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PURULENT APPENDICULAR PSEUDOMONAS PERITONITIS IN CHILDREN AND OPTIMIZATION OF ITS TREATMENT

ABSTRACT

Over the past decade (2007-2016), Pseudomonas etiology of acute purulent destructive appendicitis in children of the Central Chernozem region has been detected clinically, intraoperatively and bacteriologically in 4-5 patients per year. Totally, over this decade, Pseudomonas etiology of the disease was found in 44 children of age from 2 years 3 months to 14 years old suffering from purulent perforated peritonitis of appendicular origin. The clinical course of diffuse purulent appendicular Pseudomonas peritonitis turned out to be more severe and dangerous than in similar patients with peritonitis caused by enterobacteria: Escherichiosis, Enterococcal, Enterobacter, etc. Traditional combined treatment of such pediatric patients proved to be inefficient due to the resistance of pseudomonas flora to traditional antibacterial drugs. Combined treatment of studied patients with perforation Pseudomonas peritonitis is successfully supplemented by the newly developed differential anti-pseudomonas therapy. It has been successfully used in such patients to prevent the development of abdominal pseudomonas sepsis and to provide patients with full clinical recovery.

Keywords: children, acute gangrenous perforated appendicitis, purulent perforation peritonitis, pseudomonas aeruginosa, antibiotics, differentiated combined treatment of patients with peritonitis.

URGENCY

Improvement of the quality of diagnostics and the efficiency of combined treatment of children with gangrenous perforated appendicitis and purulent Pseudomonas peritonitis accompanied by the reduction in the incidence of sepsis and the threat to the child's life is an urgent issue of current pediatric surgery and pediatrics in general. According to the results of previous (1,2) bacteriological studies of biomaterials of the abdominal cavity with the intestinal perforation, among the causes of acute appendicitis a decrease in the frequency of Escherichia coli growth was observed, with the absolute dominance of another enterobacterial autoenterogenic flora. Among the children's population of the Central Chernozem region, intestinal dysbiosis with predominance of the Pseudomonas flora was definitely identified (3.4). According to a number of other well-known publications (1.2.3.5), intestinal contamination with Pseudomonas aeruginosa has become more frequent in children of Russia and abroad. Late diagnosis of acute gangrenous perforated appendicitis caused by Pseudomonas aeruginosa in different age groups provides frequent development of Pseudomonas peritonitis for which traditional combined treatment turned out to be low efficient.

MATERIAL AND METHODS

Over the past decade (2007-2016), Pseudomonas etiology of acute purulent destructive appendicitis in children of the Central Chernozem region has been detected clinically, intraoperatively and bacteriologically in 4-5 patients per year. Totally, over this decade, Pseudomonas etiology of the disease was icentified and investigated in 44 children of age from 2 years 3 months to 14 years old suffering from gangrenous perforation peritonitis, diffuse purulent appendicular peritonitis. Among other causative agents classified as conditionally pathogenic enterobacteria there were the following. Escherichia colli was identified as 68.5% enterococcus, 11.8% enterobacter, and 15.2% anaerobes. Klebsiellae oxytoca in 7 (5.9%) patients and Staphylococcus in 2 children were much less frequently identified. According to the age of patients with appendicular purulent Pseudomonas peritonitis, children were ranged as follows: 1 to 4 years old - 3 children, 4 to 7 years old - 11 patients, 7 to 10 years old - 12 children, 10 to 14 years old - 18 patients; as for sex groups, treatment was given to 25 boys and 19 girls. Distribution of patients by sex, age, prevalence of purulent-destructive process in the abdominal cavity in Pseudomonas appendicular peritonitis is presented in Table 1.

