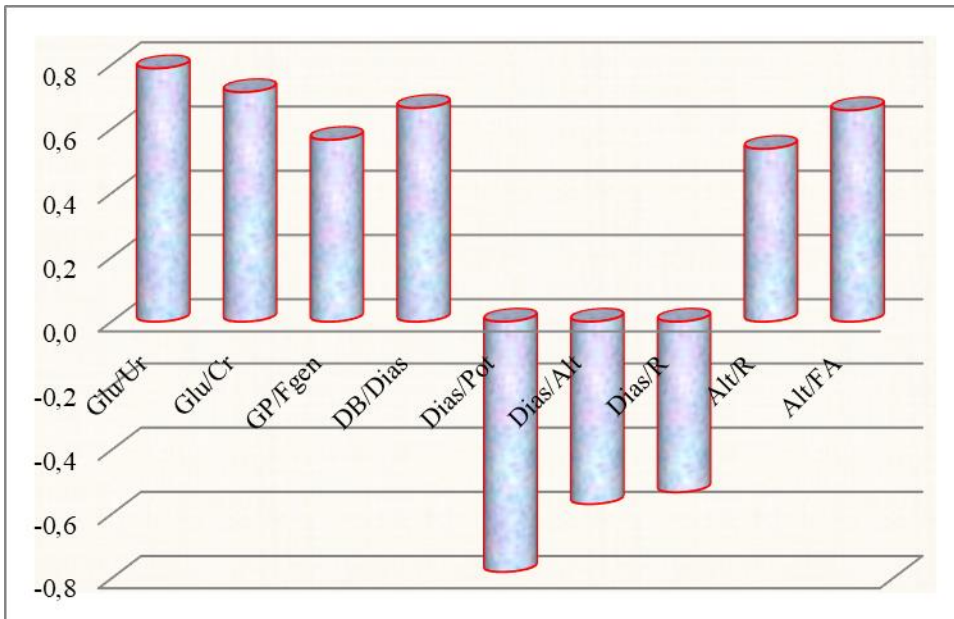


Fig. 6 Correlation links of blood biochemical parameters

Direct correlations were revealed between glucose and blood urea (0.8), glucose with plasma creatinine concentration (0.7), total protein with plasma fibrinogen levels (0.6), direct bilirubin with blood diastase (0.7), ALT and fibrinolytic activity of plasma (0.7) (fig. 6).

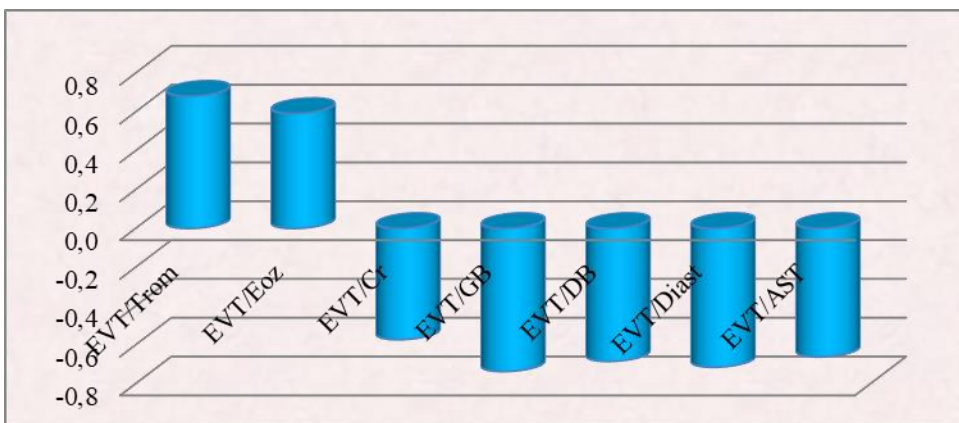


Fig. 7. Correlations between blood parameters and EVT

A moderate direct correlation was found between EVT and the number of platelets (0.7) and the number of eosinophils (0.6). While the effect of the hypersympathotonic response on trauma had

an opposite effect on creatinine levels (-0.6), total and bound blood bilirubins (-0.7; 0.7), blood diastase activity (-0.7) and AST level (-0.7) (fig. 7) in the first 8 days after CSTBI.

