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APPLICATION OF ENTEROSORBENTS IN THE TREATMENT OF INTESTINAL INFECTIONS IN CHILDREN WITH CONCOMITANT ATOPIC DERMATITIS

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Acute enteric infections (AEI) are among the widely prevalent infectious diseases worldwide. The highest incidence of intestinal infections occur in pediatric populations [1]. The main reason is biodiversity pathogens AEI: bacteria, viruses and protozoa from different taxonomic groups. Bacterial AEI can cause the genera *Salmonella*, *Shigella*, pathogenic strains of *E. coli*, spp. *Clostridium*, spp. *Campylobacter* spp., spp. *Staphylococcus* spp. *Klebsiella*, etc. Viral AEI pathogens are group A rotaviruses and noroviruses, astroviruses, F adenoviruses, sapoviruses. Discusses the role of group C rotaviruses, bocaviruses, Aichi virus, parechovirus, coronaviruses, etc. in the development of acute gastroenteritis.
Among the factors having a significant influence on the course and outcomes of AEI in children, special attention has to be to the background of somatic and immune-mediated diseases. The latter are the food allergy and atopic dermatitis. Immune imbalance, defects in mucosal immunity and the violation of microbiocenosis of the gastrointestinal tract resulting from such a combination, can lead to of atypical clinical manifestations, non-smooth and lingering infectious diseases and reduce the effectiveness of traditional treatment, long-term repeated bacterio - and viral contagiousness. In turn pathogenic enterobacteria and intestinal viruses are able to amplify the imbalance of intestinal microbiota, to violate the breakdown of food and microbial allergens, which ultimately leads to the growth of sensitization, reactivation or progression of allergic process [2, 3]. Important role and secondary pathogenetic mechanisms AEI, namely the involvement of allergic inflammation with the formation or involvement in the hearth of biologically active substances – histamine, acetylcholine, serotonin [4, 5]. Taking into account the above-said one of the key components of an integrated treatment these patients are effective recovery of mucosal barrier, sorption of toxins and allergens, as well as correction of microecological disorders.

Intestinal adsorption (Enterosorption) is an integral part of the treatment. According to the studies, a high therapeutic effect of enterosorption identified in invasive infections (dysentery, salmonellosis) in the pathogenesis of which of particular importance are the adhesion and cytotoxic agents [6, 7]. Worldwide enterosorption recognized as the effective evidence-based medicine method of etiotropic treatment of viral AEI. The use of intestinal adsorbents (enterosorbents) for fixation on their surface and excretion freely the intestinal contents of the viruses that limits the penetration of rotaviruses through the protective mucosal barrier of the intestines of animals [8], reduces the concentration of bile acids, increases the severity of the diarrhea syndrome, undigested carbohydrates and gases. Enterosorbent’s arsenal used today in clinical practice is quite wide, and is annually updated with new drugs.

The most recognized and universal classification into the following types:
• carbon sorbents (activated carbon, carblog, carbolit, carbomer, spherical carbonite rich, antralen, etc.);
• silicon-containing enterosorbents (POLYSORB, sillard P, white clay, diosmectite, etc.);

• sorbents on the basis of the organic silicon polymer compound – polymethylsiloxane polyhydrate (Enterosgel);
• natural sorbents (Mucorales, Polyphepanum, multisorb, extract, Algiers, Zosterin, mycoton, Filtrum-STI) [9].

Enterosorption therapy is quite actively used in the treatment of allergic diseases, providing an improvement of the clinical picture of the disease, increasing the duration of remission, allowing you to extend the diet for food allergies [10, 11]. It is shown that the use of enterosorbents can reduce the dose of hormones, and in some cases even cancel hormonal therapy.
At the same time, evaluation of the effectiveness of modern enterosorbents in the treatment of AEI in children suffering from atopic dermatitis, has to date not been conducted.
Under our supervision there were 99 children with AEI suffering from atopic dermatitis.
Children of the main group received sorbents (diosmectite – 53 patient and polymethylsiloxane polyhydrate [Enterosgel] – 46 patients). These drugs were administered in standard doses recommended by the manufacturer.
26 children not treated with enterosorbents (comparison group) were observed simultaneously, (table. 1). In all groups of patients received rehydration and diet treatment, according to testimony antibacterial and probiotic treatment.
The main contingent was composed of children of the first three years (82.6 to 88.8%), while the number of infants (up to years) and early (1-3 years) of age were not significant differences between the compared groups. Patients was hospitalized in the hospital mostly in the first three days of illness (60.9–73.1%, $p>0.05$, Fisher test). The most frequently recorded during the AEI with lesions of the upper gastrointestinal tract, while in the structure of decoded etiological causes of the disease prevailed diarrhea-associated viruses (rotavirus, norovirus, adenoviruses). The groups were comparable at the severity of concomitant allergic diseases, held etiopathogenetic treatment, and the frequency of the main symptoms of the AEI (table. 2).

