

THE USE OF COMBINED DECONTAMINATION AND NEUROPROTECTION IN THE TREATMENT OF SEPSIS IN CHILDREN OF THE FIRST YEAR OF LIFE

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Abstract: Global statistics indicate that sepsis is marked by a severe clinical course, involving the development of a systemic inflammatory response syndrome (SIRS) with multi-organ failure, particularly affecting infants, thus diminishing their quality of life and posing a significant medical and social challenge. It is imperative to reconsider conventional perspectives on various aspects of pediatric and surgical sepsis, especially concerning etiopathogenetic approaches to treatment and the management of the rehabilitation phase. Therapeutic interventions targeting the normalization of intestinal microflora composition, prevention of excessive antigenic burden on the immune system, and correction of endotoxemia through the binding of toxic substances, including bacterial toxins and their metabolites within the intestinal lumen, are pathogenetically justified in the treatment of sepsis in infants during their first year of life.

Keywords: sepsis, intestinal decontamination, neuroprotection, infants.

Objective of the Study. To assess the effectiveness of a method combining intestinal decontamination through selective oral antibiotic therapy and enterosorption in the treatment of sepsis in infants.

Research Materials and Methods

The study was conducted on a cohort of 246 children aged between 2 months and 1 year, all diagnosed with purulent-inflammatory diseases and treated at the 2nd Clinic of the Samarkand State Medical Institute.

Antibacterial therapy during combined intestinal decontamination involved the use of antibiotics that were non-absorbable from the gastrointestinal tract and specifically targeted opportunistic flora, while preserving bifidobacteria and lactobacilli. The duration of selective intestinal decontamination was guided by bacteriological and microscopic analyses of fecal samples from children with sepsis. Enterosorption was administered using the drug "Smekta," with the treatment duration based on the resolution of clinical and laboratory signs of intoxication, typically spanning 10-15 days.

A critical factor in the pathogenesis of sepsis in infants is the dysfunction of the autonomic nervous system (ANS), primarily due to hypoxic injuries to the central nervous system occurring during the ante- and

intranatal periods. Therefore, the use of a cerebroprotective peptide-structured drug, Actovegin, forms the cornerstone of pathogenetic intervention aimed at normalizing neurovegetative regulation.

Participants were divided into two groups for the study. The main group underwent selective intestinal decontamination in addition to standard therapy, while the comparison group received only standard therapy (systemic antibacterial therapy and detoxification therapy). The efficacy of the treatments was evaluated through several parameters, including the levels of antigen-binding lymphocytes (ASL), the spontaneous leukocyte agglomeration index (PSAL), the neutrophil nuclear segmentation index (IASN), indicators of endogenous intoxication, and an assessment of autonomic status using cardiointervalography (KIG), specifically measuring Mo, AMO, Δx , and IN.

Results of the Study

The study's findings regarding the content of antigen-specific lymphocytes (ASL) to pathogens in patients' blood throughout the therapy are detailed in Table 1. The therapeutic intervention resulted in a highly significant reduction in ASL levels in Group 1 compared to the initial values, showing a 2-3-fold decrease in ASL content for all types of pathogens ($P < 0.001$). Additionally, there was a markedly significant reduction in these indicators compared to the comparison group. It is noteworthy that the ASL content decreased concerning some pathogens, such as streptococcus ($P < 0.05$) and klebsiella ($P < 0.01$), even following traditional therapy.

In conclusion, the therapeutic intervention in infants with sepsis led to a substantial reduction in antigenic load, as evidenced by a significant decrease in ASL levels for nearly all pathogens. Although these levels did not reach the normal range, they were 2-3 times lower than in the group of patients who received traditional therapy.

