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Clinical characteristics and principles of treatment of patients with enteric infections caused by *Clostridium difficile*

Abstract: The risk factors and the development of diarrheal and intoxication syndrome in patients with intestinal infections caused by *Clostridium difficile* is an early irrational use of antibiotics, prolonged hospital stay as a source of nosocomial infections, as well as age.

Keywords: Intestinal infections, intoxication syndrome, diarrhea.

At the present stage the problem of microbial ecology associated with the effect of antibiotics on individual normal microflora of the human body is quite acute. With violation of the microecology due to extensive and occasionally unreasonable use of antibiotics is associated widespread caused by *Clostridium difficile*, clinical spectrum of symptoms that varies widely — from the carrier state and the very short-term passing of diarrhea until development of pseudomembranous colitis [1; 2; 5].

It was found that the toxins produced by these bacteria are involved in the pathogenesis of antibiotic-associated diarrhea and is currently considered as the most probable cause of colitis and diarrhea in children. All patients with diarrhea associated with antibiotics flowing with intoxication and leukocytosis, the occurrence of acute diarrhea should be associated with *C. difficile*. In samples of stool *C. difficile* cells remain viable at 5 °C to 10 days at 25 °C up to 4 days.

One of the features of *C. difficile* is the production of heat labile complex exotoxin consisting of a cytotoxin (toxin B) and enterotoxin (toxin A) with said complex binds toxic pathological changes in intestinal mucosa of the patient: ulcer formation and false-membranous colitis.

Clostridium difficile causes of pseudomembranous colitis in 100% of cases. *Clostridium difficile* intestinal infection occurs in approximately 50% of newborns. A pathogenic property of the pathogen does not occur until the end of the first year of life due to lack of or underdeveloped intestinal receptors for the toxins produced by them. At the same time, asymptomatic carriage of *Clostridium difficile* detected in a certain part of the adult population — 1–3% in Europe and 15% in Japan. In our country, a number of reasons, and primarily due to the lack of appropriate laboratory facilities, diagnosis of infections caused by *Clostridium difficile* is absent and its frequency may be judged only on the basis of individual publications.

Purposes. The purpose is study of clinical features of intestinal infections in children caused by *Clostridium difficile*.

Materials and methods. Our systematic study of the etiology of acute intestinal infections in children for the period of 2005–2012 years based on studies of 225 sick children aged 2 months to 3 years. The material for the study were samples of faeces. The study was conducted using the polymerase chain reaction (PCR) and bacteriological methods. Diagnosis by PCR analysis was installed in all cases. Of these, 14 (38.8%) children were diagnosed on the basis of bacteriological tests and 32 (88.8%) children on the basis of serological (ELISA).

The criteria for assessment of the severity of the disease were: the acuteness of infection, the severity of toxicity and exsiccosis, duration of temperature reaction and gastrointestinal disorders, the degree of involvement in the pathological process of the cardiovascular and central nervous system, blood counts and coprogram. Given these criteria of 36 examined patients were diagnosed with moderate form in 24 (76.6%) and heavy in 12 (33.4%).

To determine the causative agents of acute intestinal infection in this work first time we have used PCR.

Observed patients before admission to hospital had been treated with antibiotics, bacterial preparations received on the set in the history of various degrees and kinds of intestinal dysbiosis. These children have been carried out paraclinical methods of examination, including the study of intestinal microflora.

Results and discussion.

According to the results of research *Clostridium difficile* is found in 16% of cases of children with acute intestinal infections. The average age of patients caused by *Clostridium difficile* was $13,7 \pm 1,35$. Thus, in the age group 1–2 years among identified an acute intestinal infection predominated clostridial diarrhea. In this group of patients *Clostridium difficile* is the leading causative agent of an acute intestinal infection causing about half of all diagnosed cases of etiologically undiagnosed intestinal infections.

Our results showed that the infection is significantly more common in children younger than 2 years ($P > 0,05$) (Table 1).

Table 1. – Comparative assessment of the severity of dyspeptic symptoms

Diarrheal syndrome	Clostridium%	Salmonellosis%	Acute dysentery %	Collic infection %	AIUE%
The body temperature to 38 °C	25	31,7	40,5	34,4	10,9
The body temperature to 38 °C	62,5	63,3	40,5	43,8	69,5
Duration of t°					
Up to 2 days	0	25,0	21,4	31,3	30,4
Duration t° from 2 to 3 days	37,5	43,3	42,9	37,5	32,6
Duration t°C 7 days	50,0	26,7	16,7	9,4	17,4

Thus, in the development of the role of acute intestinal infections *Clostridium difficile* is higher than the child's age below. The study of epidemiological history revealed that the factors contributing to the emergence of pseudomembranous colitis are also crowding of patients in the wards, lack of staff, the violation of the sanitary regime and the irrational use of antibiotics. All children on the background of antibiotics and 30% of cases as “nosocomial infection” noted varying degrees of severity diarrheal syndrome and fever. More than half of children constituted the newly admitted to the hospital. In the study of comorbidity in all our children have been identified varying degrees of anemia ($P>0,05$), a rachitis ($p>0,001$), fermentopathy and dysbacterioses bowel from childbirth, perinatal encephalopathy ($P>0,05$) more often with hypertensive syndrome.

With the acute onset of the disease in the hospital received 80,6% of children and the temperature was within normal limits in 3 (8,3%), in 22 (61,1%) patients was rising to 37–38 °C, in 11 (30,6%) — above the temperature was 38 °C. Duration of the temperature in days was 16,0±4,7. The disease occurs in moderate and severe form. In 1/3 of

the patients were found mixed infection “*Clostridium salmonellosis* +”.