Biomaterial cultures for all 44 pediatric patients giving evidence of Pseudomonas origin of appendicular peritonitis, initially included: intraoperative abdominal effusion, repeated bacteriological examination of the contents of septic wounds, purulent cavities, blood, urine for microflora, and antibiotic susceptibility. Microbiological identification of microorganisms was carried out with the help of a plate reader Labsystems iEMS Reader MF using commercial microtest systems and the computer program «Microbe-automat» and «Microbe-2». The method for serum procalcitonin (PCT) determination was performed using an express-test by Brahms A.G. company as a biochemical method for diagnosing Pseudomonas sepsis in peritonitis with the assessment of its severity. For statistical processing of the results obtained, the distribution law of multidimensional quantities was used (according to A.I. Rog and V.S. Malaychuk, 1978). Antimicrobial susceptibility of microorganisms was determined by the serial dilution method and the diffusion method, which included 2 modifications - disc-diffusion test and E-test. Modern approaches to determining the antimicrobial susceptibility of bacterial pathogens are based on EUCAST (European Committee on Antimicrobial Susceptibility Testing) guidelines, as well as the «Recommendations of the NCCLS (National Committee for Clinical Laboratory Standards, USA) guidelines».

STUDY RESULTS

Over the past decade (2007-2016), acute purulent appendicular Pseudomonas peritonitis was diagnosed in 44 children of preschool and school age. This amounted to 4-5 children with

Pseudomonas peritonitis of appendicular origin annually. When revising the abdominal cavity intraoperatively appendicular Pseudomonas peritonitis was diagnosed by the characteristic infiltrative inflammation of the parietal and visceral peritoneum and fetid purulent effusion. The diagnosis in all 44 patients was reliably confirmed by the active pathogen (Pseudomonas aeruginosa) growth. The incidence of acute Pseudomonas appendicitis varied in different age groups of patients: the lowest rate was in the age of 4 years (3 children) and the highest one was observed in patients above 7 years old (30 cases). Characterizing the dynamics development of purulent Pseudomonas process in the abdominal cavity in children, it should be recognized that this process spreads more actively over the area of inflammation in perforation of the gangrenously changed vermiform appendix, which is confirmed by the data of Table 1.

Only in 8 (18.2%) patients of different ages the inflammation was local, Pseudomonas peritonitis in other 33 (75%) children was diffuse and 3 patients (6.8%) demonstrated total peritonitis. The rapid development of clinical symptoms in purulent inflammation of the abdominal cavity indicates expressed aggressiveness of the Pseudomonas aeruginosa pathogen. In all 3 patients of the age group 1-4 years old perforation of the appendix with the development of peritonitis occurred within the first 24 hours, which was confirmed by intraoperative and histopathological examination. Speedy course of the disease is typical for patients with Pseudomonas peritonitis in other age groups, too. Thus, the perforation of the gangrenous-modified vermiform appendix during the first day of the disease was confirmed intraoperatively in 13 patients, including 5 (of 11) patients aged 4-7 years, in 6 (of 12) children of the age group 7-10 years old and only in 2 girls (of 18 patients) of the age group of 10-14 years old.

The remaining patients (31 children) showed the developed purulent peritonitis with perforation of the appendix by the end of the second day. By this period of the disease in 27 children purulent appendicular peritonitis had already had a diffuse character. Among them: in 6 children with atypical location of the appendix and late diagnosis of the disease, purulent peritonitis was diffuse in 4 patients and total in 2 children. The local form of pseudomonas inflammation of the abdominal cavity in these patients in the postoperative period was complicated by an abscess of the anterior abdominal wall in the area of the operating wound (in 4 children), an abscess of the omentum (in 2 cases).

