International Journal of Medical Sciences And Clinical Research
(ISSN – 2771-2265)
VOLUME 04 ISSUE 06 PAGES: 12-17
OCLC – 1121105677
Crossref doi Google Scholar WorldCat MENDELEY

Publisher: Oscar Publishing Services

Journal Website: https://theusajournals.com/index.php/ijmscr

Research Article

THE ROLE OF CLOSTRIDIUM DIFFICILE IN THE DEVELOPMENT OF ANTIBIOTIC-ASSOCIATED DIARRHEA IN EARLY-AGED CHILDREN

Submission Date: May 31, 2024, **Accepted Date:** June 05, 2024,
Published Date: June 10, 2024
Crossref doi: https://doi.org/10.37547/ijmscr/Volume04Issue06-03

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ABSTRACT

Interest in studying the problem of diarrhea in children is due to their wide distribution (1-1.2 billion cases per year worldwide according to WHO, 2010), polyetiology, difficulty of differential diagnosis and tendency to acute and chronic course. In recent years, foreign and domestic authors have attached increasing importance to the so-called antibiotic-associated diarrhea (AAD), components: 6-40% in the structure of intestinal diseases. In the etiological structure of AAD in young children, the share of C.difficile infection was 47%. A rusk factor for development is also combination therapy with antibiotics.

KEYWORDS

Clostridium difficile, antibiotic-associated diarrhea, young children.

INTRODUCTION

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The emergence of antibiotics made it possible to treat many serious life-threatening infections and save the lives of many people. However, widespread and uncontrolled use of various groups of antibacterial drugs, especially in outpatient settings, leads to the development of many negative effects.

In the last 10 years, the use of antibiotics worldwide has increased by 36% [1]. Antibiotic resistance has led to increased use of backup antibiotics, for example, the use of carbopenems increased by 45% and polymyxins by 13%.

Antibacterial therapy affects not only intestinal microflora disorders, allergic reactions and antibiotic resistance, but also type II diabetes, metabolic syndrome, atopic dermatitis, bronchial asthma, cancer, and even myocardial infarction [2-3]. One of the frequent complications of antibacterial therapy can be the development of antibiotic-related diarrhea. According to the WHO definition, antibiotic-associated diarrhea is characterized by an increase in the frequency of stool (more than 3 times a day) that occurs during or within 8 weeks after the end of antibacterial therapy, and its volume increases, along with a change in consistency, it is represented by the appearance of pathological mixtures in the form of mucus, green and blood. According to various epidemiological observations, antibiotic-related diarrhea develops in an average of 5-30% of patients receiving antibiotics [4]. The frequency of antibiotic-related complications in children is more than 11% after the use of broad-spectrum antibiotics, and increases to 42% in immunocompromised children [5].

The incidence of antibiotic-associated diarrhea in hospitals is 20-25%, but in recent years, the free supply of drugs, including antibiotics, has led to an increase in the number of antibiotic-associated diarrhea in outpatient settings. Antibiotic-associated diarrhea may be mild in patients, and in some cases, symptoms resolve when the antibiotic is discontinued. Clinical symptoms may appear even after 8 weeks after the end of the course of antibiotic therapy and cause a deepening of the pathological process, which significantly complicates the diagnosis. Pseudomembranous colitis (PMK), which is one of the dangerous forms, develops.

Antibiotic-related diarrhea can be caused by any antibacterial drug, especially if it is highly active against anaerobes. Antibiotics that cause the greatest risk of developing antibiotic-related diarrhea are clindamycin, lincomycin, aminopenicillins, II and III generation cephalosporins. According to L.Mc Farland (1993), 5-10% of antibiotic-related diarrhea cases are caused by ampicillin, 10-25% by second-generation cephalosporins, and only 2-5% by others (tetracycline, macrolides, nitrofurans, co- develops when using trimoxazole, fluoroquinolines, aminoglycosides).

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It should be noted that the dose, method and frequency of taking antibiotics do not affect the risk of developing complications related to antibiotics. Diarrhea during antibacterial therapy can be infectious or non-infectious. Non-infectious antibiotic-related diarrhea is associated with intestinal motility disorders, toxic effects on the intestinal epithelium, bile acid and carbohydrate metabolism disorders in the intestine, etc. For example, macrolides stimulate motulin receptors, which cause contraction of the smooth muscles of the antral part of the stomach and duodenum, which subsequently leads to the development of diarrhea [6]. The toxic effect of tetracycline and neomycin on the mucous membrane of the gastrointestinal tract is manifested by the direct death of epithelial cells, infiltration of plasma cells, eosinophils and macrophages. This is accompanied by a decrease in the absorption of water and electrolytes in the intestinal villi.

The infectious nature of antibiotic-related diarrhea can be etiologically associated with various pathogens - Clostridium perfringius, Salmonella species, Clostridium difficile, which are able to colonize the intestines by replacing the normal microflora. Many researchers believe that one of the most important infectious agents is Clostridium difficile (C.difficile), which accounts for 10-25% of all antibiotic-associated diarrhea and 90-100% of cases of pseudomembranous colitis.

