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Results of the impact of antiproteinase hemosorbent on the dynamics of clinical and laboratory indicators in children with generalized peritonitis

Wyniki wpływu hemosorbentu antyproteinazowego na dynamikę wskaźników klinicznych i laboratoryjnych u dzieci z uogólnionym zapaleniem otrzewnej

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Keywords
children, peritonitis, abdominal sepsis, hemoperfusion

Słowa kluczowe
dzieci, zapalenie otrzewnej, posocznica brzuszna, hemoperfuzja

Summary

Introduction. Despite the undoubted success of modern medicine, peritonitis in children remains not only a surgical, but also a general pathological problem, the relevance of which does not decrease. The use of efferent therapy methods, in particular hemosorption, imitating the natural mechanisms of detoxification of the body, are promising in the complex therapy of children with peritonitis.

Aim. The aim of the study was to establish the effectiveness of the antiproteinase hemosorbent "Hemo-proteazsorb" in the complex intensive care of children with generalized peritonitis.

Material and methods. A prospective randomized study of 60 children with generalized peritonitis was conducted. In the main group, there were 30 patients who underwent hemosorption in complex intensive care, and the comparison group also included 30 patients who underwent traditional treatment. The examined groups were comparable in terms of the nature of the pathology and the severity of the condition.

Results. During hemoperfusion, a significant increase in blood saturation was established from 95.1 (93.2; 97.1)% to 97.3 (95.5; 98.7)%, with an improvement in oxygen transport (ctO_2, mmol/l) from 6.9 (6.4; 7.9) to 8.8 (1.5; 9.7) and a decrease in lactate level (mmol/l) from 1.7 (1.5;2.1) to 1.1 (0.9;1.3), which indicates normalization of blood oxygenation and improvement of microcirculation. After 24 hours, there was a significant decrease in the amount of points on the pSOFA scale, from 4.5 (3.0; 6.0) to 0.5 (0; 2.0), $p < 0.001$, normalization of body temperature, restoration of intestinal function was noted in 15 (50.0% CI: 32.1-67.9) children, which indicates a decrease in multiple organ dysfunction and improvement of the condition. When compared in the second group, the studied indicators changed much more slowly.

Conclusions. The data obtained as a result of the study on the positive dynamics of clinical and laboratory parameters prove the high effectiveness of the use of the Belarusian hemosorbent "Hemo-proteazsorb" in the complex of intensive care of generalized peritonitis.

Conflict of interest
Konflikt interesów
None
Brak konfliktu interesów

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Streszczenie

Wstęp. Pomimo niewątpliwego sukcesu współczesnej medycyny, zapalenie otrzewnej u dzieci pozostaje nie tylko problemem chirurgicznym, ale także ogólnym problemem patologicznym, którego znaczenie nie maleje. W kompleksowej terapii dzieci z zapaleniem otrzewnej obiecujące jest zastosowanie metod terapii eferentnej, w szczególności hemosorpcji, naśladującej naturalne mechanizmy detoksykacji organizmu.

Cel pracy. Celem pracy było określenie skuteczności hemosorbentu antyproteinazowego „Hemo-proteazsorb" w złożonej intensywnej terapii dzieci z uogólnionym zapaleniem otrzewnej.

Materiał i metody. Przeprowadzono prospektywne randomizowane badanie 60 dzieci z uogólnionym zapaleniem otrzewnej. W grupie głównej było 30 pacjentów poddanych

hemosorpcji na złożonej intensywnej terapii, grupa porównawcza również obejmowała 30 pacjentów poddanych tradycyjnemu leczeniu. Badane grupy były porównywalne pod względem charakteru patologii i zaawansowania stanu.

Wyniki. Podczas hemoperfuzji stwierdzono istotny wzrost wysycenia krwi z 95,1 (93,2; 97,1)% do 97,3 (95,5; 98,7)%, przy poprawie transportu tlenu (ctO_2, mmol/l) z 6,9 (6,4; 7,9) do 8,8 (1,5; 9,7) oraz spadek poziomu mleczanów (mmol/l) z 1,7 (1,5;2,1) do 1,1 (0,9;1,3), co wskazuje na normalizację natlenienia krwi i poprawę mikrokrążenia. Po 24 godzinach nastąpił istotny spadek liczby punktów w skali pSOFA z 4,5 (3,0; 6,0) do 0,5 (0; 2,0), $p < 0,001$, normalizacja temperatury ciała, przywrócenie funkcji jelit odnotowano u 15 (50,0% CI: 32,1-67,9) dzieci, co wskazuje na zmniejszenie dysfunkcji wielonarządowej i poprawę stanu. W porównaniu z drugą grupą badane wskaźniki zmieniały się znacznie wolniej.