Clostridial infection in all patients manifest in dry and pale skin and mucous membranes, weakness and lethargy. In 97,2% of patients noted a violation of appetite, at 58,4% — a sleep disorder.

Dyspeptic symptoms like abdominal pain met — at 88,9%, with a duration of 6,5 ± 0,72 days, bloating — 61,1%–66,7% rumbling intestines, sigmoid pain — 30,6% tenesmus and its equivalents — 25%, single vomiting episode in — 50,0%. In 27 (75,0%) patients experienced children diarrhea with mucus and 25% — streaked with blood, with more than half of the patients stool frequency was noted more than 8–10 times a day. The duration of diarrhea in days was –12,4±1,62. As well it was characteristic of generalization of infection, sepsis especially in “mixed” infection.

An objective examination, 83,3% of patients found hepatomegaly, at 38,9% — splenomegaly, at 61,1% — abnormal noise at the top of the heart and the lungs rhonchuses (table 2).

Table 2. – Comparative assessment of the severity of diarrhea syndrome

Diarrheal syndrome	Clostridium%	Salmonellosis%	Acute dysentery%	Collic infection %	AIUE%
Duration abdominal migraine					
Duration from 4 days	61,1	21,7	38,1	40,6	39,0
Duration t° from 4 to 7 days	66,7	50,0	42,9	25,0	37,0
Duration from 7 days	37,5	21,7	9,5	9,4	8,7
Other symptoms					
Incompletely closed anus	62,5	78,3	76,2	65,3	71,7
Vomiting single	62,5	61,7	47,6	53,1	60,9
Manifold single;	12,5	13,3	7,1	37,6	8,7
Frequency duration t° from 2 to 3 days 5–8 paz	62,5	55	57,1	43,8	60,9
Frequency 10 and more	37,5	38,3	23,8	0	10,9
Bloating	61,1	61,7	57,1	40,6	69,6
Tenesmos	25	13,3	40,5	15,6	17,5
Borborygmus	37,5	71,7	38,1	53,1	56,5

Due to the fact that the violations of stool persisted after resolution of the inflammatory process and the discontinuation of antibiotic therapy for all children was conducted microbiological studies of feces. Conducted analysis of the microflora of the colon revealed that children were studied pronounced shifts in the gut microbiota,

namely, 61,1% of children have no bifidobacteria in 66,7% — lactobacilli, while *E.coli* deficit was observed in 38,8% of patients. Strains of *E.coli* with hemolysing activity were identified in 22% of children. In some of the children in the relevant credits were sown fungi of the genus *Candida*, *Klebsiella* and *Proteus*.

Questions to treat diarrhea caused by *Clostridium difficile* hitherto not fully developed. List of antibacterial drugs used in the treatment of intestinal infections caused by *Clostridium difficile*, including metronidazole, vancomycin, Bactrim, rifampicin and fluoroquinolones. Currently, the most promising direction in the treatment of this infection is the use of probiotics. In the treatment of moderate forms of the disease, we used metronidazole tablets in age dosage in the treatment of severe diseases include therapy metrogil i/v and rifampicin injections. To correct the identified dysbiotic shifts all children were assigned -immunobifidum. The control groups of 10 children were treated for 20 days standard bifidumbacterin (10 doses per day).

Domestic drug "Immunobifidum" manufactured by the original technology of "Orom-biological product" (Tashkent), consists of a complex of probiotic "Bifidobacterium bifidum" and extract fetal "immunoaktivina" does not contain artificial colors or preservatives. 1 tablet contains 10 doses of viable bifidumbacterin. The drug was administered to children under 1 year 1 tablet and aged 1 to 3 years 2 tablets before going to bed. The course of therapy was 20 days.

Upon completion of the full course of therapy normalization of stool, the disappearance of signs of inflammation in the intestines

scatological study and microbiological improvement was observed for all the children of the main group. After the event frequency of dysbiosis of III degree decreased by 3 times (68,0% – 26,6%) and II degree — 2 times (28% – 14,3%). The positive effect was observed in 62,5% of children.

Thus, clinical analysis showed that intestinal infections caused by *Clostridium difficile* is also characteristic symptoms of diarrhea and intoxication syndrome. The risk factors and the development of the disease is the early irrational use of antibiotics, prolonged hospital stay as a source of nosocomial infections, as well as age of the children.

Qualitative and quantitative changes in intestinal microflora are considered as one of the mechanisms that support and aggravating for the main disease

Conclusions:

1. The presented data give reason to treat an intestinal infection caused by *Clostridium difficile* as a serious problem that requires a specific approach to the diagnosis and the corresponding complex treatment

2. The obtained results allowed us to draw a reasonable conclusion about the usefulness of the drug "Immunobifidum" in the treatment of intestinal infection caused by *Clostridium difficile*.

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Efficiency estimation of multi-modal approach to anesthetic management of long-term, abdominal operative interventions

Abstract: 86 patients has been examined and divided into 3 groups depending on the method of anesthesia have been investigated. Patients of 1st and 2nd groups were made traditional general anesthesia. Patients of 3rd group were made general anesthesia on the principle of multi-modal anesthesia.

Multi-modal approach to anesthetic management with the force to all parts of pain pathogenesis promotes the stability of hemodynamic indications in post-operative period, to minimum tension of homeostasis, less expressed reaction of sympathoadrenal system due to good neurovegetative protection.

Keywords: multi-modal analgesia, epidural analgesia, pain

Introduction

Multy-modal analgesia foresees the simaltenious usage

of 2 or more analgesics having different acting mechanisms and allowing to reach the adequate narcosis at minimum side-