Research Article

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The Effect of the Enteral Homeostasis Correction Program on the Hemorheological Pattern in Acute Poisoning With Corrosive Substances

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BACKGROUND Poisonings with corrosive substances in Russia retains a high proportion among acute exotoxemias. They are accompanied by severe homeostasis disorders with changes in hemorheological pattern in particular.

AIM OF STUDY To evaluate the effect of the enteral correction of homeostasis (ECH) on the hemorheological patterns in patients with acute poisoning with corrosive substances.

MATERIAL AND METHODS Patients with chemical burns of the mucous membrane of the esophagus of the 2nd-3rd degree and stomach of the 2nd-3rd degree who were treated at the N.V. Sklifosovsky Research Institute for Emergency Medicine in 2017–2021 were examined. In 73 patients, ECH was performed (study group), and 35 patients received standard treatment (comparison group). Indicators of hemorheological status were examined on the 1st, 3rd and 5th days in the course of ongoing therapy, as well as before and after intestinal lavage in patients of the study group. Statistical data analysis was carried out using the Statistica 10 software package (StatSoft, Inc., USA).

RESULTS The first stage of ECH, characterized by the use of intestinal lavage, has no negative effect on hematocrit, plasma viscosity and erythrocyte aggregation indices.
The use of a glucosated enteral solution led to a decrease in plasma viscosity under normal hematocrit conditions at all follow-up periods. In patients of both groups, there was a decrease in blood viscoelasticity under conditions of high shear potential at all stages of the study, which indicates violations of the deformability of red blood cells. This process is more significant in individuals of the comparison group. The conducted studies have shown that standard treatment and ECH for poisoning with corrosive substances have a corrective effect on the hemorheological profile aimed at stabilizing blood circulation, however, according to a number of indicators, the effect of ECH is more pronounced.

CONCLUSION The program of enteral correction of homeostasis and standard treatment for poisoning with corrosive substances have a unidirectional effect on the indicators of the hemorheological pattern. In cases of application of the enteral homeostasis correction program, the outstripping improvement of the majority of the studied hemorheological parameters is seen.
Keywords: transcranial magnetic stimulation, TMS, eloquent brain areas, preoperative planning, neuronavigation
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CS – corrosive substances
ECP – enteral correction program
ES – enteral solution
GES – glucose enteral solution
IA – red blood cells aggregation index at rest
IA_1 – red blood cells aggregation index in motion
IL – intestinal lavage
MCV – mean cell volume

RELEVANCE

Despite the changes that occurred at the beginning of the 21st century in the general structure of acute exotoxicoses, poisoning with corrosive substances (CS) retains a high proportion [1, 2]. According to the CIS specialized toxicological centers in 2001–2016, patients with acetic acid poisoning averaged from 7.2 to 14.6% of the total number of patients with acute exogenous poisoning [2–5].

Corrosive substances have a local and resorptive effect on the body, which leads to significant disturbances in homeostasis, including hemorheological status.

Since the first half of the 20th century, the contribution of the rheological properties of blood to the efficiency of blood flow and tissue perfusion has been the subject of extensive research. The particular importance in blood viscosity was given to impairment of the deforming and aggregation properties of red blood cells when assessing microcirculation, which manifest themselves at any level of hematocrit and in vessels of any diameter; these disorders were directly associated with the processes of oxygen exchange in tissues [6–8]

Studies were carried out to study violations of hemorheology and in patients with acute poisoning, mainly with psychotropic drugs. It was found that already in the first hours of chemical injury there are disorders of viscous, viscoelastic and aggregation parameters of blood. Their severity depends on the severity of poisoning and the exposure of the toxicant in the body; they play an important role in the dynamics of the pathological process. In this regard, sufficient attention was paid to the development of methods for their correction, as well as the influence of the applied treatment methods on their dynamics [9–11].

The aim of the study was to evaluate the effect of the enteral homeostasis correction program on the hemorheological profile in patients with acute CS poisoning.

