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A DIFFERENTIATED APPROACH TO INFUSION-TRANSFUSION THERAPY FOR LARGE BLOOD LOSS IN PATIENTS WITH POLYTRAUMA

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ABSTRACT

| Received: 26 November 2020 | With polytrauma, more than 30% of victims are diagnosed with severe |
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| Accepted: 05 February 2021 | blood loss, grade III MARINO of the leading components is transfusion |
| Published: 10 February 2021 | therapy, which aims to restore the erythron system and improve the |
| KEYWORDS polytrauma, blood loss, oxygen transport system, postoperative period. | - runctional state of the oxygen transport system. The addition to intensive care of substances that affect lipid peroxidation and energy status of cells can reduce the number of heterogeneous transfusions and thus reduce the number of complications in the postoperative period. Such substances may be a solution of ceruloplasmin with a leading antioxidant effect and a solution of D-fructose-1,6-diphosphate sodium salt of the hydrate with an energetic effect. Criteria for exposure to these substances should be indicators such as blood levels of hemoglobin, phosphorus, malonic dialdehyde and lactate / pyruvate ratio. |

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Introduction. Analysis of injuries in recent years has shown a significant (3 times) increase in the number of victims with combined trauma complicated by shock with blood loss [1, 2]. Mortality in this group of victims reaches 68-90% [3, 4]. One of the leading conditions in providing emergency care to victims with combined chest and abdominal trauma with polytrauma is intensive care, the focus and significance of which depends on the timely diagnosis of the severity of the victim, volume, degree and rate of blood loss [5]. Despite the significant progress made in recent decades in compensating for acute massive blood loss and prevention of possible postoperative complications, mortality from it remains quite high and varies from 30 to 90% [6, 7].

Tactics of perioperative infusion-transfusion therapy is based on clinical assessment of blood loss, mean blood pressure, heart rate, hemoglobin, hematocrit, acid-base parameters and blood gases and other parameters [8]. The analysis of the depth of changes in these indicators, central hemodynamics, parameters of cellular, humoral and gas systems of the body, oxygen transport function of the blood and peripheral circulation are very important in the acute period of blood loss. With adequate infusion-transfusion therapy, primarily with the possibility of reinfusion, the clinical condition of patients improves from the first day of stay in the intensive care unit [9, 10].

Today, there are many algorithms for the correction of blood loss in various clinical situations, including patients with polytrauma. However, the issues of metabolic adaptation of circulating erythron in response to different options for the introduction of hemo- and plasma correctors are still unresolved. This is why the issues of intensive care of blood loss, including patients with polytrauma,

need detailed study and scientific substantiation, followed by the provision of recommendations for examination, intensive care and intensive care.

The aim of the study was to increase the effectiveness of treatment of patients with polytrauma with hemorrhagic shock through the development and implementation of a differentiated approach to infusion and transfusion therapy based on the clarification of the mechanisms of systemic oxygen transport in the postoperative period

Materials and methods. This study is based on the analysis of the results of a comprehensive clinical-instrumental and laboratory dynamic study of hemodynamic, biochemical in 96 patients with polytrauma who were treated at the polytrauma department and intensive care unit for patients with combined trauma in Kharkiv City Clinical Emergency Hospital in the period 2017 - 2020, which evaluated the effectiveness of the proposed treatments in the process of cohort prospective randomized simple open-label clinical trial. The conditions for selecting patients for the study were age up to 60 years, the presence of polytrauma, the possibility of productive contact with the patient at admission (14-15 points for GCG), obtaining informed consent, compensation at the time of injury of any comorbidities, no history blood, cancer, severe heredity, alcoholism, mental disorders, allergic reactions, blood transfusions, the use of immunocorrectors, glucocorticoids.

Criteria for non-inclusion were age over 60 years, the presence of damage to the craniofacial anatomical and functional area, as well as abdominal organs, musculoskeletal system on the severity scale (AIS), which belonged to the category of "critical injury, survival is unlikely", the presence of post-traumatic heart attack.

In order to stratify patients, the severity of the injury was taken into account according to the ISS scale (Injury Severity Score) – all patients had 9-24 (medium severity) points, its combination, mechanogenesis, concomitant somatic pathology, time since injury, anesthesia and surgery. All victims at the time of admission had a deficit of circulating blood volume (BCV) of III degree according to MARINO (1998) – 30-40%. BCV deficit was calculated with the formula: BCV def. = BCV p.-BCC f., where BCCp. – proper BCC (for women 60 ml / kg, for men 70 ml / kg, pregnant and overweight 75 ml / kg); BCV f. – actual BCV = body weight, kg / part by weight of Ht (hemoglobin). All patients during the operation, against the background of diuresis control as a component of infusion-transfusion therapy were transfused 1 dose – 450 \pm 45 ml – donor erythrocytes to maintain normal oxygen transport function of the blood in the postoperative period.

