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PECULIARITIES OF ANTIBIOTIC-ASSOCIATED DIARRHEA
DEVELOPMENT IN CHILDREN WITH ACUTE RESPIRATORY INFECTIONS

ODMIENNOŚCI ROZWOJU BIEGUNKI POANTYBIOTYKOWEJ
U DZIECI Z OSTRYMI INFEKCJAMI GÓRNYCH DRÓG ODDECHOWYCH

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ABSTRACT

Introduction: Acute respiratory infections (ARI) are the main cause of morbidity in most countries. The probability of complications and age determine antibiotics administration.

Antibiotic associated diarrhea (AAD) is one of the side effects of antibiotics.

The aim: The study of the prevalence rate of AAD and the characteristics of its development in children with ARI.

Materials and methods: The study included 75 children aged from 1 to 12 y diagnosed with ARI, who were treated with age-specific doses of antibiotics. The influence of children’s anamnesis, parents’ health on the development of AAD was studied with odds ratio calculation (OR).

Results: In general, AAD incidence was 52%. The highest frequency 59.3% was observed in children under 3 y. AAD most often developed in children treated with amoxicillin – 92%. The greatest dependence of AAD development was connected with breastfeeding less than 6 months – OR was 7.65, preterm birth – 2.9, functional GIT disorders in anamnesis – up to 3.14, allergy – 2.33. The risk of AAD development increased with the age of parents more than 35 y – 5.03, at the age of parents less than 18 and older than 35 y – 4.09, parents’ allergies - 3.74 and parents smoking - 2.43.

Conclusions: The most important factors of AAD development on antibiotics therapy in children with ARI are breastfeeding less than 6 months, functional GIT disorders and allergic conditions in anamnesis. Suboptimal age and parents’ health (GIT disorders, allergic conditions and unhealthy habits) also increase the risk of AAD development.

KEY WORDS: Antibiotic associated diarrhea, children

INTRODUCTION

Acute respiratory infections (ARI) are the main cause of morbidity and mortality in both developed and developing countries [1; 2]. A child may have up to 6-8 cases of acute respiratory infection during a year. The incidence of acute respiratory infections is recorded throughout the year but more abundantly in the autumn and winter. Around 90% of children have respiratory pathology during flu epidemic. Viruses dominate the etiology of ARI, they are considered to constitute 55-90% of cases [3]. Respiratory syncytial virus is most often revealed. It is pointed out that it is responsible for the development of acute respiratory disease in 60% of children and in 80% of infants at the peak of viral season [4]. A number of authors emphasize the role of rhinovirus in infants (human rhinovirus, HRV), which can be detected in 38% of infants with ARI. Respiratory syncytial virus is detected less often in children of above mentioned group – 5-7% of cases. [3]. The frequency of bacterial infection at ARI in infants can reach 10%, however, the frequency of its detection depends on viruses present in the body [3]. In general, the availability of bacteria as etiological factor may be 27% for all age groups of children [1].

The probability of bacteria presence, ARI severity, du-ration, age and other factors condition antibiotics admin-istration. Unfortunately, despite the high probability of complications of antibiotic therapy, the frequency of their use at acute respiratory infection is rather high. It is pointed out that it constitutes 52-66% depending on the type of ARI [1]. The number of side effects of antibiotic therapy is large and includes the development of allergic condi-tions, the formation of pathogenic microflora resistance, the formation of intestinal microbiome disorders and the development of antibiotic associated diarrhea (AAD).

THE AIM

The research aim is to study the prevalence rate of AAD and the characteristics of its development in children with ARI.

MATERIALS AND METHODS

We have examined 75 children aged from 1 to 12 years old diagnosed with of ARI bacterial etiology treated in in-pa-tient department. All of them were treated with age-spe-
specific doses of antibiotics. The children were divided into 3 groups depending on age, group 1 – children aged from 2 months to 3 years old, group 2 – children aged from 4 to 6 years old, group 3 – children aged from 7 to 12 years. Each group was divided into 2 subgroups depending on the presence or absence of AAD signs. Antibiotic-associated diarrhea was defined as 3 or more cases of loose stool after antibiotic administration [5].

The influence of some factors of children’s anamnesis, the peculiarities of parents’ health, their age and some habits on AAD development in a child on the background of ARI and antibiotic therapy were studied.

The obtained results were processed by descriptive statistics methods calculating average error share, mean, its error, obtaining of odds ratio (OR), calculation of significance test $\chi^2$, F-test (F), Student’s t-test ($t$).

RESULTS

The incidence rate of antibiotic-associated diarrhea was 52% for all examined patients (Table I). There was a ten-dency to large values in infants, although there was no significant difference in the study groups. The highest frequency - 59.3% was noted in the children of group 1 under the age of 3 years old. The lowest value was recorded in the patients of group 3 - 47.4%. The further analysis of OR value showed that the age-dependent value less than 1 year and AAD development in group 1 was 1.75 at $p = 0.69$. The calculation of analogous dependence for three groups revealed the value of OR as 2.17 at $p = 0.34$.

