JOURNAL OF CRITICAL REVIEWS
ISSN- 2394-5125 VOL 7, ISSUE 04, 2020

EFFICIENCY OF PLASMAPHERESIS IN THE TREATMENT OF MULTIPLE ORGAN FAILURE IN CHILDREN

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ABSTRACT

A total of 46 children aged 3 months to 14 years with diagnosed multiple organ failure were under observation in the anesthesiology and intensive care unit (AICU) and in the paediatric department of the RRCEM. Children were divided into the following age groups: infants (5), aged 3 to 7 years (19) and 7 to 14 years (22). In each age group, children were divided into two subgroups: children who received standard treatment (control group - 24) and children who received plasmapheresis along with standard treatment (main group - 22 children). In children from the main group after plasmapheresis in a short period of time there was a change in clinical manifestations towards, normalization of indicators, a significant decrease in breathing frequency and heart rate, increased blood oxygen saturation, normalization of blood pressure. All 46 children in groups 1 and 2 (after plasmapheresis) underwent immunocorrection with the immunological medication Octagam, in a dose of 30-50 mg/kg once a day, and repeat after a week. Inclusion of Octagam in the complex therapy led to a more rapid increase in the initially reduced indices of the cellular component of immunity, stabilization of the humoral immunity, shortening the time of antibacterial therapy, shortening the time of hospitalization in children of the main group (with plasmapheresis) than in children without plasmapheresis.

KEY WORDS: multiple organ failure syndrome, clinic, plasmapheresis, children.

INTRODUCTION

The progress achieved in the medicine of critical conditions has initiated a fundamentally new approach to the interpretation of the severity of the pathological process - the concept of a single pathogenesis and the interdependent progression of organ failure. Multiple organ failure is a universal lesion of all organs and tissues of an body by aggressive mediators of critical condition, with temporary prevalence of symptoms of insufficiency of one or another organ system [1,6,11,16].

In recent years, the number of children with multiple organ failure of various etiologies has increased. The high predisposition for the development of multiple organ failure syndrome (MOFS) in children compared with adults is explained by the imbalance in children of the mechanisms regulating the inflammatory response, the vulnerability of the homeostasis system and metabolic reactions, the immaturity of the immune and endocrine systems, which predispose them to contracting the infection and which further contributes to the progression of MOFS [3,7,12,14].

Despite some success to date in the treatment of MOF there is still no reliable effective therapy and the lethality rate from MOF remains high, within 35-45% [3,8,13,14].

According to opinion of some authors, in the treatment of MOF, special attention should focus on methods that can simultaneously affect several key components of pathogenesis and reduce the degree of organ dysfunction. One such method is plasmapheresis. [2,4,15]. It is a universal efferent method that allows the removal of toxic substrates of any nature, molecular weight and electrochemical charge. Plasmapheresis has a pronounced detoxifying, immunomodulating, deplasminating and draining effect, which allows it to affect all liquid fields of the body [7,9,10]. Accordingly, in recent years there has been renewed interest in the use of plasmapheresis in the treatment of multiple organ failure in children.

The aim of the research is to evaluate the effectiveness of plasmapheresis in the treatment of multiple organ failure in children.

MATERIALS AND METHODS

A total of 46 children aged 3 months to 14 years with diagnosed polyorganic insufficiency were under observation in the anesthesiology and intensive care unit (AICU) and in the paediatric department of the RRCEM. Multiple organ failure syndrome in children was defined as the presence of dysfunction of two or more body systems. Children were divided into the following age groups: infants (5), aged 3 to 7 years (19) and 7 to 14 years (22). In each age group, children were divided into two subgroups: children who received standard treatment (control group - 24) and children who received plasmapheresis along with standard treatment (main group - 22 children). Plasmapheresis was carried out by a «Hemofenix» apparatus. It is a membrane filtration type device. The continuous process of membranous plasmapheresis on this device is carried out according to the single-needle scheme in a sterile extracorporeal circuit of single application. During the procedure, the form elements are returned to the patient's bloodstream, plasma is collected in a special receiver and plasma substitution is performed.

Vascular support was provided by catheterization of the subclavian vein. An extracorporeal circuit was connected to the catheter, which was assembled directly at the patient's bedside under aseptic conditions. At the same time, a femoral vein catheterization was performed, which was used for medication support of the procedure and current appointments.

All patients were subjected to clinical examination: general examination of children using physical research methods. Non-invasive methods were used to determine blood oxygen saturation, body temperature, heart rate, respiration rate and blood pressure. Functional indices were determined using monitoring monitors of vital organs of Space Labs (USA), Dash 2000 "GE Medical Systems" (USA)."GE Médical Systems" (USA).

Also, all patients were carried out general clinical examination, biochemical blood tests (total protein, urea, creatinine, bilirubin, potassium, ALT, AST, lactate level, medium-molecular peptides), acid-alkaline state of blood, instrumental methods of examination (chest X-ray, ECG, according to the indications of echocardiography, CT-research). In addition, all patients were conducted immunological tests.