The selection of patients was carried out in accordance with the goal and objectives.

After the analysis of the obtained indicators at the screening stage against the background of no probable difference between the figures of the obtained indicators in each of the groups – the number of points and the APACHE II scale averaged 13.1 ± 1.6 points – we combined all data and took the average values with the interval min-max.

To implement the study and study the impact of a differentiated approach to the correction of blood loss on the consequences of the course of patients with traumatic disease, patients were divided into 3 randomized groups: group 1, 26 patients (16 men, 10 women) with mean age 47.7 \pm 4.6 years, time from the moment of injury 2.02 \pm 0.47 hours; group 2 – 32 people (20 men, 12 women) with average figures of age 48.1 \pm 3.8 years, time from injury 2.01 \pm 0.61 hours, who were additionally prescribed D-fructose-1.6 -disophate sodium salt hydrate 150 mg / kg 2 times a day intravenously at a rate of 10 ml per minute for 14 days; group 3 – 34 persons (20 men, 14 women) with average age of 47.1 \pm 3.9 years, time from injury 2.06 \pm 0.42 hours, who in addition to the developed algorithm of intensive care was prescribed a solution of ceruloplasmin in a daily dosage of 5 mg / kg, diluted in 200 ml of 0.9% sodium chloride solution at a rate of 30 drops per minute intravenously for 14 days in patients with polytrauma with heavy blood loss.

Given the fundamental differences in pharmacodynamics and pharmacokinetics of additionally prescribed substances for the functional state of the oxygen transport system in patients with massive blood loss in the postoperative period, it was important to control the number of repeated blood transfusions to achieve a satisfactory state of homeostasis in patients. 3 and 10 days of the postoperative period were selected as control points: the state of erythrocyte metabolism was determined by monitoring the level of hemoglobin, phosphorus, malonic dialdehyde in the blood of patients, and the lactate / pyruvate ratio was determined. 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. Since the transfusion of donor erythrocytes is aimed at restoring the volume of circulating erythrocytes and maintaining normal oxygen transport function of the blood, clinically it reproduces a decrease in shortness of breath, tachycardia, increased hemoglobin in the blood. The effectiveness of the erythrocyte transfusion procedure depends on the initial parameters of the hemoglobin level, the presence or absence of cessation of bleeding, the hematocrit of the transfusion medium and its shelf life.

Given that the decrease in physical and muscular activity is accompanied by a decrease in the body's need for oxygen, against this background, excessive desire to quickly restore hemoglobin levels can lead to the development of cardiovascular failure and increase thrombogenic hazard.i Especially dangerous is the desire in case of hemorrhagic shock. very often accompanied by the development of intravascular coagulation syndrome. Erythrocyte transfusion always exacerbates this syndrome in such situations.

Since there are no absolute indications for heterologous blood transfusion, and the severity of the patient's bleeding does not depend on the level of hemoglobin and hematocrit, it is important to differentiate the approach to infusion and transfusion therapy in victims with polytrauma with heavy blood loss.

When performing a statistical analysis of hemoglobin in the blood, the number of blood transfusions with a single dose $(450 \pm 45 \text{ ml})$ of erythrocyte mass in order to maintain the functional state of the oxygen transport system at a satisfactory level in patients groups 1, 2 and 3 at the time of admission (table 1), 3-th (table 2) and the 10th day (table 3) of intensive care, the data were obtained, which are presented in table 1.

| Table 1. | | | |
|---|--------------------------|--------------------------|--------------------------|
| Indicators | Group 1 (26 patients) | Group 2 (32 patients) | Group 3 (34 patients) |
| Hemoglobin, g / l | 92,7±8,1 | 87,4±9,6 | 90,9±7,2 |
| Number of heterogeneous blood transfusions | 1,2±0,4 | 1,1±0,2 | $1,1{\pm}0,1$ |
| Phosphorus, mmol / 1 | 1,06±0,22 | 1,07±0,19 | $1,06\pm0,17$ |
| Malonic dialdehyde, µmol / l | $1,24{\pm}0,08$ | 1,21±1,1 | $1,22\pm1,1$ |
| Lactate / pyruvate | 122,4±14,1 | 126,1±12,9 | 122,8±10,6 |

Table 2.