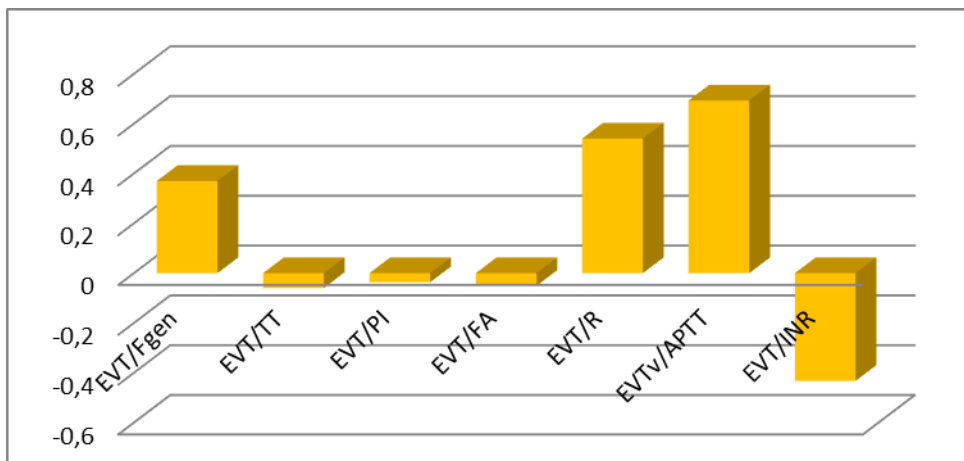


Fig. 8. Correlations between the components of the hemostasiogram and EVT

The relationship between the autonomic response and the hemocoagulation system in the first week after severe trauma is shown in Fig. 8. It reliably reflected the stimulating effect of the hypersympathotonic response to APTT (0.69), to a lesser extent on clot retraction (0.54), and the plasma fibrinogen level (0.4). At the same time, there was a tendency to the formation of feedback between EVT and INR (-0.4). It should be noted that the obtained indicators are the result of intensive therapy with timely correction of deviations from physiological standards with an average value of the mesor of the circadian rhythm EVT of $1.67 \pm 0,07$ units

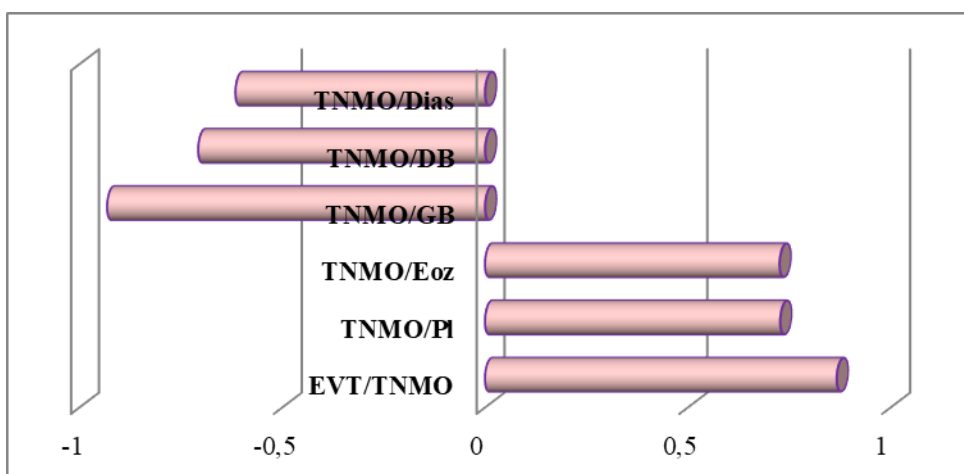


Fig. 9. Relationship of blood parameters with TNMO

The ongoing treatment of the early acute period of traumatic illness also changed the correlation between hemostasis indicators and myocardial oxygen demand, which on average increased during the first week to $108 \pm 0.3\%$. Thus, a direct strong dependence of TNMO on EVT (0.87) was revealed, as well as a direct relationship between myocardial oxygen demand and the