However, for the development of manifest forms of infections caused by C.difficile, not only the colonization of the intestine with toxigenic strains of the pathogen, but also the presence of risk factors are of great importance, including the use of certain groups of antibiotics, the age of patients, the characteristics of the main and concomitant diseases, hospital stay The period of eating, the condition of the intestinal microflora, etc. can be the cause. A high risk factor for the development of diarrhea associated with C.difficile in children of early age is more characterized by the polymorphism of clinical manifestations in the gastrointestinal tract, which is of great importance for timely diagnosis and adequate therapy.

Currently, the role of Clostridium difficile in antibiotic-associated diarrhea has been studied more in older patients [8.9]. On the contrary, in pediatric practice, many aspects of this problem are related to Clostridium difficile infection, and the differential diagnostic issues of antibiotic-related diarrhea of non-infectious origin have not yet been fully resolved, and the nature of infectiousness has not yet been sufficiently studied. In addition, criteria for early diagnosis, taking into account risk factors for the development of Clostridium difficile infection, have not been developed, and the degree of damage in the gastrointestinal tract and the informative value of signs of inflammation of the large intestine have not yet been fully studied.

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The purpose of the study: to determine the role of Clostridium difficile infection in early-aged children with antibiotic-associated diarrhea.

METHODS

This study was conducted in the Samarkand regional multidisciplinary medical center (head doctor-prof. M.K. Azizov), 68 children aged 2 months to 1.5 years with antibiotic-related diarrhea were observed.

Antibiotic-associated diarrhea is defined as 3 or more episodes of loose stools over 2 or more days, unless another cause is identified (WHO, 2002).

76.5% (52 children) of the examined patients with antibiotic-related diarrhea are children under one year of age. In age groups older than 1 year - 23.5% (17 patients).

38 (55.8%) of the examined children were boys, 30 (44.1%) were girls, gender differences were not identified. Children with antibiotic-related diarrhea treated in gastroenterology and pulmonology departments were included in the study.

According to the characteristics of the degree of damage in antibiotic-related diarrhea, 3 main forms of gastroenteritis, enterocolitis and hemocolitis were identified. More than half of children (57.5%) had antibiotic-related diarrhea with symptoms of gastroenteritis (39 patients), 22 (30.1%) patients developed enterocolitis, 7 (10.2%) patients developed hemocolitis.

Depending on the severity and duration of toxicosis and exicosis, vomiting and diarrhea syndrome, fever, etc., 62 patients (91.2%) and 6 patients (8.8%) with severe form found in children.

Laboratory examinations include general blood analysis, coprology, biochemical blood analysis and bacteriological examination of feces. In addition, laboratory tests include the detection of Clostridium difficile and its toxins A and B using the QIAGEN GmbH (Germany) equipment by polymerase chain reaction. The specificity of the test is 96.2%, the sensitivity is 95.8%.

RESULTS

Clostridium difficile infection was detected in 32 out of 68 patients with antibiotic-related diarrhea, which is 47%. Toxins A and B were detected in children with antibiotic-related diarrhea during hospitalization, and this is 18.7% (6 people).

When analyzing the prevalence of Clostridium difficile infection among children treated with different nosologies, it was found that its ratio is high among children with gastroenterological pathology during the use of antibacterial therapy, which is related to the degree of damage to the gastrointestinal tract and the

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severity of the disease, as well as the degree of inflammation in the intestines was found to be related.

When studying the effect of the method of using antibacterial therapy on the detection of Clostridium difficile infection, the risk of developing this infection when taking antibiotics enterally, the manifestation of clinical manifestations of antibiotic-related diarrhea was 68%, and 31.25 when taking parenterally found in % of cases.

We found that a risk factor for the development of Clostridium difficile infection was combined antibiotic therapy: the frequency of combined therapy was 65.6% (22 patients). This is explained by the fact that taking several antibiotics at the same time increases their negative impact on the microecological relationship in the gastrointestinal tract, expands the range of toxic effects and, as a result, creates additional conditions for the growth and colonization of Clostridium difficile. In our study, it was found that ampicillin (34.4%) and III generation cephalosporin (28.2%) were the most common antibiotics in the formation of C. difficile toxins and the development of the disease.

A risk factor for the development of C. difficile infection is combination therapy with antibiotics:C. difficile-positive group used this treatment option more frequently than C. difficile-negative group (59% significantly higher than 37.70%, respectively, p=0.011). This is explained by the fact that taking several antibiotics at the same time increases their negative impact on the microecological relationship in the gastrointestinal tract, expands the range of toxic effects and, as a result, creates additional conditions for the growth and colonization of C. difficile.

CONCLUSION

In conclusion, the share of C. difficile infection in the etiological structure of antibiotic-related diarrhea in early-aged children is 47%. A risk factor for development is antibacterial therapy combined with antibiotics.

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