ISSN: 2755-0281

Journal of Pediatrics Research Reviews & Reports

SCIENTIFIC Research and Community

Research Article

Open Access

Antibiotic-Associated Syndrome in Clinical Practice

Golden LB, Ploskireva AA* and Akimkin VG

Golden Lika Borisovna, GBUZ Infectious Diseases Clinical Hospital #2 Department of Health of the City of Moscow

ABSTRACT

Purpose of Research: Establishing clinical features of an antibiotic- associated diarrhea and extra-intestinal manifestations of an antibiotic- associated syndrome in children

Patients and Methods: In 2017-2019 on the basis of GBUZ Infectious clinical hospital No. 2 DZ of Moscow a prospective clinical surveillance was carried out 200 patients aged 3 months to 13 years who were hospitalized with a diagnosis of acute pneumonia and received antibacterial therapy. All patients were evaluated for antibiotic-associated diarrhea (development of diarrhea, vomiting, dyspepsia, stomatitis) and manifestations of antibiotic-associated syndrome in children (condition of the skin and appendages of the skin, nervous system, development of inflammatory changes in the external genitals) within a month after antibiotic therapy. Comparative analysis of the effectiveness of probiotic prevention of antibiotic-associated syndrome was conducted in two groups: group 1 (23 children who received a drug containing Lactobacillus acidophilus, polysaccharide of kefir fungus in parallel with antibacterial therapy), group 2 (122 patients who received a medication containing Lactobacillus acidophilus, Bifidobacterium infantis, Enterococcus faecium).

Results: 29% of patients had symptoms of antibiotic-associated syndrome. AAD symptoms were diagnosed in 13% of patients. Abdominal pain (32.8%), dyspepsia symptoms (22.4%), bad breath (17.2%), flatulence (17.2%), stomatitis (10.3%), and constipation (1.7%) associated with antibiotic therapy were found among the manifestations of antibiotic-associated gastrointestinal syndrome. Dry skin was observed in 15.5% of patients, diaper rash-3.4%, brittle nails-15.5%, peeling of the skin-3.4% of patients, increased irritability in 17.2%, inflammatory changes in the external genitals-in 1.7% of patients. Comparative analysis of various probiotic prophylaxis of AAD showed that 1 group patients were significantly more likely to have stomatitis ($p<0.01$) and dry skin ($p<0.05$) than patients in group 2.

Summary: New term " antibiotic-associated syndrome» implies the development of a wider range of clinical manifestations associated with the use of antibacterial agents than the development of antibiotic-associated diarrhea. The use of probiotic prophylaxis with a medication containing Lactobacillus acidophilus, Bifidobacterium infantis, Enterococcus faecium demonstrates high efficiency compared to the comparison group.

***Corresponding author**

Ploskireva Antonina Alexandrovna, Central Research Institute of Epidemiology of Rospotrebnadzor, Russia. Tel: 972-533-432-658:
E-mail: antonina@ploskireva.com

Received: July 18, 2022; **Accepted:** July 25, 2022; **Published:** July 30, 2022

Keywords: Antibiotic-Associated Diarrhea, Antibiotic-Associated Syndrome, Probiotics

Antibacterial medicaments are important a tool in the arsenal of the modern doctor. However, in practice, patients may be concerned about the safety of this type of therapy. This fact can be justified in particular by the risk of developing antibiotic-associated diarrhea (AAD). Currently, AAD is understood as "the presence of at least three or more episodes of unformed stool associated with the use of antibacterial drugs within 4-8 weeks after their withdrawal, unless another cause of diarrhea is identified" [1].

In the pathogenesis of AAD, three main links are leading:
*Side effects of antibacterial drugs (allergic, toxic, pharmacological);
*Cosmotic diarrhea as a result of impaired metabolism of bile acids and carbohydrates in the intestine, mainly characteristic of cephalosporins;
* Destabilization of the microflora of the gastrointestinal tract (GI) [2].

In this case, the violation of the gastrointestinal microbiocenosis is the most significant factor that leads not only to destabilization system of microbiocenosis, but increases the risk of developing AAD, *Clostridium difficile*-associated infection [3].

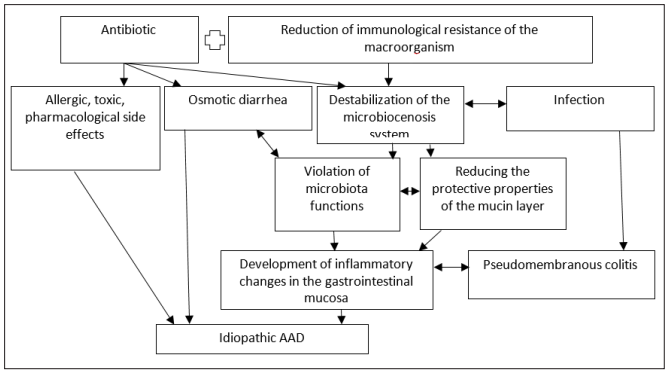

Figure 1: The Pathogenesis of AAD

Given this fact, as well as modern ideas about the role of microbiocenosis in the human body, it can be assumed [4-7] that the clinical manifestations associated with antibacterial therapy are not limited to the development of diarrhoeal syndrome, but are much broader in nature. In this regard, the purpose of this study was to establish the features of clinical manifestations of the syndrome associated with the use of antibacterial medicaments.