Intraoperatively, fetid pus in the abdominal cavity was evacuated by an electric pump in the amount of 100-200 to 250 ml. In 16 (36.4%) of the patients studied, the appendix was located in the small pelvis, in the other 17 (38.6%) patients it was located retrocetically. Involvement of the cecum and omentum into inflammation was taken into account during the sanation and the need for drainage of the abdominal cavity. Removal of the appendix in all 44 children was carried out with a purse-string technique, without any technical difficulties. Sanitation and drainage of the abdominal cavity were performed in pediatric patients taking into account the severity of the purulent-destructive process. Resection of omentum sections was carried out within healthy tissues with the severity of inflammation in 20 patients. In 3 children, when performing the abdomen revision, abscesses in the infiltrated omentum were tapped. In 4 cases of appendicular Pseudomonas peritonitis, the disease was complicated by the formation of abdominal infiltrates, which were successfully sanitized with conservative methods. For all 44 patients, the prevalence and severity of the purulent process were taken into account in surgical technique and intensive care. In all cases, the operation was completed with draining the abdominal cavity. Drainages were installed in the abdominal cavity in the flanks and to the bed of the appendix. They functioned and remained in the abdominal cavity of the operated child for 3-4 postoperative days.

Results of the histopathological study of the drug: «destructive gangrenous-perforated appendicitis, massive fibrinous-purulent periappendicitis, mesenteriolitis, purulent omentitis.» Intraoperatively, all 44 children underwent bacteriological swab test of the abdominal effusion for the flora and antimicrobial susceptibility. In 35 (79.5%) of 44 patients, abundant growth of Pseudomonas aeruginosa monoculture, sensitive to amikacin, ciprofloxacin, cefepime, ceftazidime, carbenicillin, and tazobactam, was found. In other 9 patients with Pseudomonas peritonitis the causative agent of the disease helped to reveal a Pseudomonas mix-infection, including its combinations with other enterobacteria (with Enterobacter cloacae in 1 patient and Escherichia coli in 3 children) after 2-3 days of the disease (repeated sampling of the abdominal effusion). In 3 other cases, a combination of Pseudomonas aeruginosa with epidermal staphylococcus - Staph. Epidermalis was detected. Among the detected pathogens of Pseudomonas peritonitis of appendicular etiology, except for Pseudomonas aeruginosa, other Pseudomonas strains (Pseudomonas fluorescens in one patient and Pseudomonas putida in another patient) demonstrated an active growth of the culture. But these strains of Pseudomonas infection were no less aggressive than Pseudomonas aeruginosa, causing a very severe course of perforation peritonitis. Pseudomonas fluorescens and Pseudomonas putida, were also sensitive, like Pseudomonas aeruginosa, to amikacin, cefotaxime, ceftazidime, cefepime, meropenem, ticarcillin.

Discussion of the results: Acute appendicitis in children of different ages is still among the difficultly diagnosed childhood diseases in public health. In the conducted studies, pseudomonas inflammation and destruction of the appendix with the development of peritonitis proceeded classically and was diagnosed in the preoperative period at the end of the first day of the disease in 13 (29.5%) children. The disease developed acutely, beginning with abdominal pain, nausea, vomiting, general weakness,

Table 1

Distribution of pediatric patients by sex, age, prevalence of purulent-destructive process in the abdominal cavity in Pseudomonas appendicular peritonitis (n=44)

Age	Boys	Girls	Local	Diffuse	Total
1-4 years old (n= 3)	2	1	-	1	2
4-7 years old (n= 11)	6	5	2	8	1
7-10 years old (n=12)	6	6	2	10	-
10-14 years old (n= 18)	10	8	4	14	-
Total = 44	25	19	8	33	3

subfebrile condition (up to 37.5C). Abdominal pain was pronounced and permanent. The diagnosis of acute appendicitis in this group of patients, including children aged 1 to 4 years old, was made in the first day of the disease without difficulties and doubts, by means of objective examination by a first contact physician. In pre-school and school-age patients, Pseudomonas peritonitis was diagnosed by an objective examination of the doctor after 24 hours from the onset of the disease. These children, within 2-3 days after the onset of the disease, have demonstrated total purulent fecal peritonitis, purulent omentitis, mesadenitis. Studies of the susceptibility for cultures of Pseudomonas strains in 44 children with perforated peritonitis have shown that in recent years the microbe still remains sensitive to a large number of antibacterial drugs, as indicated in Table 2.