MATERIAL AND METHODS

An open prospective randomized study was conducted on the basis of the Department of Acute Poisoning and Somatopsychiatric Disorders of the N.V. Sklifosovsky Research Institute for Emergency Medicine in the period 2017–2021 after the approval of the Biomedical Ethics Committee (Minutes No. 5–16 dated November 21, 2016). The selection of patients was carried out in accordance with the inclusion criteria (age up to 65 years, the time of oral administration of CS no more than 6 hours before hospitalization, the presence of a chemical burn of the mucous membrane of the mouth, pharynx, esophagus and stomach of the 2nd–3rd degree according to the classification of S.V. Volkov and co-authors [12]). The diagnosis of chemical burns and subsequent monitoring of the condition of the mucous membrane of the upper gastrointestinal tract was set using esophagogastroduodenoscopy.

Seventy-three patients were examined, of which 38 people (24 men and 14 women) aged 47 (34.0; 57.5) years who underwent the program of enteral homeostasis correction (ECP) constituted the study group; the comparison group with standard treatment included 35 people (24 men and 11 women) aged 42 (32.5; 54.5) years.

On the first day of hospital stay after the administration of analgesics, antispasmodics and gastric tube lavage patients underwent intestinal lavage (IL) using enteral solution (ES). The composition of this solution includes: sodium phosphate, sodium chloride, sodium acetate, potassium chloride, citric acid, complexone disodium salt of ethylene diaminetetraacetic acid, as well as calcium chloride and magnesium sulfate, drinking purified water. ES was prepared from a set of commercially available mineral acid concentrate. To do this, the concentrate was dissolved in a given volume of water according to the manufacturer's instructions attached to the set of concentrates. The osmolarity of the solution is 290–310 mOsm/l (depending on the volume of water used to dissolve the salts), pH≈5.8 [13]. The solution, the temperature of which was 18–22°C, was given to the patient to drink 200 ml every 5 minutes. In 1.5–2 hours the diarrhea developed. IL was carried out until light translucent water appeared from the rectum, after which the patient stopped drinking the solution. During the next 30–40 minutes, defecation continued, then spontaneously stopped. The total volume of the solution ranged from 3 to 4.5 liters. The IL procedure lasted an average of 3 hours. Patients tolerated it satisfactorily, there were no reactions or complications. In cases where patients, due to the severity of the condition, could not independently take ER, it was administered through a nasogastric tube. In the next 4 days, fractional oral administration of a glucosated enteral solution — GER (GER is an ER supplemented with 2 g of glucose per liter) of 200 ml at regular intervals in a total volume of 3–4 liters per day was carried out. "Hilak forte" was added to the GER, 60 drops 3 times a day, and "Pektovit" 5.5 g 3 times a day was also prescribed. At the same time, intravenous administration of saline and plasma-substituting solutions was excluded.

Standard treatment included detoxification infusion therapy and forced diuresis, followed by maintenance infusions of 2–3 liters per day. Patients of both groups received the same pathogenetic and symptomatic treatment.

The hemorheological status indicators were studied on the 1st, 3rd and 5th days during the therapy, as well as before and after the IL in the patients of the study group.

The study of blood viscosity and elasticity was performed on a VioProfiler capillary viscometer (USA). The analysis of the results included the evaluation of the parameters corresponding to the rheological model: at a high shear rate (62.8 s^{-1}) corresponds to the start of the formation of "coin columns" of RBC [14]. Aggregation indices of RBC at rest (IA) and in motion at a shear rate of 3s^{-1} (IA_1) were determined by the MA-1 aggregometer (Myrenne GmbH, Germany) [15], hematocrit was determined by the Act diff 2 Beckman Coulter hematological analyzer (USA). Parameters obtained during examination of 45 blood donors (30 men and 15 women) aged 20–40 years were used as normal values.