1-The content of circulating ASL to sepsis pathogens in infants with DMK, % (M=m)

ASL to pathogens	Control, n=30	Before treatment, n=129	After treatment	
			Main, n=56	Comparison group (post-trad. therapy), n=38
Staphylococcus	2,3±0,4	12,9±0,6	4,6±0,3 ^{^^^}	11,7±0,2 ^{°°°}
Streptococcus	1,8±0,2	8,9±0,8	3,8±0,7 ^{^^^}	7,4±0,7 ^{°°°}
Klebsiella	1,5±0,1	16,8±0,5	5,6±0,3 ^{^^^}	14,8±0,6 ^{^^°°°}
Proteus	1,7±0,3	14,3±0,9	7,0±0,1 ^{^^^}	12,7±0,8 ^{°°°}
Pseudomonas aeruginosa	1,3±0,04	15,2±0,8	4,9±0,2 ^{^^^}	14,7±0,5 ^{°°°}
Fungi of the genus Candida	1,9±0,5	22,8±0,6	12,2±0,4 ^{^^^}	22,5±0,7 ^{°°°}

Note:

- Differences concerning the healthy group data are significant (- $P < 0.001$)
- [^]: Differences concerning the data before treatment are significant (^{^^} - $P < 0.01$, ^{^^^} - $P < 0.001$)
- [°]: Differences concerning the data of Group 1 are significant (^{°°°} - $P < 0.001$)

Results of Endogenous Intoxication Indices

In the assessment of endogenous blood intoxication indices in infants within the first year of life, the first subgroup exhibited favourable dynamics compared to the comparison group (Table 2). Specifically, on the 10th day of combined decontamination and Actovegin administration, the concentration of medium-sized molecules (MSM) in the blood serum of infants in this group was significantly lower than in those who received only basic therapy ($P < 0.05$).

It is well-established that during chromatographic analysis of the protein composition of chyme in the intestinal contents of children with purulent-septic diseases, MSM proteins are predominant [64]. The level of MSM content in the blood is largely influenced by the intestinal condition, particularly by intestinal hypercolonization, which contributes to an increase in MSM levels in the intestinal lumen and may be a key factor in the mechanism of endotoxemia, including sepsis. Consequently, it is logical that combined intestinal decontamination leads to a reduction in MSM content in the intestinal lumen, which in turn decreases their levels in the blood.

Table 2: Indicators of Endogenous Intoxication in Children with Sepsis using Selective Decontamination Strategy (SDS) and Neuroprotection (M±m)

Indicators of endotoxemia	Control, n=30	Patients with septicaemia			
		Before treatment n=106	First subgroup, n=56		Comparison group (post-trad. therapy), n=38
			On day 10-12 of treatment	After treatment	
IMS a.u.	0,25±0,02	0,52±0,01	0,31±0,02	0,24±0,01 [^]	0,37±0,03
CIC, units	1,04±0,02	3,1±0,1	2,5 ±0,09	2,1±0,04 ^{^^^}	3,5±0,14 ^{°°°}
PTC, units.	27,5±1,1	47,2±2,5	31,2±2,4	28,1±2,7 ^{^^^}	49,3±1,4 ^{°°°}
LII, units.	1,96±0,18	4,51±0,41	3,5±0,43	2,3±0,23 ^{^^^}	4,4±0,15 ^{°°°}

Note:

- : Differences concerning the healthy group data are significant (- P<0.05, - P<0.01, - P<0.001)
- [^]: Differences concerning the data before treatment are significant ([^] - P<0.05, ^{^^} - P<0.01, ^{^^^} - P<0.001)
- [°]: Differences concerning the data of Group 1 are significant (^{°°} - P<0.01, ^{°°°} - P<0.001)

Study Results. Circulating Immune Complexes (CIC) and Blood Toxicity Indices

The content of circulating immune complexes (CIC) in the first subgroup of patients decreased 1.4 times compared to pre-treatment values (P<0.001), and 1.5 times compared to the group receiving traditional therapy post-treatment (P<0.001). However, when compared to healthy children, the CIC levels in the first subgroup and the comparison group remained 2.2 and 3.4 times higher, respectively (P<0.001).