According to Table 2, the susceptibility of Pseudomonas cultures to different antibiotics in patients with acute purulent perforated peritonitis is different: it is the highest in imipenem - 93%, ceftazidime - 90.3%, amikacin - 87%, meropenem - 83.3%, ticarcillin - 83.3%. Significantly less sensitive are cefepime - 71% and ciprofloxacin - 55%. The lowest sensibility was demonstrated by Pseudomonas to carbenicillin, amoxiclav and other antibiotics. The most highly effective anti-Pseudomonas drugs in our studies were antiseptics, which showed a high level of antimicrobial effect: chlorhexidine 71%, bacoderm -71%.

Empirical antimicrobialc therapy of patients with purulent appendicular Pseudomonas peritonitis was started in the perioperative period in the intensive care unit environment. Its efficiency was significant in the combined treatment of a pediatric patient who was in critical condition. Patient's condition was evaluated by the degree of subsidence of clinical signs of peritonitis in the early postoperative period. In a modern pediatric surgical hospital, it is reliably confirmed clinically and in laboratory, even before obtaining the result of identification of the microorganism – the causative agent of peritonitis. Persistent fever, oliguria, intoxication, toxic intestinal paresis, which persisted in a patient in the first days after the operation, required a search for the cause of the pronounced activity of the infection of the abdominal cavity after its intraoperative sanation. It was established through the joint efforts of pharmacologist, a pediatric surgeon and an emergency physician on the basis of available objective clinical and biochemical tests of the patient's condition as a reason for the low effectiveness of starting postoperative intensive care. Traditionally, it is known that the expected results of the bacterial test of the effusion are received by the attending physician from the laboratory only by the end of the 3rd day of bacteriological diagnostics, while the data on the antibiotic susceptibility of the microbial culture - only on the 5th day of the bacterial swab test. Therefore, all doubts about the inefficiency of starting antibiotic therapy were resolved in favor of the patient. The substitution of the antibiotic with a drug more significant in the treatment of pediatric patients with peritonitis has now become a rational kernel of getting a therapeutic effect in patients with a complicated course of autoenterogenous disease - acute appendicitis in the environment of a modern surgical clinic.

Evaluating in this study the efficiency of a traditional starting antibiotic therapy in patients with appendicular Pseudomonas peritonitis, it was established that it was not always effective enough against Pseudomonas infection. Traditionally, starting empirical antibacterial therapy for such patients included antibacterial drugs, which, according to the results of their use, always proved to be highly effective, as indicated in Table 3.

According to Table 3, the absence of the expected clinical effect of the use of cefazolin, ceftriaxone, amoxiclave, ampicillin in 26 patients with perforation Pseudomonas peritonitis make the doctor substitute these drugs taking into account the data of bacterial swab tests. The antibiotic was changed for drugs with a high rating of therapeutic effect in pediatric patients with suspected or identified Pseudomonas infection (ceftazidime, amikacin, meropenem, imipenem). The revealed tendency to the formation of abdominal wall infiltrates (3 patients) and abdominal infiltrates in the other two patients with Pseudomonas peritonitis is explained by the administration (together with a pharmacologist) of more effective drugs (vicef, imipenem, meropenem) to these patients. Such decisions to replace the antibiotic with a more effective, considering the data of bacterial swab tests for a certain patient, were taken collectively during the treatment of the child in the intensive care unit and reanimation in accordance with the established standard. If against intensive therapy after 4 - 5 days of the postoperative period the patient with appendicular peritonitis of any etiology continued to fever and the hyperleukocytosis in the peripheral blood persisted, it is carried out in-depth analysis of the course of the surgical pathology, the patient was evaluated with the effectiveness of antibiotic therapy and infusion therapy, also the patient was screened for sepsis, postoperative infiltration, an abscess, an abdominal pyogenic abscess which was formed but not diagnosed in the abdominal cavity or beyond it. Replacement antibiotic with reserve preparations (thienam, meronem, imipenem), detoxification tratment expansion, transfer to complete parenteral nutrition (aminoplasmal, lipofundin) eliminated the risk of sepsis and other complications of the purulent process in the abdominal cavity. This was particularly true for children who were operated in the later stages of the disease. Among these patients, there were 2 children with total Pseudomonas appendicular peritonitis who had already been operated in the stage of developed abdominal sepsis and septic pneumonia, but with favorable results of combined treatment - recovery.