AAD most often developed in children who were treated with antibiotics of penicillin line. We have treated 92% of patients with amoxicillin, who later developed symptoms of antibiotic-associated diarrhea. We have detected 86% of ADD cases in children who were treated with third generation cephalosporins. The incidence rate of AAD at macrolides therapy was the lowest – 25% of patients who took these antimicrobial drugs.

The assessment of gender composition showed a tendency for boys to prevail in groups 1 and 2 among children with antibiotic-associated diarrhea (Table II). At the same time, these differences were not significant. The maximum number of boys was in the group 1d, where they constituted 62.5%. The group 2d included less number of boys – 57.1%. At the same time, the girls predominated in the group 3d. The indices of physical development did not have significant differences in the study groups either depending on age or presence or absence of diarrhea. Nevertheless, there was a tendency to large values of mass and height in the groups of AAD children.

The value of odds ratio was studied to determine the dependence of some anamnesis features and development of antibiotic-associated diarrhea (Fig. 1). The values of OR were determined for preterm birth, previous signs of functional diarrhea and/or vomiting, intestinal colic, allergy and also breastfeeding less than 6 months. The highest value of OR was obtained for a pair of breastfeeding less than 6 months and AAD development – 7.65. The influence value of preterm birth on AAD development was 2.9. The presence of functional disorders in anamnesis also increased the risk of AAD development from 2.7 to 3.14 units. The value of dependence of AAD development on allergy was somewhat less – 2.33. All these values were significant.

The next group of indices included the hereditary history peculiarities, age and lifestyle of the parents of the studied children (Fig. 2). The greatest value of OR was determined for pairs of parents’ age and AAD development. At the parents’ age over 35 years old the frequency of AAD inCREASED by 5.03 units. Odds ratio at the age of less than 18 years old was 2.91, but its value was not significant. The indices combination of parents’ age less than 18 years old and older than 35 years old increased the risk of AAD development by 4.09 times. The presence of allergic conditions also increased the probability of AAD. In this case, OR was 3.74 units. In fact, the risk of AAD in children in the study groups increased by the same value at periodic bowel disorder in parents’ anamnesis.

The influence of parents’ smoking and alcohol on the risk AAD development in children of the study groups was
studied. The index in the pair of smoking – AAD appeared to be 2.43, while OR for the pair alcohol consumption – AAD was only 0.76 units.

**DISCUSSION**

Our data showed that the incidence rate of antibiotic-associated diarrhea was 52% in all examined children. This complies with the data of other researchers. The literature indicates that AAD frequency can be from 5 to 60% [5, 6, 7, 8]. The dependence of AAD development on age is also mentioned by some authors [9] for 2-year-old children and younger. At the same time, other researchers deny the existence of such connection [10]. Our data did not show any significant differences as to age, although such trend existed, especially for children under 1 year old according to odds ratio. The possibility of such influence can be determined by the formation of intestinal microflora, which is modulated by breastfeeding, mother’s diet and introduction of complementary feeding in infants [11, 12, 13].

Among the antibiotics, amoxicillin most often caused the development of AAD, less often – cephalosporins and macrolides. The literature also indicates that amoxicillin with clavulanic acid often caused the development of AAD which is confirmed by our data [7, 9, 10].

The most significant increase in risk of AAD development was observed at breastfeeding less than 6 months. The role of breastfeeding in the development of microbiome and immune system is extremely important and crucial [14, 15]. It has been established that breast milk has its own microbiota [16]. Not only its direct transfer to a child is possible, but also the indirect influence of other factors on the microflora formation of a child such as pro- and prebiotics, oligosaccharides, immunoglobulin, immunomodulation
The dependence of some parents’ intestinal microbiome are allergic in a child’s birth, the studies that the unhealthy habits on the unhealthy habits on the differences in response condition [27, 28]. The role of hereditary factors in the formation of diseases is widely recognized. The role of hereditary factors in disorders formation of axis connection “brain-intestine” [23, 29]. Probably, preterm birth also plays a certain role in dissociation of this connection.

Also, the dependence of some parents’ unhealthy habits on the risk of AAD development in a child was found. In particular, the influence of alcohol and smoking was studied. Smoking increased by 2 times the probability of antibiotic associated diarrhea in a child. Perhaps, this influence was mediated through the duration of feeding in socially disadvantaged families.

CONCLUSIONS
The most important factors of antibiotic-associated diarrhea in children with ARI are breastfeeding less than 6 months as well as signs of previous functional disorders and allergic conditions. A number of features of parents’ health – bowel disorders, allergic conditions, suboptimal age of parents at child’s birth, unhealthy habits – increase the risk of developing antibiotic associated diarrhea in children with ARI.

REFERENCES
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