Wnioski. Uzyskane w wyniku badań dane dotyczące dodatniej dynamiki parametrów klinicznych i laboratoryjnych świadczą o wysokiej skuteczności stosowania białoruskiego hemosorbentu „Hemo-proteazsorb" w kompleksie intensywnej terapii uogólnionego zapalenia otrzewnej.

INTRODUCTION

Generalized peritonitis is a severe form of abdominal infection and can be considered as intraabdominal sepsis. With the generalization of inflammation, the body loses the ability to localize the infection and control its spread beyond the primary focus of infection. In this situation, it is believed that there is a translocation of bacteria from the intestine into the bloodstream, due to a violation of the integrity of the intestinal mucosa, as a result of which an uncontrolled septic process is triggered (1-3). Over the past century, medicine has made great progress in understanding of the pathological processes that occur not only in the focus of inflammation, but also in the entire body under the influence of inflammatory agents. Nevertheless, the range of problems that arise in the treatment of severe forms of peritonitis is only expanding. This, in turn, encourages the search and introduction of new technologies in the complex therapy of abdominal sepsis (2, 4-6).

In addition to surgical intervention and conventional nonoperative therapy, timely pathogenetic therapy aimed at removing inflammatory mediators, toxic substances and tissue metabolism products from the body is very important in the treatment of generalized peritonitis. Hemoperfusion (HP) is one of the main methods of correcting the body's dysregulatory response to infection. Currently, the following selective hemosorbents are used in world clinical practice: a cartridge with immobilized polymyxin B (Toraymyxin 20R, Japan), an LPS Adsorber cartridge (Alteco Medical AB, Sweden), a MATISSE-Fresenius system (Fresenius SE, Germany), a Toxipak column (NPF "POKARD", Russia) and a CytoSorb hemoperfusion cartridge (CytoSorbents, Monmouth Junction, New Jersey, USA) (1-3). Belarusian researchers have proved the effectiveness of the domestic selective hemosorbent "Ovosorb" in the treatment of severe pancreatitis, peritonitis and burns in adult patients, as a result of the adsorption of proteases, pro-inflammatory cytokines from the blood, the release of which increases hundreds of times in these pathological processes (7). However, by now, there are no sufficiently convincing results in pediatric detoxification obtained on the basis of randomized controlled trials, and this limits the introduction of many methods into practice. Epidemiological and prospective studies aimed at studying the practical aspects of extracorporeal methods of treatment in children are relevant and have high practical significance.

AIM

To establish the effectiveness of the antiproteinase hemosorbent "Hemo-proteazsorb" in the complex intensive care of children with generalized peritonitis.

MATERIAL AND METHODS

A prospective randomized study examined 60 children with generalized peritonitis, the main cause of which was acute appendicitis. The patients were treated in the Anesthesiology and Intensive Care Unit (AICU) of the Grodno Regional Children's Clinical Hospital. This study was conducted in accordance with the standards of bioethics, was approved by the ethics committee of the institution and complies with the principles of the Helsinki Declaration. Each legal representative of the child has received an informed consent for hemosorption and blood sampling, followed by the use of the obtained medical data.

Upon admission, all patients were randomized using a random number generator program to form 2 groups. The first main group included 30 patients who underwent HP through the "Hemo-proteazsorb" sorbent using the "MultiFiltrate" device (Fresenius, Germany). Operation parameters: the rate of blood perfusion along the main line is 50-70 ml/min, with a perfusion volume of 1.0-1.5 volumes of circulating blood, the sorption duration was 60-90 minutes. Anticoagulation was performed with unfractionated heparin at a dose of 100 U/kg by bolus administration at the beginning of the procedure. The second comparison group included 30 patients who underwent conservative treatment according to the clinical protocol for the diagnosis and treatment of children with a general surgical profile.