The level of cytokine (IL-1β , 6) in blood serum was determined by solidphase immunoenzyme analysis using test systems of Vector-Best LLP (Novosibirsk).

The data obtained were statistically processed using the Statistica 6.0 software.

All 46 children with multiple organ failure after plasmapheresis underwent immunocorrection by immunological drug Octagam, solution for infusions transparent, 20 ml 1g, 30-50 mg/kg 2 times, once a week (production of OCTAPHARMA Pharmazeutika Produktionsges, m.b.H (Austria) OCTAPHARMA NORDIK AB (Sweden)).

OCTAGAM is a solution for infusions transparent or slightly opalescent, from colourless to light yellow. 1 ml plasma protein 50 mg, including at least 95% IgG. The form of release 20 ml bottle contains 1g of active substance - normal human immunoglobulin, for children were prescribed 30-50 mg / kg once a day, a week later.

RESULTS AND DISCUSSION

The main systems of organs involved in the pathological process were respiratory, cardiovascular and central nervous systems. Acute respiratory insufficiency in combination with acute heart failure of the 2nd degree were observed in all 46 (100%) children, respiratory and cardiovascular insufficiency in combination with cerebral insufficiency in 29 (63%) children, cardiovascular insufficiency in combination with toxic lesions of the liver, kidneys and intestinal insufficiency syndrome in 17 (37%) cases.

The cause of multiple organ failure syndrome was inflammatory diseases in the lungs - 35 (76.1%), combined and associated injuries - 7 (15.2%), sepsis - 4 (8.7%). Often cases of multiple organ syndrome development were noted against the background of congenital heart defects - 9 (19.6%).

All children showed clinical signs of intoxication syndrome in the form of tachypnoea, tachycardia, moderate arterial hypertension. There was a reliable increase in respiration rate up to 51.2±3.1 min. on average, increase in heart rate up to 158.5±4.1 min. on average, increase in systolic blood pressure up to 77.2±7.4 mm Hg on average. The saturation rate (oxygen saturation of capillary blood) was 78.5±4.1% on average. Respiratory and cardiovascular disorders in children were accompanied by a sharp drop in blood oxygen saturation, which required all patients to use additional oxygen supply.

20 (43.5%) of children with respiratory insufficiency of III degree were transferred for forced ventilation by SAVINA (Germany), VELLA (USA). The criteria of indications for transfer to ALV were progressive respiratory insufficiency, pathological type of breathing, persistent tachycardia, indices of oxygen saturation in blood less than 90% despite oxygen therapy, pCO_2>70 mmHg and blood pH <7,30.

The body temperature measured in the axillary region was elevated in all children in research groups I and II. Diuresis was significantly reduced in 10 (21.7%) children almost three times compared to normal, in blood chemistry tests - creatinine levels exceeded the norm and reached 2.74±1.9 μmol/l, urea 9.9±6.1 mmol/l.

In the blood analysis, mainly there was high leukocytosis with the blood formula shift to the left, toxic neutrophil granularity (++++), high ESR, hypochromic anemia. The number of red blood cells decreased by 2.6 times and platelets by 1.9 times compared to normal values. The leukocyte index of intoxication (LI) in the latter increased on average 6.8 times, the level of average molecular peptides - 5.1 times compared to the normal values.

During bacteriological examination (sowing tank from the throat) of children the following pathogenic microorganisms were identified: Staphylococcus aureus (34.9%), Klebsiella pneumoniae (39.1%), Pseudomonas aergenosa (26%) and others.

The severity of the children's condition was assessed with the Pediatric Multiple Organ Dysfunction Score (PEMOD). The system evaluates 6 key organ systems: Each of them has one clinical or laboratory criterion.

The severity of the condition was also assessed using the scale **S**equential **O**rgan **F**ailure **A**ssessment (SOFA), which is designed to assess and describe the sequence of complications in critical patients. The SOFA scale is based on the evaluation of six organ systems: respiratory, cardiovascular, liver, coagulation, renal and neurological, from mild dysfunction (0 points) to severe failure (4 points).

Table 1. Evaluation of patient severity on prognostic scales

Reason MOFS	Number of patients	Number of points on the scale	
		PEMOD	SOFA
Respiratory diseases	35	11 (10-14)	2,5 (2-3)
Combined and associated injuries	7	16 (15-17)	3 (2-4)
Sepsis	4	12 (9-12)	3 (2-4)

The clinically most severe on all prognostic scales used in the study were patients with combined and associated trauma who underwent emergency surgical interventions.

For 22 children of the main group, plasmapheresis was performed with the «Hemofenix» apparatus. The advantage of membranous plasmapheresis is the greater uniformity of the outflow and flow of blood in the external circuit and the reduction of the damaging effect of the procedure on the blood cells.

The indications for plasmapheresis were: expressed endotoxicosis, generalization and progression of infection process, immunity failure, low efficiency of the methods and means of intensive therapy.