number of platelets in the blood (0.72), and eosinophils (0.72) (fig. 9). That is, despite the ongoing anti-inflammatory therapy during the first 8 days, signs of the activity of factors causing prolonged myocardial hypoxia were found, this is the severity of the inflammatory response, activation of hematopoiesis, hypersympathetic response. That is, the ongoing stress-limiting therapy was not effective enough in terms of protecting the myocardium from oxygen starvation, which inevitably leads to a decrease in compensatory activity and adaptive hemodynamic capabilities already in the first week after CSTBI.

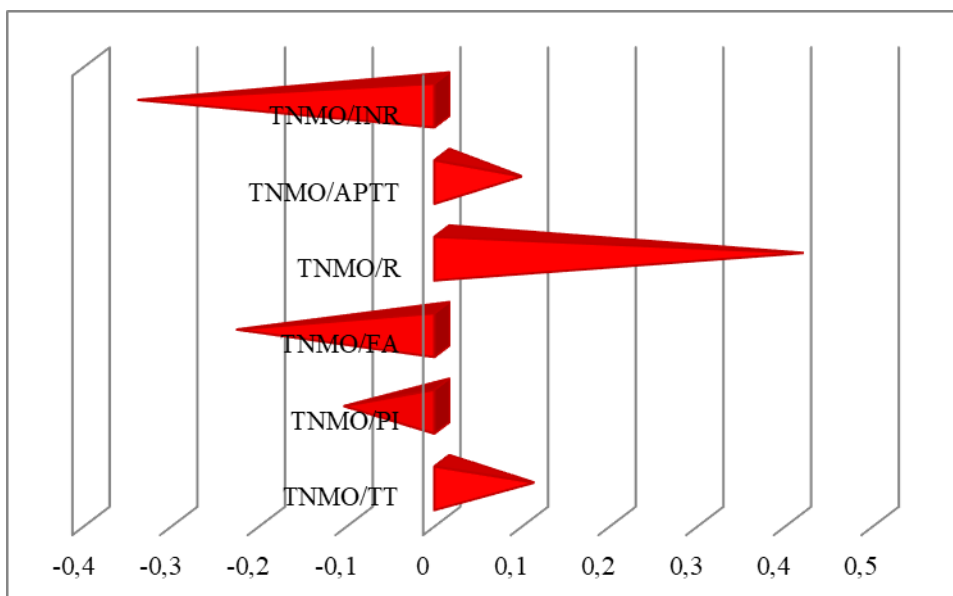


Fig. 10. Correlation of hemostasis parameters with TNMO in the first 8 days after injury

The ongoing intensive therapy somewhat reduced the negative effect of changes in hemostasis parameters on TNMO (fig. 10). Thus, there was a tendency to increase TNMO with an increase in the retraction time of the blood clot (0.41). The conducted stress-limiting therapy proved to be insufficiently effective in protecting the myocardium from oxygen starvation, which inevitably leads to a decrease in compensatory activity and adaptive hemodynamic capabilities already in the first week after CSTBI.

Conclusions. Timely blood transfusion therapy made it possible to maintain the parameters of erythrocytes, hemoglobin, hematocrit within the normative values. The tendency to an increase in glucose in the blood was revealed on day 4.5, which corresponds to the acrophase of the about-week rhythm of the inflammatory reaction. On the 5th day, an increase in stabs was noted up to $11 \pm 4.8\%$ and up to $13 \pm 2\%$ on the 6th day. Hyperglycemia in the acrophase of a weekly biorhythm on days 4-5 caused a decrease in immune tolerance and an exacerbation of the systemic inflammatory response on days 6. The trend towards an increase in AST throughout the observation period caused a trend towards hypercoagulability, decreasing APTT (-0.89). The

synergism of the functional activity of the hematopoietic function and the immune response in the acute period of CSTBI was revealed.

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