In the first subgroup, the initial indices of blood toxicity and the leukocyte index of intoxication (LII) statistically significantly decreased by 1.7 and 1.9 times, reaching normal values. Conversely, in the comparison group, these indices only showed a tendency to decrease and remained significantly above normal values, being 1.8 and 2.2 times higher, respectively.

Following treatment, the first subgroup of patients exhibited a significant reduction in the index of spontaneous agglomeration of leukocytes compared to pre-treatment values and the comparison group post-treatment (P<0.001 in each case). This reduction is an indirect indicator of decreased inflammatory activity in the patients' bodies (Table 3).

Table 3: Indices of Spontaneous Leukocyte Agglomeration in Children with Sepsis Using SDS and Neuroprotection (M±m)

3 - Dynamics of PSAL and IUSN in children during treatment of sepsis with CDC (M±m) (n=40)

parameter norm	Before treatment n=20	First subgroup, n=56		Comparison group (post-trad. therapy), n=38
		10-12 день	After treatment	
PSAL 3,72±0,12 (n=25)	13,1±0,5 P<0,001	11,3±0,6 P<0,001 P1<0,05	7,1±0,53 P<0,001 P1<0,001	10,7±0,65 P<0,001 P1<0,001
ИЯСН 2,67±0,04 (n=25)	2,35±0,03	2,29±0,04	2,45±0,03	2,41±0,04

Note:

- P: Reliability of differences in comparison with the norm
- P1: Reliability of differences in comparison with baseline data

Analysis of Combined Decontamination and Actovegin on Adaptive Mechanisms

The analysis of the impact of combined decontamination and Actovegin on the adaptive mechanisms, as measured by cardiointervalography (CIG) in infants with sepsis, revealed that such treatment tends to increase AMo and Δx values while decreasing IN, accompanied by a slight, though not significant, reduction in Mo values (Table 4). Despite these changes, the achieved CIG values during sepsis treatment remain significantly different from the normative values. Specifically, patients exhibit lower Mo values (P<0.05), higher AMo values (P<0.001), higher IN values (P<0.001), and lower Δx values (P<0.001).

Although combined decontamination and Actovegin positively influence the indices of adaptive reactions during treatment, these improvements are not fully realized. This partial success is expected given the severity of the disease, which maintains a certain level due to the activity of various pathophysiological processes impacting adaptive mechanisms. This is evidenced by the persistence of hypersympathicotonia in the examined children.

Table 4: Indices of Cardiointervalography (CIG) in Children with Sepsis Using Combined Decontamination and Actovegin (M±m)

4 - Indices of cardiointervalography in patients depending on the method of treatment

CIG indicators	Control n=38	First subgroup, n=56		Comparison group (post-trad. therapy), n=38
		initial data	After treatment	
Mo, sec.	0,46±0,02	0,38±0,01	0,38±0,01	0,42±0,01
AMo, %	44±1,9	61±3,74	62±2,7	63±3,6
Δx, sec.	0,32±0,006	0,032±0,006	0,039±0,003 [^]	0,041±0,02 [°]
IN, units.	478±17	2501±261	2381±257	2137±237
Note: -	- Differences concerning the data of the healthy group are significant (- P<0.05, - P<0.01, - P<0.001), [^] - differences with respect to the data of the group before treatment are significant ([^] - P<0.05), [°] - differences with respect to the data of group 1 are significant ([°] - P<0.05).			

Conclusion

In conclusion, the implementation of a novel antibacterial therapy strategy, characterized by a protective approach to the development of bifidobacteria and lactobacilli, and the proactive management of endogenous intestinal flora through selective intestinal decontamination and combined anaerobic therapy, alongside neuroprotective therapy with Actovegin, proves highly effective. This approach successfully mitigates hypercolonization, prevents excessive antigenic overload, restores the intestine's natural detoxification function, and enhances its adaptive capacity. A significant advantage of this method is its applicability not only in specialized clinics but also in peripheral areas, broadening its potential impact on pediatric healthcare.

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