Statistical data analysis was carried out using the *Statistica* 10 software package (*StatSoft Inc.*, USA). The nature of the distribution of the obtained data was assessed using the Shapiro–Wilk test, and, in accordance with the result, nonparametric tests were used. Descriptive statistics of quantitative traits are presented as medians and quartiles in Me (LQ; UQ) format. Comparative statistics of intergroup differences were assessed according to the Wilcoxon criteria (at the stages of the study) and Mann-Whitney (differences between groups and from the norm). The threshold level of significance (*p*) was taken to be less than 0.05.

RESULTS

The data presented in Table 1 show that after IL there was a normalization of slightly elevated hematocrit, plasma viscosity and IA. At the same time, IA_1 , although it showed a tendency to normalization, remained increased compared to the norm by 21.6% ($p \geqslant 0.05$).

Table 1

Influence of intestinal lavage on some hemorheological parameters in case of poisoning with corrosive substances (n=38)

Indicators	Research stages			
	Norm	Before IL	After IL	Δ, %
Hematocrit, vol.%	40.4 (40.05; 40.76)	44.3 (40.3; 49.5)	39.8[1] (36.5; 42.4)	-10
Plasma viscosity, mPa·s	1.80 (1.78; 1.82)	1.91 (1.85; 2.3)	1.76 (1.5; 1.9)	-8
Resting RBC aggregation index (IA)	15.6 (15.02; 16.18)	17.0 (15.8; 21.3)	15.7 (15.3; 16.2)	-8
Index of erythrocyte aggregation in motion (IA_1)	18.9 (18.17; 19.63)	24.8* (19.3; 27.6)	23.0 (18.7; 26.3)	-7.5

Notes: * - statistically significant difference from the norm (p<0.05 according to the Mann-Whitney test); [1] — statistically significant difference between the stages of the study (p<0.05, according to the Wilcoxon test). IL - intestinal lavage

From the data presented in Table 2, it follows that the hematocrit at all stages of the study did not have a statistically significant difference from the normal value. The plasma viscosity in the subjects of the study group at all stages of the study was below the norm by an average of 1.4-fold. In the comparison group, it increased from normal values to exceeding the norm on the 3rd and 5th days by 10% and 25%, respectively.

Table 2

Comparative evaluation of the influence of the program of enteral correction of homeostasis and standard treatment on the dynamics of hemorheological parameters in patients with acute poisoning with corrosive substances