| Indicators | Group 1 (26 patients) | Group 2 (32 patients) | Group 3 (34 patients) |
|---|--------------------------|--------------------------|--------------------------|
| Hemoglobin, g / l | 92,7±8,1 | 87,4±9,6 | 90,9±7,2 |
| Number of heterogeneous blood transfusions | 3,2±0,6 | 1,9±0,4* | 2,1±0,2** |
| Phosphorus, mmol / 1 | $0,78{\pm}0,04$ | 0,82±0,01 | 1,02±0,04**° |
| Malonic dialdehyde, µmol / l | $1,09\pm0,02$ | $0,62{\pm}0,01$ | 1,02±0,02° |
| Lactate / pyruvate | 76,2±10,4 | 45,8,1±16,9* | 54,2±7,4** |
| * - $p < 0.05 - probable difference be$ | tween groups 1 and 2. | | |

* - p<0,05 – probable difference between groups 1 and 2; **- p<0.05 – probable difference between groups 2 and 3;

 $^{\circ}$ - p<0,05 – probable difference between groups 1 and 3.

Table 3.

| Indicators | Group 1 | Group 2 | Group 3 |
|---|-----------------|---------------|---------------|
| | (26 patients) | (32 patients) | (34 patients) |
| Hemoglobin, g / l | 112,6±4,7 | 109,2±5,2 | 111,4±3,9 |
| Number of heterogeneous blood transfusions | 3,2±0,8 | 1,9±0,6* | 2,1±0,4** |
| Phosphorus, mmol / 1 | $1,04{\pm}0,24$ | 1,02±0,17 | 1,37±0,02** |
| Malonic dialdehyde, µmol / l | 0,92±0,16 | 0,22±0,07* | 0,76±0,19° |
| Lactate / pyruvate | 42,7±7,2 | 37,8±6,4 | 18,6±2,9**° |

* - p<0,05 – probable difference between groups 1 and 2;

**- p<0,05 – probable difference between groups 2 and 3;

 $^{\circ}$ - p<0,05 – probable difference between groups 1 and 3.

Statistical analysis revealed that at the time of admission, all groups of patients were randomized for hemoglobin, phosphorus, malonic dialdehyde in the blood, lactate / pyruvate ratio and the number of heterogeneous blood transfusions performed during surgery. Subsequently, on the 3rd day of intensive

care, patients in group 2 had a minimum number of blood transfusions, 1.9 ± 0.4 , which were performed to achieve the target level of hemoglobin in the blood as a leading component of the oxygen transport system. With. Also, these patients had a minimum level of malonic dialdehyde in the blood and the ratio of lactate / pyruvate, which indicated a minimal effect of anaerobic processes on the course of traumatic disease. Finding the level of phosphorus at the minimum allowable reference level, 0.82 ± 0.01 mmol / l, also indicated a satisfactory condition of the erythron system and blood buffers.

On the 10th day of intensive care there was a tendency of the predominant effect of differentiated infusion-transfusion therapy in patients of group 2 on the general state of homeostasis. Thus, patients in group 2 had significantly fewer heterogeneous blood transfusions, which meant the leading pathogenetic mechanism of complications in patients with polytrauma with massive blood loss. Although on the 10th day of treatment, lactate / pyruvate ratios were best in group 3 patients, and in group 2 patients they were also within the reference range. Given that the decisive factor in the results of the study was the number of heterogeneous blood transfusions, which were necessary to maintain homeostasis in patients with polytrauma with blood loss of III degree according to MARINO, the appointment of ceruloplasmin solution with leading antioxidant action was not the most period of traumatic illness in these patients.

Conclusions. Developed and implemented an algorithm for infusion and transfusion therapy in the perioperative period in patients with massive blood loss in polytrauma, which are prescribed to: influence the process of lipid peroxidation - additional introduction of ceruloplasmin solution in a daily dosage of 5 mg/kg, diluted in 200 mg % sodium chloride solution at a rate of 30 drops per minute intravenously for 14 days - allowed to minimize the number of heterogeneous blood transfusions and, in turn, the number of complications in the postoperative period.

Developed and implemented an algorithm for infusion and transfusion therapy in the perioperative period in patients with massive blood loss in polytrauma, which are prescribed to: influence the process of energy metabolism, including erythrocytes - additional introduction of a solution of D-fructose-1,6-diphosphate sodium salt hydrate 150 mg / kg 2 times a day intravenously at a rate of 10 ml per minute for 14 days - allowed to improve the systemic rate of systemic oxygen transport by accelerating the recovery of aerobic metabolism in tissues.

The study of the effect of the combination in the composition of infusion-transfusion therapy as a differentiated approach of ceruloplasmin solution and solution of D-fructose-1,6-diphosphate sodium salt of hydrate as substances that have fundamentally different mechanisms of action, but may reduce the transfusion of heterogeneous and heterogeneous compounds is promising, the course of traumatic illness.

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

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