It is established that complex AEI treatment in children suffering from atopic dermatitis, using the enterosorbents were effective in 88.7-89.7%, including at 60.8–67.9% had a complete clinical efficacy that was characterized by the relief of most of the pathological symptoms by the end of the third day of inpatient treatment. The effectiveness of treatment of patients in the comparison group without the use of enterosorbents did not exceed 81%, full recovery – 57.6 per cent.
In patients treated with enterosorbents, showed a significant reduction in terms of relief of symptoms of intoxication (including lethargy, loss of appetite) relative to the comparison group (table. 2). The binding and elimination of toxins, pathogens, pathological products of metabolism reduced their penetration into the blood system, which is clinically manifested by improved health, appetite. In the subgroups of patients receiving enterosorbent, terms of relief of fever were significantly less than 0.8-0.9 days ($p<0.05$) than in the comparison group.

In Fig. 1 shows the daily dynamics of relief of diarrhea syndrome in compared groups.
When analyzing the dynamics of relief of gastrointestinal disorders there was statistically significant reduction in the duration of diarrhea syndrome and bloating when included in the treatment natural enterosorbent or organosilicon enterosorbent.
Application of enterosorbents contributed to the complete cessation of diarrhea by the 5th day of treatment in the of 78.5-79.3 percent children, comparing to 57.9 per cent in the comparison group ($0.05<p<0.01$, Fisher test).
After 5-7 days of treatment complete clinical recovery was achieved in 73.6% of patients receiving diosmectite, and 76.1% – enterosgel. In other patients the stools remain fluid with frequency from 3 to 6 times a day with pathological impurities, was observed flatulence, loss of appetite. In the comparison group, the proportion of such patients was significantly higher – 43.4 compared to 26.4 and 23.9% ($p<0.05$, the Fisher test).
A significant result is statistically significant shorter duration of symptoms of exicosis in the subgroup of patients treated with Enterosgel, not only with the comparison group, but also with a group of

children who received diosmectite ($p<0.05$, Student test). Analysis of the results viral and bacterial tests after treatment showed (tab. 3) that the eradication effectiveness of enterosorbents was comparable to their clinical efficacy and amounted to 73.4% in relation to bacterial pathogens AEI and 80.6% viral pathogens. Eradication efficacy of standard therapy did not exceed 57.2 – 62.5%, but differences between groups did not show a statistically significant difference.

To assess the detoxification effectiveness of different treatments schemes, we evaluated the dynamics of leukocyte index of intoxication (LII) (PL. 4).
It is established that in the period of clinical manifestations AEI average LII in all compared groups was statistically significantly above the norm. A significant greater LII showed during the disease in patients treated with enterosorbents. Significant differences in the effectiveness of detoxification between the compared groups treated with enterosorbents was not detected.
To assess the impact of the treatment on the severity and dynamics of clinical manifestations of concomitant atopic dermatitis, an analysis was conducted of the frequency of the timing and duration of exacerbation of atopic dermatitis from the beginning of the infectious disease, the severity score used for atopic dermatitis (SCORAD) (table. 5, Fig. 2).
It's estimated that more than 80% of children in the comparison group AEI was accompanied by strengthening of cutaneous manifestations of allergic process (strengthening and increasing the area of hyperemia, increased itching, soak and scratching of skin elements), regarded as the exacerbation of atopic dermatitis. The inclusion of enterosorbents in the treatment regimen of patients of the main group was associated with a statistically significant decrease of 58-63% frequency of exacerbation of atopic dermatitis (table. 5). In this case the decisive factor was the timing of the start of enterosorption: early (1-2 days of illness) the appointment of enterosorbents exacerbation of atopic dermatitis were recorded only at 18.9–23.9% of patients of the main group; in the use of enterosorbents with 3-4 days of illness the frequency of exacerbation of atopic dermatitis was significantly higher is 32.1 and 32.6%, and had no significant differences with the comparison group.

The inclusion of enterosorbents in the complex therapy AEI patients the core group has had a positive impact on the severity of clinical manifestations and duration of exacerbation of atopic dermatitis, which was significantly decreased by 3.9 to 4.8 days depending on what kind of enterosorbent was used ($p<0.05$). In the main group of patients showed a decrease in the severity of skin manifestations of allergy (swelling, redness, rash, crusting), a decrease in the intensity of pruritus, sleep disturbance, which was accompanied by a significant decrease of SCORAD index (Fig. 2).
A significant decrease of the average value of SCORAD index to the end of therapy (7 days) marked as in mild and moderate atopic dermatitis in patients treated with enterosorbents (Fig. 2). In the comparison group by the end of the course of basic therapy the severity of clinical manifestations of atopic dermatitis and the value of SCORAD index had a significant positive dynamics.
During the study there were no identified side effects and allergic reactions to investigational drugs.
Thus, the results of the study indicate a high clinical and laboratory efficiency of modern enterosorbents in AEI in children suffering from atopic dermatitis, which leads to more rapid control of symptoms of intoxication and fever, reduces the time normalization of stool, and also reduces the risk of exacerbation and the severity of clinical manifestations associated with allergic diseases in an early start of therapy.