Inclusion criteria: age from 1 month to 18 years, underwent surgical interventions for peritonitis, hospitalization after surgery in the AICU, written informed consent of legal representatives to conduct a HP and blood sampling with subsequent use of the obtained medical data.

Exclusion criteria: age less than 1 month, the presence of significant congenital anatomical or functional abnormalities, the presence of oncological, hematological diseases, immunodeficiency conditions, as well as the presence of absolute contraindications to HP (terminal condition, ongoing internal or external bleeding, unstable hemodynamics).

Clinical signs were recorded in all patients upon admission to the AICU – respiratory rate (RR), heart rate (HR), body temperature (BT), mean blood pressure (BPmean), central venous pressure (CVP) and diuresis. The severity of each patient's condition in dynamics was assessed by the pSOFA scale (Pediatric Sequential Organ Failure Assessment Score), which allows us to objectively assess the effectiveness of new therapeutic measures and characterize patients for inclusion in clinical trials. A general blood test (GAT) with the calculation of the leukocyte formula and the number of platelets was performed using an XP-300 analyzer (Systems Corporation, Japan). The determination of blood biochemical parameters with the study of the level of total protein, urea, creatinine, ions was performed using biochemical analyzers BS 200 (Mindray, China) and AU-480 (Beckman coulter, USA). The study of the state of the hemostasis system was analyzed using the ACL 10 000 coagulometric analyzer (Instrumentation Laboratory, USA).

The study in the main group was conducted after surgery (initial data, or before the HP session), immediately after the completion of the HP, as well as after 24 and 48 hours. In the comparison group, clinical and laboratory parameters were monitored after surgery (baseline data), after 24 and 48 hours. Statistical data analyzing was carried out using the STATISTICA 10.0 statistical data processing program. Quantitative tests were used to test the hypothesis of the normality of the distribution: Kolmogorov-Smirnov, Lillifors, Shapiro-Wilk. The methods of nonparametric statistics are used in connection with the abnormal distribution of features. The statistical significance of the differences for independent samples was determined using the Mann-Whitney U-test, and the Wilcoxon criterion was used for dependent groups. The differences were considered significant at $p < 0.05$, highly significant at $p < 0.01$ and $p < 0.001$, and not significant at $p > 0.05$. Quantitative variables are expressed as the median and standard deviation: Me (L; U) Me (25%; 75%). The confidence interval was calculated for 95% probability.

RESULTS AND DISCUSSION

All patients were admitted to the hospital with an acute appendicitis clinic, with a disease duration of 48.0 (24.0; 72.0) hours. All children had abdominal pain, an increased body temperature was recorded in 93.0% (CI 86.5-99.5) of children, vomiting was present in 73.0% (CI 61.8-84.2) of cases, diarrhea were observed in 33.0% (CI 21.2-44.9) of patients. All these clinical signs are risk factors for the development of a severe septic condition. The gender distribution of children was as follows: 35 boys (58.0% CI 45.5-70.5), 25 girls (42.0% CI 29.5-54.5). The average age was 7.5 (4; 12) years. The comparative characteristics of patients in the study groups are presented in table 1.

Tab. 1. Comparative characteristics of patients in the study groups

Parameters	Group 1, n = 30	Group 2, n = 30	p
pSofa scale (points)	2.0 (2.0; 3.0)	2.0 (1.0; 2.0)	0.048*
Gender, male, n (%)	20 (66.7%)	15 (50.0%)	0.542
Female, n (%)	10 (33.3%)	15 (50.0%)	
Age (years)	7.0 (4.0; 11.0)	8.0 (5.0; 12.0)	0.538
Body weight (kg)	23.5 (18.0; 36.0)	25.5 (18.0; 38.8)	0.662
Duration of the disease (hour)	48.0 (24.0; 72.0)	42.0 (24.0; 48.0)	0.438
Average bed-day in the AICU (days)	4.0 (3.0; 5.0)	4.5 (3.0; 6.0)	0.469
Average total hospital stay (days)	14.0 (11.0; 18.0)	15.0 (12.0; 20.0)	0.305

p – the reliability of differences between groups
*statistical significance

The average duration of the disease ($p = 0.438$) and the time from the moment of admission to the hospital to surgery ($p = 0.26$) did not significantly differ in both groups. Surgical treatment consisted in the removal of a destructively altered appendix, sanitation and drainage of the abdominal cavity. There were no significant differences in age ($p = 0.539$), weight ($p = 0.662$), gender ($p = 0.27$) in the groups. The indicator of the average stay in the intensive care unit for group I was 4.0 (3.0; 5.0) days versus 4.5 (3.0; 6.0) days in the second, and the indicator of the average total hospital stay was 14.0 (11.0; 18.0) days versus 15.0 (12.0; 20.0) days. The examined groups were comparable in terms of the nature of the pathology and the severity of the condition.