Today it is necessary to recognize the particularly important diagnostic role of

Table 2

Results of studies on antimicrobial susceptibility of Pseudomonas cultures in children with perforation peritonitis (n=44), in bacteriological swab tests of abdominal effusion

Drug	Number of patients with peritonitis	Number of studied bacterio-logical swabs of Ps. aeruginosa	Antibiotic susceptibil-ity, %
ceftazidime	44	28	90,3
amikacin	44	27	87
cefepime	44	22	71
ciprofloxacin	44	17	55
cefotaxime	44	9	29
imipenem	14	13	93
meropenem	12	10	83,3
ticarcillin	12	10	83,3

Table 3

Drugs of empiric antimicrobial therapy used (%) for treating pediatric patients with perforation Pseudomonas peritonitis of appendicular origin (n=31)

Drug	Susceptibility of a Pseudomonas microbe	Number of treated patients (n=)	Percentage	Drug substitution
Amikacin	++++	13	42	no
Ceftazidime	++++	10	32,2	no
Ciprofloxacin	++++	3	9,7	no
Cefotaxime	+++	16	51,6	no
Cefazoline	+	7	22,6	yes
Ceftriaxone	+	8	25,8	yes
Amoxiclav	+	9	29	yes
Amoxicillin	+	2	6,5	yes

modern high-tech devices (ultrasound and X-ray CT of the abdomen) to identify the unclear causes of fever and other manifestations of purulent complications in patients with peritonitis. Among 6 (13.6%) severe patients, radiation diagnostic methods (ultrasound, X-ray CT) revealed intraperitoneal infiltrates in 2 patients (4.5%), purulent infiltrates in the area of the postoperative wound in 3 other patients (6.8%), and an intra-abdominal abscess was diagnosed in 1 child. To treat these patients, different methods of treatment have been successfully used: both traditional treatment such as tapping and emptying the omentum abscess (in 1 patient), and conservative treatment of intra-abdominal infiltrates (in 2 pediatric patients) and infiltrates of the anterior abdominal wall. Conservative treatment of infiltrates occuring on the 8th-19th day of the disease, along with antibiotic therapy, included modern physiotherapy: magnetotherapy No. 5-7, iruksol phonophoresis, and laser therapy. Anti-adhesion therapy included administration of electrophoresis with KJ, lidase No. 10 on the right iliac region, laser therapy No. 8-10. There were no cases of early adhesion in the studied 44 children with appendicitic Pseudomonas peritonitis. In this group of patients, disability was not recorded either, while the outcome in abdominal sepsis was diagnosed only in 2 patients (4.5%) admitted to the hospital at the stage of generalization of the purulent infection. There were no cases of lethality among 44 children of different ages.