In 9 (40.9%) patients of group 2, due to low blood and venous pressure, tachycardia, anemia, infusion therapy was carried out to prepare for plasmapheresis. Hemodynamic parameters (blood pressure, central venous pressure, heart rate and saturation) were studied in each patient during plasmapheresis before plasmapheresis, after plasmapheresis.

Table 2. Hemodynamic indicators

№	Indicators	Before plasmatheresis	After plasmapheresis
1	SBP	70,5±4,3	65,5±3,5
2	HR	95,5±0,7	90,0±0,45
3	CVP	7,0±0,5	6,3±0,7

As the results of plasmapheresis show, it was not accompanied by reliable changes in the values of heart rate, SBP, and CVP.

Plasma-substitution was carried out with freshly frozen donor plasma and was heated before plasma injection. The total volume of plasma substitution in one session of plasmapheresis was: in children under 3 years of age - 120-240 ml, from 3 to 7 years - 240-360 ml, from 7 to 14 years - 360-400 ml.

The analysis showed that plasmapheresis, used in intensive care in children, did not adversely affect the indicators of homeostasis, coagulation and anticoagulation of the blood. After plasmapheresis and substitution plasmatransfusion, there was an increase in the total plasma protein and its fractions. To achieve a good clinical effect in children, was conducted course of plasmapheresis in 2 sessions at intervals of 3-5 days.

We have not recorded a single case of a serious complication of plasmapheresis. In 2 (0.9%) children, against the background of donor plasma infusion of the corresponding group and rhesus, there was individual intolerance in the form of immediate allergic reactions, which were suppressed by disposable intravenous injections of dexamethesone.

Considering that interleukin-6 (IL-6) belongs to the group of cytokines with proinflammatory action and also serves as an early marker for determination of polyorganic insufficiency, we conducted a study of serum content of IL-1 β and IL-6. The level of IL-1β in patients before plasmapheresis was 31.9 times higher

than in children of the control group (p<0.001) and averaged 829±0.9 pg/ml. IL-6 production in children was 4.6 times higher (31±1.51 pg/ml) than in the control group (6.8±0.2 pg/ml) (Table 3).

Table 3. Serum cytokine content in children, pg/ml

Indicators	Control «Probably healthy» n=10	Main group		
		Before plasmatheresis n=22	After plasmapheresis n=22	After treatment n=22
IL-1 β	IL-1 β	IL-1 β	IL-1 β	IL-1 β
IL-6	6,8±0,2	31,0±1,5[6]	18,0±1,1[6]	6,2±0,63

Remark: a - p<0.05, b - p<0.001 compared to the control

The received data allows to think about the presence of certain dependence of level of production of IL-1β and IL-6 on character of pathological process that is proved by rather high level of its secretion. After plasmapheresis in the main group, the concentrations of IL-1β and IL-6 decreased sharply. This indicates a decrease in the severity of the systemic inflammatory response.

All patients underwent complex etiopathogenetic therapy aimed at elimination of multiple organ failure manifestations, provision of adequate gas exchange, stabilization of central and peripheral hemodynamics and maintenance of adequate cerebral perfusion. Antibiotic therapy was carried out by the introduction of at least two broad-spectrum antibiotics (3rd generation cephalosporins + aminoglycosides), further on the sensitivity of the infection to antibiotics. Symptomatic therapy includes infusion and detoxification, medications that improve the rheological properties of blood (direct and indirect anticoagulants), sedatives.

All 46 children of the 1st and 2nd groups - after plasmapheresis immunocorrection with the immunological drug Octagam was carried out, in a dose of 30-50 mg/kg once a day, after a week again.

CONCLUSION

Thus, the use of plasmapheresis in the complex treatment of multiple organ failure in children reduces the time of the procedure, has a great detoxifying effect.

In children from the main group, after plasmapheresis, changes in clinical manifestations towards normalization of indices were observed in a short period of time, breathing frequency and heart rate decreased significantly, blood oxygen saturation increased, blood pressure, body temperature and diuresis indices were normalized to 1.8±2.2 ml/hour, practically to normal.

The use of plasmapheresis in patients of the main group allowed to reduce the level of leukocytes and platelets in the blood of children in comparison with the initial level, the average value of LII was significantly reduced, creatinine content was reduced, bilirubin concentration was reduced.

As a result of application in complex therapy of plasmapheresis in children with multiple organ failure it is marked decrease in time of stay in intensive care unit on the average on 4,9±2,1 beds/day, decrease in time of stay on a TRS on the average on 3,6±0,5 days and decrease in level of lethality on the average on 6,6±0,3 % from level of the general lethality.

The effectiveness of plasmapheresis in MOF in children was also assessed based on cellular and humoral immunity. There was a faster decline in the IL-6 level, which was an early indication of the effectiveness of the therapy.

Inclusion of Octagam in the complex therapy has led to a more rapid increase in the initially reduced indices of the immunity cellular link, stabilization of the humoral immunity, shortening the period of antibacterial therapy, shortening the period of hospitalization in children of the main group (with plasmapheresis) than in children without plasmapheresis.

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