When selective HP was included in the complex intensive therapy, a positive dynamics of clinical and laboratory parameters was noted, manifested in a decrease in the severity of endogenous intoxication and in the stabilization of the patient's condition. The data was monitored 3 hours after the end of the hemoperfusion session, the data are presented in table 2.

To objectify the condition of patients and its control in dynamics, a point assessment of the state of organs and systems on the pSOFA scale was used (fig. 1). An increase in the amount of points by more than 2 during the day from the initial one predicts organ failure and a severe outcome of the disease.

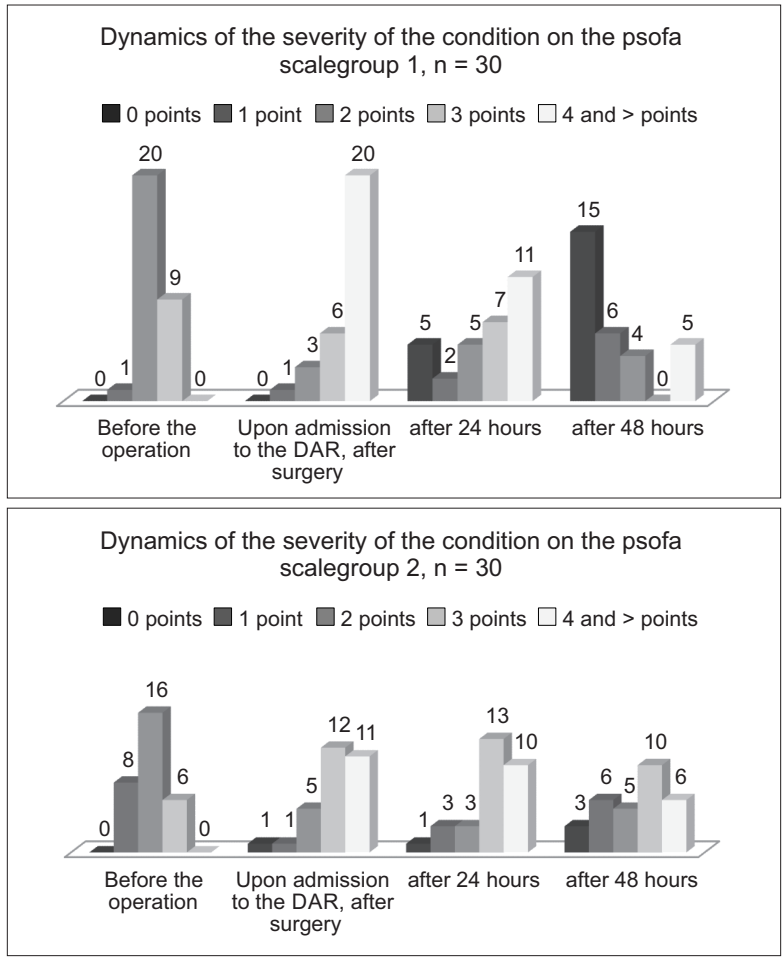
As a result of the HP procedure, there was a significant decrease in the sum of points on the pSOFA scale, from 4.5 (3.0; 6.0) to 0.5 (0; 2.0), $p < 0.001$ within 48 hours, which indicates a decrease in multiple organ dysfunction and improvement of the condition. In the second group, there was only a slight change from 3.0 (3.0; 4.0) to 3.0 (1.0; 3.0), $p = 0.002$.