Table 1. Characteristics of the compared groups of patients

Indicators	Main group, n=99		Comparison Group , n=26
	Diosmectite, n=53	Polymethylsiloxane polyhydrate, n=46	
Age of children %			

Up to 1 year	43.4	30.4	34.6
1-3 years	43.4	52.2	50
Over 3 years	13.2	15.4	17.4
Hospitalization period of onset, %			
1-3 days	66	60.9	73.1
The clinical form of the disease, %			
gastritis, gastroenteritis, enteritis	75.4	80.4	76.9
gastroenterocolitis, enterocolitis, colitis	24.6	19.6	23.1
The severity of atopic dermatitis, %			
Mild	32.1	34.6	36.9
Moderate	64.2	54.3	57.7
Severe	3.7	8.7	7.7
Etiology AEI, %			
AEI bacterial etiology	26.9	17	13
AEI viral etiology	39.6	32.6	30.8
AEI unknown etiology	43.4	42.3	54.4

Table 2. Comparative characteristics frequency and duration of major clinical manifestations AEI depending on the kind of treatment

Symptoms		Main group, n=99		Comparison group, n=26
		Diosmectite, n=53	Polymethylsiloxane polyhydrate, n=46	
Intoxication	All, %	93.5	100	84.6
	The average duration in days	3.1±0.41*	3.4±0.34*	4.1±0.41
Fever	All, %	84.9	84.7	76.9
	The average duration in days	2.8±0.4*	2.9±0,4	3,7±0.2
Vomiting	All, %	81.1	76	65.3
	the average duration in days	2.5±0.4	2.6±0.3	2.7±0.3
	the average duration in days from the start of therapy	1.4±0.2	1.9±0.2	1.6±0.1
Exsicosis I–II degree	All, %	15	23.9	26.9
	the average duration in days from the start of therapy	2.3±0.2	1.6±0.1*#	2.5±0.2
Bloating	All, %	81.1	73.9	80.8
	the average duration in days from the start of therapy	3.1±0.2*	2.8±0.1*	4.1±0.3
Diarrhea	All, %	95.6	98.1	100
	the average duration in days	5.6±0.6*	5.6±0.6*	7.2±0.5
	the average duration in days from the start of therapy	3.2±0.5*	3.4±0.4*	4.8±0.3
The frequency increase in 1-3-day treatment	stool, %	15.1	19.2	13
	vomiting, %	9.5	19.2	13

The increase of fever in 1-3-day treatment, %		7.6	8.7	15.3
Clinical treatment efficiency	full, %	67.9	60.8	57.6
	incomplete %	20.8	28.3	23.2
	no, %	11.3	10.8	19.2

Note. Significant differences at p<0.05: * the comparison group, # group diosmectite.

Table 3. Eradicating effectiveness of enterosorbents in AEI in children suffering from atopic dermatitis

Symptoms		Main group (diosmectite + polymethylsiloxane polyhydrate)*, n=51	Comparison group, n=15
Was isolated pathogen, abs.	bacteria	15	7
	viruses	36	8
Stopped allocating pathogen after 1 course of treatment, abs/%	bacteria	11/73.4	4/57.2
	viruses	29/80.6	4/50

* The analysis is performed for the combined group of patients taking into account the previously obtained data on comparative clinical effectiveness.

Table 4.

LII dynamics during the therapy of AEI in children suffering from atopic dermatitis (AD)

The timing of the study	Main group, n=99		Comparison group, n=26
	Diosmectite, n=53	Polymethylsiloxane polyhydrate, n=46	
When you receive	3.1±0.2*	2.7±0.1*	3.3±0.1*
After treatment (5-7 days)	0.82±0.1**#	0.6±0.1**#	1.6±0.2#
Norm	1.6±0.5		

Note. Statistically significant differences (p<0.05) with: * indicators of physiological norm, ** comparison group, # from the beginning of the observation.