CONCLUSION

Pseudomonas etiology of acute appendicitis in children, established by clinical, intraoperative and bacteriological study in appendicular peritonitis, which has become more frequent in recent years, turned out to be the result of intestinal dysbiosis. Among the identified opportunistic pathogens of appendicular Pseudomonas peritonitis, an active growth of the culture was observed predominantly for the Pseudomonas aeroginosae strains (in 42 pediatric patients) and rearly for Pseudomonas fluorescens in 1 patient and Pseudomonas putida in another patient. These strains of Pseudomonas infection were no less aggressive than Pseudomonas aeruginosa, and caused a very severe course of perforation peritonitis. The obvious reason for the insufficient effectiveness of combined treatment of patients was considered to be the resistance of the Pseudomonas flora to the majority of traditional starting antibacterial drugs, especially in patients with the thriskreat of development of abdominal sepsis. Due to the successful application of modern high medical technologies (ultrasound, laparoscopy, bacteriological, biochemical and X-ray computer studies) in the studies undertaken, it has now become possible to provide patients with early diagnosis of the etiology of appendicular peritonitis and early effective treatment, to prevent the development of abdominal sepsis and multiple organ failure. In patients with appendicular peritonitis and the suspicion or identification of Pseudomonas flora, the need for correction of starting antibiotic therapy is reliably confirmed, with the administration of carbapenems or cephalosporins of III-IV generation in combination with aminoglycosides (amikacin, selemycin). Pseudomonas fluorescens and Pseudomonas putida are particularly sensitive to amikacin, cefotaxime, ceftazidime, cefepime, meropenem, ticarcillin, chlorhexidine. These drugs in modern conditions largely provide the clinical effeciency of starting antibiotic therapy, until the results of bacterial swab tests for abdominal effusion are obtained. Today, for children with purulent appendicular Pseudomonas peritonitis, early targeted anti- Pseudomonas antibacterial therapy is the basis of the therapeutic effect of postoperative intensive therapy and the prevention of Pseudomonas abdominal sepsis and multiple organ failure.

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RESULTS OF TREATMENT OF CHRONIC COLOSTASIS AND HIRSCHSPRUNG'S DISEASE

Chronic colostasis (CCS) is an actual and not fully resolved problem in pediatrics in general, and in pediatric surgery [4,5]. Despite the modern development of coloproctology, many aspects of diagnostic and treatment algorithm, as well as questions of rehabilitation after conservative and surgical treatment are still unresolved, controversial and are in need of further verification and clarification [4, 7, 8].

During the literature review of surgical treatment of children with CCS and Hirschprung's disease (HD), in a sufficient percentage (up to 30-40%), in a further period a large number of complications such as, gas and stool incontinence, relapses on constipation, stenosis of anastomoses [1, 4, 5, 6,]. A significant number of patients after multiple surgical interventions, have expressed adhesion processes in abdominal cavity, what is directly related to the traumatic nature of reconstructive operations, and lengthens the terms for rehabilitation [3]. These groups of children are placed on a list and treated in specialized departments, more often in Republican and Federal centers, as they require adequate rehabilitation therapy, which are unable to carry out in clinic services in central cities of Russia, not talking of remote areas. The reasons for such appeals, for a purpose to provide medical assistance, are persistent functional disorders, due to which child becomes disabled.

The **aim** of the study was to evaluate the immediate and long-term results of conservative and surgical treatment of CCS and HD.

To achieve the goal, we examined and treated 108 children with various forms of chronic colostasis. Patients were divided in to 3 groups according to a clinical classification of CCS by A.I. Lyonyushkin. In group with compensated form of chronic colostasis, were included children with episodic disorders in functioning of colon. Constipations with a presence of an independent defecation lasted for 2-3 days. In subcompensated form of disease children complained about periodic constipations with a followed independent defecation, that did not bring relief. Children were ill during several years and the: abdominal pain, flatulence, and accumulation of fecal matter in the colon appeared. In children with decompensated form of CCS clinical picture was characterized by a more noticeable disorders in functioning of colon. The delay of stool was persistent and lasted up to 7 days and more, independent defecation did not bring relief. The abdomen was enlarged, paradoxical encopresis was observed.

Compensated form of chronic colostasis was diagnosed in 37 (34,26%) children, subcompensated in 48 (44,44%) and decompensated in 23 (21,29%) (Diagram 1)

Study included children aged from 1 to 17 years. The detailed distribution of children by age and form of CCS is illustrated in Table 1.

In 37 patients with compensated form, the treatment began of following conservative measures: diet, laxatives, physiotherapy, exercise therapy and massage of anterior abdominal wall. The diet included vegetables, salads on