Tab. 2. Dynamics of clinical parameters in the study groups

Indicators	pSofa scale (points)	Body temperature (°C)	HR (per min)	RR (per min)	CVP (mmHg)	BPmean (mmHg)
1 group with HP, n = 30						
Initial data	4.5 (3.0; 6.0)	37.2 (36.9; 37.6)	116.0 (108.0; 123.0)	23.0 (20.0; 26.0)	80.0 (25.0; 95.0)	80.0 (76.0; 87.0)
After the HP		37.2 (37.0; 37.4)	114.5 (108.0; 120.0)	23.0 (20.0; 26.0)	77.5 (30.0; 100.0)	80.0 (76.0; 84.0)
p		0.239	0.791	0.514	0.614	0.206
After 24 hours	3.0 (2.0; 4.0)	37.0 (36.6; 37.4)	107.5 (100.0; 114.0)	24.0 (20.0; 26.0)	50.0 (30.0; 80.0)	78.0 (75.0; 84.0)
p_1	< 0.001*	< 0.001*	0.009*	0.523	0.085	0.372
After 48 hours	0.5 (0; 2.0)	36.8 (36.6; 37.0)	97.5 (88.5; 111.5)	24.0 (19.0; 25.0)	50.0 (25.0; 77.0)	80.0 (76.0; 84.0)
p_2	< 0.001*	< 0.001*	< 0.001*	0.226	0.003*	0.688
Group 2 without HP, n = 30						
Initial data	3.0 (3.0; 4.0)	37.8 (37.4; 38.2)	117 (109; 127.0)	24.0 (22.0; 26.0)	75.0 (60.0; 100.0)	76.0 (68.0; 82.0)
After 24 hours	3.0 (3.0; 4.0)	37.5 (37.2; 37.8)	111.5 (108.0; 120.0)	24.0 (22.0; 26.0)	70.0 (45.0; 85.0)	77.0 (70.0; 80.0)
p_1	0.529	< 0.001*	0.032*	0.391	0.15	0.273
After 48 hours	3.0 (1.0; 3.0)	37.5 (37.1; 37.9)	111.0 (102.0; 122.0)	24.0 (22.0; 26.0)	50.0 (40.0; 82.5)	75.5 (73.0; 79.0)
p_2	0.002*	< 0.001*	0.004*	0.503	0.544	0.058
p_3	0.003*	0.007*	0.482	0.282	0.797	0.067
p_4		< 0.001*	0.251	0.214	0.95	0.135
p_5	0.52	< 0.001*	0.032*	0.391	0.15	0.273
p_6	0.002*	< 0.001*	0.004*	0.503	0.544	0.058

p – reliability of differences in comparison before and after HP; p1 – reliability of differences in comparison with the initial data and after 24 h; p2 – reliability of differences in comparison with the initial data and after 48 h; p3 – reliability of differences in the initial data between groups; p4 – reliability of differences in comparison of group 1 after HP with the initial data of group 2; p5 – reliability of differences in comparison between groups after 24 h; p6 – reliability of differences in comparison between groups after 48 h
*statistical significance

Fig. 1. Dynamics of the severity of the condition the scale pSOFA in the study groups



*the data is presented in absolute numbers

When analyzing the dynamics of clinical indicators in the first group, the normalization of BT was noted in 16.6% (5) children after the completion of HP. After 24 hours, a decrease in BT was recorded in 33.3% (10) children from 37.2 (36.9; 37.6) 0C to 37.0 (36.6; 37.4) ^{0}C p = 0.0009 and by the third day, BT was significantly normalized in 15 (50.0% CI 32.1-67.9) children (36.8 (36.6; 37.0)), p < 0.001. At the same time, this was accompanied by a decrease in HR and normalization of RR in accordance with age, while a significant increase in blood saturation was established from 95.1 (93.2; 97.1)% to 97.3 (95.5; 98.7)%, with an improvement in oxygen transport (ctO_2, mmol/L) from 6.9 (6.4; 7.9) to 8.8 (1.5; 9.7) and a decrease in lactate level (mmol/L) from 1.7 (1.5;2.1) to 1.1 (0.9;1.3), which indicates normalization of blood oxygenation and improvement of microcirculation (4). It should be noted that the HP session did not significantly affect the changes in BPmean and CVP – these indicators were within the age norm, which indicates a slight effect of HP on central hemodynamics. During the HP auscultation, a distinct increase in intestinal peristalsis was recorded. Subsequently, after 24 hours, the intestinal peristalsis was restored in 24 (80.0% CI: 65.7-94.3) children in the study group I, and after 48 hours in 100% of patients. There was a tendency to increase the hourly diuresis against the background of the standard volume of infusion therapy from 3.5 (2.9; 5.0) to 4.2 (3.5; 5.3) ml/kg/hour, p < 0.001. When compared in the second group, the studied indicators changed much more slowly. For 48 hours, the elevated body temperature persisted (37.5 (37.1; 37.9) ^{0}C, p < 0.001), relative tachycardia was recorded (111.0 (102.0; 122.0) per minute, p = 0.004), signs of a systemic inflammatory response syndrome, signs of respiratory failure, intestinal paresis persisted.