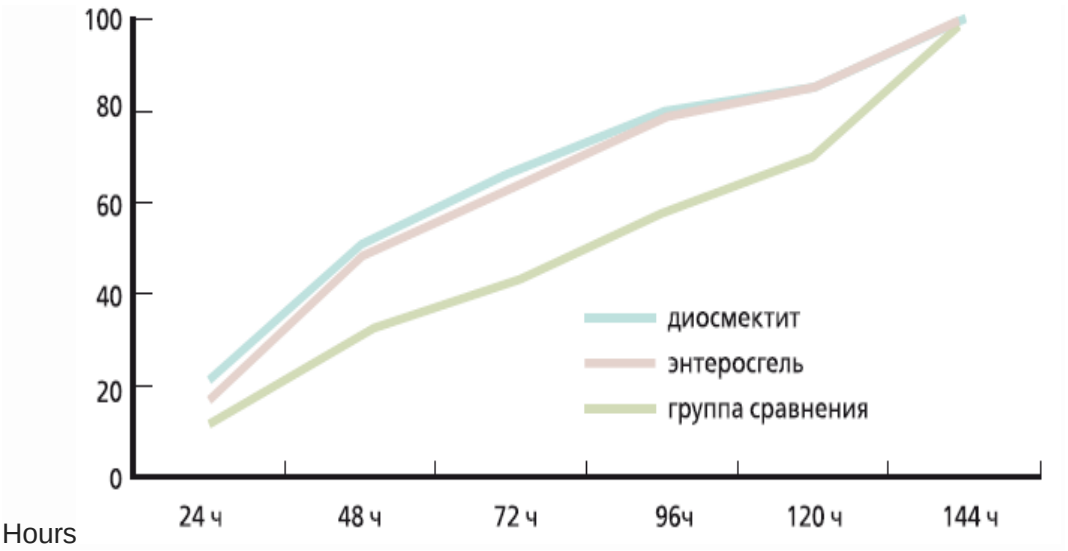
Table 5. The influence of the therapy on the course and severity of atopic dermatitis in children with AEI

Index		Main group, n=99		Comparison group, n=26
		Diosmectite, n=53	Polymethylsiloxane polyhydrate, n=46	
Strengthening clinical manifestation or exacerbation of atopic dermatitis in the acute period of the AEI, %		50.9*	56.5*	80.8
Strengthening	Early initiation of	18.9*	23.9	42.3

clinical manifestations of atopic dermatitis taking in account the initiation of treatment, %	treatment (1-2 days AEI)			
	Delayed treatment (3 and later day course of the AEI)	32.1	32.6	38.5
The average duration of exacerbation of atopic dermatitis after AEI, day		18.2±1.1#	17.3±1.8#	22.1±1.6

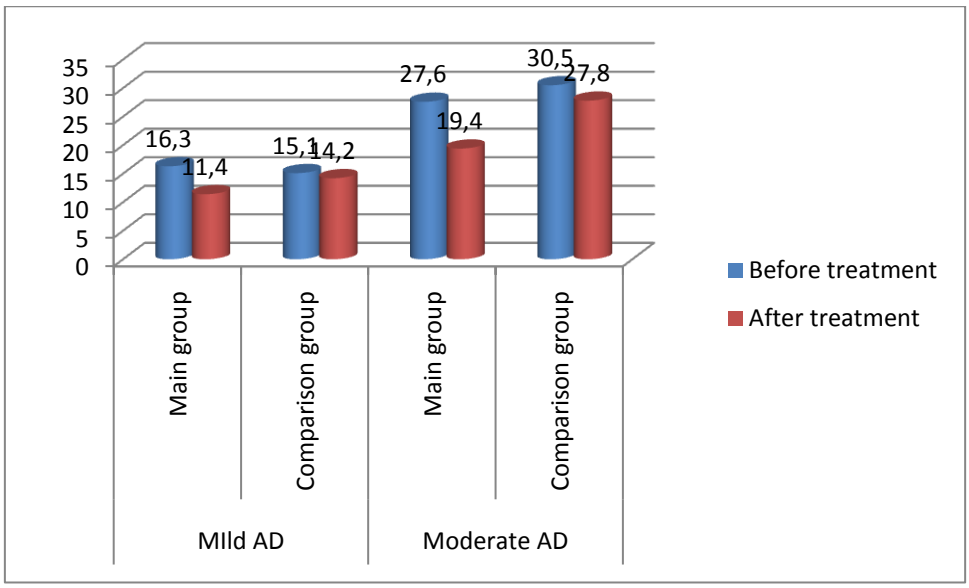
* Statistically significant differences with the comparison group ($p<0.05$, Fisher test); # statistically significant differences with the comparison group ($p<0.05$, Student test).

Figure 1. Stool normalization depending on kind of treatment, hours



Diosmectite – blue line, enterosgel - pink, comparison group - green

Figure 2. SCORAD index during the treatment children with acute enteral infection and atopic dermatitis



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