Indicators	Norm	Research stages					
		1st day		3rd day		5th day	
		Study group	Group comparisons	Study group	Group comparisons	Study group	Group comparisons
Hematocrit, %	40.4 (40.05; 40.76)	43.15 (39.20; 48.05)	38.2 (36.2; 45.7)	40.75 (38.05; 45.20)	39.5 (27.5; 43.9)	40.20 (37.40; 44.05)	42.7 (40.9; 48.0)
Plasma viscosity, mPa s	1.80 (1.78; 1.82)	1.30^{*2} (1.23; 1.39)	1.76 (1.33; 2.2)	1.27^{*2} (1.18; 1.38)	1.95 (1.41; 2.5)	1.28^{*2} (1.20; 1.32)	2.35 (2.00; 2.5)
Resting RBC aggregation index (IA)	15.60 (15.02; 16.18)	15.50 (13.90; 16.10)	11.9* (9.1; 17.4)	15.55 (12.55; 16.05)	15.4^{1} (12.7; 19.65)	16.35^{2} (14.45; 17.30)	21.25 (16.9; 23.9)
RBC aggregation index (IA_1)	18.90 (18.17; 19.63)	24.90 (18.10; 27.70)	22.0 (17.3; 27.0)	25.50* (22.35; 26.45)	26.7^{*1} (22.25; 30.7)	27.75* (24.30; 31.25)	31.40* (26.6; 36.1)
Platelet count, $\times 10^{9}$/l	196 (187; 204)	207.0 (175; 249)	200.5 (157; 267)	167.5 (129.0; 199.0)	168 (95; 295)	179.5 (131.5; 207.0)	227.5 (165; 294)
Blood viscosity, mPa·s at shear rate:							
2.5 s^{-1}	5.9 (5.75; 6.05)	5.24 (4.38; 6.01)	4.1* (3.02; 5.03)	5.39 (4.65; 8.60)	4.18* (2.34; 5.12)	5.66 (4.97; 8.19)	4.6 (4.32; 6.54)
12.6 s^{-1}	4.8 (4.68; 4.92)	4.20 (3.38; 4.96)	3.44* (2.24; 4.15)	4.6 (3.78; 5.55)	3.62 (1.95; 4.37)	4.73 (4.06; 5.62)	3.95* (3.89; 5.41)
62.8 s^{-1}	4.1 (4.02; 4.15)	4.19 (3.51; 4.68)	3.24* (2.62; 4.03)	4.11 (3.70; 5.67)	3.20* (2.65; 3.79)	4.54^{2} (3.69; 6.01)	2.85 (2.56; 3.82)
Viscoelasticity, mPa·s, at shear rate:							
2.5 s^{-1}	3.13 (3.02; 3.24)	2.98 (2.06; 3.66)	1.94* (1.27; 2.65)	3.13 (2.53; 3.95)	2.01* (0.83; 3.02)	3.49 (2.73; 4.09)	2.92 (2.4; 3.48)
12.6 s^{-1}	1.55 (1.48; 1.62)	1.53 (1.00; 2.05)	1.0 (0.58; 1.56)	1.58 (1.22; 2.97)	1.16 (0.48; 1.83)	1.91 (1.43; 3.26)	1.55^{1,2} (1.33; 1.75)
62.8 s^{-1}	0.61 (0.57; 0.65)	0.28* (0.21; 0.33)	0.21* (0.13; 0.42)	0.28* (0.21; 1.91)	0.23* (0.18; 0.42)	0.29 (0.25; 1.97)	0.37* (0.28; 0.40)
MCV	80–100	90.55 (86.5; 92.75)	94 (90.9; 97.0)	90.2 (86.2; 91.4)	95.0 (88.6; 99.05)	90.7 (87.05; 91.65)	95.3 (93.3; 103.0)

Notes: * — statistically significant difference from the norm ($p<0.05$ according to the Mann-Whitney test); ^{1} — statistically significant difference between the stages of the study ($p<0.05$, according to the Wilcoxon test); ^{2} — statistically significant difference from the comparisons indicator ($p<0.05$, according to the Mann–Whitney test). MCV — Mean Cell Volume

In patients of the study group, IA during the study did not have statistically significant differences with the norm. At the same time, the initially reduced indicator in the comparison group showed an increase in the study in dynamics and on the 5th day was higher than the norm by 26.5%. The values of IA_1 in patients of both groups at all stages were above the norm from 14 to 39.8%, to a greater extent in the comparison group. The number of platelets had no statistically significant differences from the norm.

The blood viscosity at a low shear rate in the study group of patients in the course of treatment was within the normal range. In the compared group, it was below the norm initially by 30% and on the 5th day — by 22%, that is, it showed a tendency to normalization. At an average shear rate, no statistically significant differences in blood viscosity with the norm were found in the subjects of the study group, while in the comparison group it was initially reduced by 28%, and on the 5th day by 17.7%. In the study group, at a high shear potential rate, blood viscosity was within the reference values. In the compared group, it was initially reduced and subsequently had a negative trend.

In the study group, at low and medium shear rates, blood viscoelasticity did not have statistically significant differences from the norm. In patients of the comparison group, it was initially reduced, and in dynamics showed a tendency to normalization. At a high rate of shear potential, this indicator was statistically significantly below the norm in both groups of patients at all stages of the study. In all cases, the mean erythrocyte volume was within the normal range.

DISCUSSION

Efficient tissue perfusion and oxygenation is provided only with an optimal ratio of microcirculation parameters, blood rheological profile and its oxygen capacity [16, 17]. The main integral rheological characteristic of blood is its dynamic viscosity. It is determined by plasma viscosity, hematocrit value; aggregation properties of blood cells and deformability of erythrocytes [18]. Each of the above factors can play a certain role in changes in tissue perfusion [8, 19]. There is evidence that plasma viscosity, hematocrit, and erythrocyte deformability are involved in the regulation of functional capillary density and arteriole tone [20]. However, the contribution of each of the factors to the efficiency of tissue blood flow is currently insufficiently studied.