After hemoperfusion, a positive trend was established in relation to the indicators of the general blood test responsible for the inflammatory process. The results of the study of hemogram indicators in dynamics are presented in table 3.

One of the simple and generally available methods of controlling endotoxemia is counting the number of white blood cells and determining the leukocyte formula with the calculation of the neutrophil-lymphocyte index (NLI). Before the HP, the leukocyte level was 10.9 (8.7; 14.6) × 10^9, and immediately after the HP it significantly decreased to 9.4 (7.7; 12.3) × 10^9, p < 0.001 and after 48 hours it was 8.2 (6.0; 11.1) × 10^9. The level of rod-shaped neutrophils decreased from 12.0 (10.0; 25.0)% to 9.5 (6.0; 15.0)%, p < 0.001, followed by an increase in the number of lymphocytes from 12.0 (8.0; 19.0)% to 17.0 (13.0; 24.0)%, p = 0,0001. At the same time, the value of the NLI compared to the initial data after HP decreased by 35% (from 6.58 (4.0; 9.7) to 4.3 (2.8; 5.9), p < 0.001), and subsequently, after 24 and 48 hours, there was a positive dynamics of this indicator (from 3.8 (2.2; 6.5) to 3.0 (1.7; 5.2), p = 0.023). In the group without the use of HP, the studied indicators remained at high values after 24 hours: white blood cells – 10.6 (8.9; 14.4) × 10^9, rod-shaped neutrophils – 7.0 (4.0; 12.0)%, NLI – 5.8 (3.6; 8.7). It should be noted that in the course of the study, the facts of the negative effect of HP on the level of hemoglobin, red blood cells, platelets were not recorded.

Tab. 3. Dynamics of inflammatory parameters in the studied groups

Indicators	WBC (x 10^9)	PLT (x 10^9)	Segmented neutrophils (%)	Rod-shaped neutrophils (%)	Percentage of neutrophils (%)	Percentage of lymphocytes (%)
1 group with HP, n = 30						
Initial data	10.9 (8.7; 14.6)	238.5 (193.0; 273.0)	63.0 (53.0; 70.0)	12.0 (10.0; 25.0)	79.5 (76.0; 86.0)	12.0 (8.0; 19.0)
After the HP	9.4 (7.7; 12.3)	233.0 (191.0; 264.0)	60.5 (52.0; 70.0)	9.5 (6.0; 15.0)	73.0 (67.0; 79.0)	17.0 (13.0; 24.0)
p	< 0.001*	0.091	0.478	< 0.001*	< 0.001*	< 0.001*
After 24 hours	9.6 (7.2; 11.4)	243.0 (214.0; 294.0)	59.5 (54.0; 66.0)	8.0 (5.0; 12.0)	69.5 (62.0; 78.0)	18.0 (12.0; 28.0)
p_1	< 0.001*	0.601	0.039*	< 0.001*	< 0.001*	< 0.001*
After 48 hours	8.2 (6.0; 11.1)	272.0 (228.0; 350.0)	60.0 (47.0; 67.0)	6.0 (4.0; 13.0)	66.0 (56.0; 78.0)	22.0 (15.0; 31.0)
p_2	< 0.001*	0.105	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Group 2 without HP, n = 30						
Initial data	14.3 (11.9; 19.6)	246.5 (214.0; 337.0)	74.0 (64.0; 80.0)	9.0 (4.0; 17.0)	84.5 (80.0; 89.0)	10.5 (5.0; 15.0)
After 24 hours	10.6 (8.9; 14.5)	245.0 (226.0; 390.0)	68.0 (62.0; 76.0)	7.0 (4.0; 12.0)	77.5 (70.0; 84.0)	13.5 (9.0; 20.0)
p_1	0.006*	0.976	0.01*	0.952	0.015*	0.026*
After 48 hours	9.9 (7.9; 11.7)	256.0 (227.0; 288.0)	62.5 (55.0; 70.0)	5.0 (3.0; 9.0)	70.0 (64.0; 76.0)	18.0 (13.0; 27.0)
p_2	0.209	0.27	0.099	0.215	0.246	0.246
p_3	0.012*	0.183	0.002*	0.023*	0.022*	0.096
p_4	< 0.001*	0.103	0.001*	0.52	< 0.001*	< 0.001*
p_5	0.022*	0.976	0.01*	0.952	0.015*	0.026*
p_6	0.209	0.27	0.099	0.215	0.246	0.246

p – reliability of differences in comparison before and after HP; p1 – reliability of differences in comparison with the initial data and after 24 h; p2 – reliability of differences in comparison with the initial data and after 48 h; p3 – reliability of differences in the initial data between groups; p4 – reliability of differences in comparison of group 1 after HP with the initial data of group 2; p5 – reliability of differences in comparison between groups after 24 h; p6 – reliability of differences in comparison between groups after 48 h

*statistical significance

When studying the indicators of biochemical blood analysis in the first and second groups, no significant differences were obtained. The obtained data may indirectly indicate that the HP procedure did not have a significant effect on the change in the concentration of total protein, albumin, urea, creatinine and electrolytes in blood plasma, the data are presented in table 4.

During HP, the patient's blood passes through the extracorporeal circuit, directly contacting the sorbent, which may be accompanied by activation of the hemostasis system. In order to prevent

Tab. 4. Dynamics of biochemical parameters in the studied groups

Indicators	Urea (mmol/L)	Creatinine (mkmol/L)	Total protein (g/l)	K^+ (mmol/L)	Na^+ (mmol/L)	Cl^- (mmol/L)
1 group with HP, n = 30						
Initial data	2.4 (2.0; 3.4)	45.1 (36.0; 51.5)	54.0 (50.0; 58.0)	3.9 (3.6; 4.1)	136.0 (134.6; 137.2)	103.9 (101.5; 106.0)
After the HP	2.0 (1.7; 2.5)	42.0 (32.4; 58.1)	55.0 (51.0; 57.0)	3.5 (3.3; 3.9)	137.9 (135.0; 140.0)	103.4 (101.3; 107.0)
p	0.011*	0.516	0.913	0.047*	0.032*	0.803
After 24 hours	2.4 (1.8; 3.0)	44.5 (39.0; 52.0)	59.0 (52.0; 61.0)	4.0 (3.8; 4.4)	137.1 (135.4; 140.0)	104.3 (102.0; 106.0)
p_1	0.005*	0.657	0.8	0.229	0.005*	0.515
After 48 hours	2.6 (1.9; 3.2)	44.4 (35.5; 50.0)	58.2 (55.1; 64.0)	4.4 (4.1; 4.7)	136.0 (133.8; 138.8)	102.4 (101.1; 105.6)
p_2	0.03*	0.018*	0.049*	< 0.001*	0.033*	0.668
Group 2 without HP, n = 30						
Initial data	3.2 (2.7; 4.0)	53.0 (47.3; 62.0)	58.0 (52.0; 66.0)	4.0 (3.8; 4.16)	136.0 (134.1; 138.4)	102.0 (99.0; 105.0)
After 24 hours	2.4 (2.0; 2.7)	50.0 (45.0; 60.0)	54.0 (49.5; 57.0)	3.9 (3.8; 4.0)	138.0 (136.0; 139.0)	101.0 (100.0; 103.0)
p_1	0.635	0.037*	0.042*	0.183	0.688	0.001*
After 48 hours	2.2 (1.9; 2.8)	48.0 (44.0; 57.0)	57.0 (54.0; 60.0)	4.2 (4.1; 4.5)	138.0 (137.0; 140.0)	101.0 (100.0; 102.0)
p_2	0.49	0.006*	0.07	0.224	0.065	0.021*
p_3	0.01*	0.014*	0.094	0.176	0.911	0.047*
p_4	< 0.001*	0.032*	0.205	0.003*	0.164	0.04*
p_5	0.636	0.037*	0.042*	0.185	0.689	0.001*
p_6	0.491	0.006*	0.071	0.225	0.066	0.022*

p – reliability of differences in comparison before and after HP; p1 – reliability of differences in comparison with the initial data and after 24 h; p2 – reliability of differences in comparison with the initial data and after 48 h; p3 – reliability of differences in the initial data between groups; p4 – reliability of differences in comparison of group 1 after HP with the initial data of group 2; p5 – reliability of differences in comparison between groups after 24 h; p6 – reliability of differences in comparison between groups after 48 h
*statistical significance