Our studies have established that the first stage of ECP, characterized by the use of IL, does not adversely affect hematocrit, plasma viscosity, and RBC aggregation indices. In general, this contributes to their stabilization at normal or subnormal levels.

At the second stage, the use of GER, a decrease in plasma viscosity was found in the study group under conditions of normal hematocrit. This effect was maintained throughout the observation period.

Plasma is a complex biological medium that includes proteins, carbohydrates, lipids, metabolic intermediates, various salts, hormones, other biologically active compounds, and dissolved gases [21, 22]. Therefore, a change in the concentration of plasma proteins and, especially, fibrinogen and immunoglobulins can significantly affect the value of plasma viscosity [23].

In the regulation of blood flow, the viscosity of whole blood, plasma and hematocrit play a certain role. Previously, it was shown that optimally high values of blood viscosity, plasma and/or hematocrit are required for optimal microvascular perfusion [24, 25].

Information has been obtained that, during hemodilution, a decrease in plasma viscosity can contribute to a decrease in shear stress on the wall and a lower production of nitric oxide by vascular endothelial cells [26]. This has a negative effect on microcirculation processes. At the same time, a moderate increase in hematocrit under hemodilution conditions can be effective for a regulatory increase in the density of functioning capillaries and for the production of nitric oxide by the vascular endothelium [24, 27].

The decrease in blood viscoelasticity found by us under conditions of high shear potential in patients of both groups at all stages of the study indicates violations of the deformability of erythrocytes. This process is more pronounced in the persons of the comparison group, which is confirmed by their lower viscoelasticity at other shear potential rates.

Deformability is determined by such factors as cytoplasmic viscosity, membrane viscoelasticity, cell shape and volume [28–30]. Changes in deformability are observed in various diseases and pathological conditions [8]. Their causes are numerous, including changes in the protein and lipid structures of the erythrocyte membrane induced by oxidative stress, as well as changes in the lipid layer of the membrane [17].

It can be assumed that, in our studies, one of the factors contributing to this process is oxidative stress, which occurs in the first hours of chemical injury, persists at an early stage of the disease, and leads to damage to the lipid layer of the erythrocyte membrane [31]. There is no change in the average volume of these cells. Violation of the deformability of erythrocytes leads to disorders of their aggregation. In our studies, this is indicated by increased values of the erythrocyte aggregation index in motion.

It is traditionally believed that erythrocyte aggregation significantly affects blood viscosity at relatively low shear rates [17, 32]. Therefore, when blood flow slows down, one can assume an increase in aggregation and an increase in its contribution to the viscous resistance to blood flow [17]. However, in some cases, erythrocyte aggregation has a positive effect on blood flow, for example, it is involved in the formation of the Fahraeus effect and reduces hematocrit in microvessels [33]. Since endothelial function is modulated by shear stress acting on the vessel walls, erythrocyte aggregation can affect the viscosity and thus the radial distribution of RBC flow in the vessel [34].

In our opinion, in patients with CS poisoning, a moderate decrease in deformability and an increase in erythrocyte aggregation, detected at the stages of the study, are compensatory in nature, aimed at maintaining the microcirculation level that is optimal for a given physiological situation.

Thus, the conducted studies have shown that the standard treatment and the program of enteral correction of homeostasis in case of poisoning with corrosive liquids have a corrective effect on the hemorheological profile, aimed at stabilizing blood circulation.

CONCLUSION

1. The program of enteral correction of homeostasis and standard treatment for poisoning with corrosive substances have a unidirectional effect on the parameters of the hemorheological panel.

2. In cases of application of the program of enteral correction of homeostasis indicators, the outstripping positive dynamics of the majority of the studied hemorheological parameters is determined.

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