Tab. 5. Dynamics of parameters of the state of the hemostatic system in the studied groups

Indicators	APTT (s)	PT (s)	INR	Fibrinogen (g/l)
1 group with HP, n = 30				
Initial data	32.3 (29.5; 37.0)	18.8 (17.0; 20.7)	1.3 (1.2; 1.5)	5.8 (4.9; 6.7)
After the HP	31.5 (28.4; 37.2)	17.6 (16.0; 18.7)	1.2 (1.1; 1.3)	5.5 (5.1; 7.0)
p	0.375	0.009*	0.004*	0.592
After 24 hours	31.7 (28.7; 37.2)	17.6 (16.3; 18.1)	1.2 (1.1; 1.3)	6.0 (5.0; 7.0)
p_1	0.893	0.03*	0.049*	0.0705
After 48 hours	32.3 (28.3; 35.3)	17.7 (15.5; 18.9)	1.2 (1.1; 1.3)	5.8 (4.6; 7.2)
p_2	0.28	0.004*	0.002*	0.123
Group 2 without HP, n = 30				
Initial data	30.8 (29.7; 32.6)	18.0 (16.5; 18.7)	1.2 (1.2; 1.3)	5.4 (4.4; 6.7)
After 24 hours	31.5 (28.7; 33.9)	18.3 (16.8; 19.0)	1.3 (1.2; 1.4)	6.1 (4.8; 6.6)
p_1	0.622	0.172	0.25	0.792
After 48 hours	31.0 (29.1; 33.5)	16.7 (15.8; 17.3)	1.1 (1.1; 1.2)	6.6 (5.6; 7.1)
p_2	0.642	0.303	0.447	0.16
p_3	0.167	0.048*	0.063	0.529
p_4	0.439	0.48	0.71	0.371
p_5	0.622	0.172	0.25	0.792
p_6	0.642	0.304	0.16	0.447

p – reliability of differences in comparison before and after HP; p1 – reliability of differences in comparison with the initial data and after 24 h; p2 – reliability of differences in comparison with the initial data and after 48 h; p3 – reliability of differences in the initial data between groups; p4 – reliability of differences in comparison of group 1 after HP with the initial data of group 2; p5 – reliability of differences in comparison between groups after 24 h; p6 – reliability of differences in comparison between groups after 48 h
*statistical significance

thrombosis of the sorption column, heparinization of the system is traditionally used to ensure hypocoagulation. The risk of developing iatrogenic hypocoagulation bleeding is a deterrent to the use of HP in the early postoperative period, especially when performing conversion (changing the operative access: laparoscopic – to laparotomic). As can be seen from table 5, the following changes in the coagulogram were observed immediately after the HP session: shortening of prothrombin time (PT) and a decrease in the international normalized ratio (INR) with stable indicators of activated partial thromboplastin time (APTT). On the first day after the operation, the hemostasis indicators in group I normalized and did not significantly differ from the hemostasis indicators of group II. On the second and third days after the operation, these indicators were the same in both groups.

CONCLUSIONS

1. The data obtained as a result of the study indicate a faster decrease in the dynamics of symptoms of endogenous intoxication (leukocytosis, NLI, body temperature) in the main group, whose therapy included hemoperfusion.
2. The use of biospecific hemoperfusion as an additional method in the complex therapy of peritonitis provides a real opportunity to improve the treatment results of this category of patients.
3. The absence of evidence of a negative effect on central hemodynamics, the level of hemoglobin, red blood cells, platelets, biochemical blood parameters during the study indicates the safety of using the method in children.
4. Hemoperfusion performed in the early postoperative period does not cause significant changes in hemostasis and does not require specific therapy.

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