Patients and Methods

In 2017-2019 on the basis of GBUZ Infectious disease clinical hospital No. 2 a prospective clinical surveillance was carried out for 200 patients aged 3 months to 13 years who were hospitalized with a diagnosis of acute pneumonia

The criteria for including patients in the study were:
1) Diagnosis of acute pneumonia;

2) The need for an ABT for at least 7 days;

3) The patient's anamnesis vitae do Not have information about the available
previous diseases and / or complaints about the digestive system;

4) Signed informed consent of parents/legal representatives to participate in the study.

The criteria for not including the patient in the study were:
1) Severe forms of acute pneumonia;

2) The Presence of severe decompensated comorbidities of kidney, liver, digestive tract, cardiovascular, respiratory, and other body systems;

3) Established diagnosis of cancer, mental illness, tuberculosis, HIV infection;

4) Participation of the participant of clinical observation in other clinical clinical follow-up x during the last 3 months prior to the present disease;

5) Lack of readiness of the participant/parents/legal representatives of the patient to cooperate with the doctor.

Patients were selected for clinical observation by continuous screening. Duration of observation for each the patient was 1 month old. The monitoring included:
General clinical examination in dynamics, laboratory testing examinations (for all patients: clinical blood analysis, general urine analysis, determination of the etiology of acute pneumonia by bacteriological methods. serological methods, chest radiography, and also, biochemical blood analysis, ultrasound examination of organs abdominal cavity, etc. according to indications).

The etiology of acute pneumonia was established in 22 patients: 11 patients Mycoplasma infection was established, 6-pneumococcal infection, 2 –chlamydia, 3-combined (Mycoplasma was found in 2 patients' infection and pneumococcus, 1-Mycoplasma and chlamydia infections).

All patients received conventional treatment for acute pneumonia, which includes antibacterial, mucolytic and symptomatic therapy. All patients received probiotic therapy to prevent AAD.

Patients in probiotic therapy were analyzed separately which used various medications. In one group of patients (23 people, group 1) as prevention of AAD probiotic therapy was performed with Acipol (Lactobacillus acidophilus) at least 107 CFU, kefir fungus polysaccharide 0.4±0.1 mg in 1 capsule) for 1 cap. 2-3 times (3-4 times a day, depending on age) for 30 minutes before meals. In another group (122 patients, group 2) - Linex (Lactobacillus acidophilus, Bifidobacterium infantis, Enterococcus faecium at least 1, 2X107 live lyophilized lactic acid bacteria in a capsule) 1 capsule (up to 2, depending on age) 3 times a day. The groups were comparable in the main parameters (gender, age, and therapy). The establishment of antibiotic-associated syndrome was conducted during clinical examination and by questioning parents/legal patient representatives using a specially designed questionnaire. Was evaluated for the condition of the digestive system (diarrhea, vomiting, dyspepsia, stomatitis), the condition of the skin and appendages of skin (dryness of the skin, diaper rash, brittle nails, hair, etc.), nervous system (development of sleep disturbances, disorders in psycho - emotional sphere), the development of inflammatory changes of the outer genitals, was considered an aggravation of allergic diseases, the development of repeated episodes of acute respiratory infections (ARI) within one month after antibiotic therapy.

Statistical processing of the obtained data was performed on the basis of GOST R 50779.21-96 using methods of variational statistics on a computer using licensed programs Microsoft Excel tools. The statistical analysis included an assessment the analysis of variables was carried out by calculating the values of the sample fraction (W) and its standard error (SE). Comparison of the reliability of differences in quantitative and ordinal variables between groups was performed after checking the assumptions for the use of parametric multivariate one-dimensional variance analysis, followed by calculation of the achieved significance levels by t-criteria for related and unrelated samples or non-parametric criteria. The differences were considered reliable at $p°0.05$, highly reliable at $p<0.01$ and $p<0.001$, and unreliable at $p°0.05$ [8].

Research Result

Of the 200 patients examined, symptoms of the associated syndrome were found in 58 patients (29%), and in 142 children – these clinical manifestations were not detected (71%). Most frequent clinical manifestations of the associated syndrome were diagnosed in children under age of 3. However, a comparison of the age structure of groups of patients with symptoms of antibiotic-associated syndrome and none showed that in the group of patients older than 10 years, this syndrome was significantly more often diagnosed. While for children aged 1 to 3 years, there is an inverse relationship-the proportion of patients of this age with antibiotic-associated syndrome is less than among patients who did not have clinical manifestations of this syndrome (Figure.2).

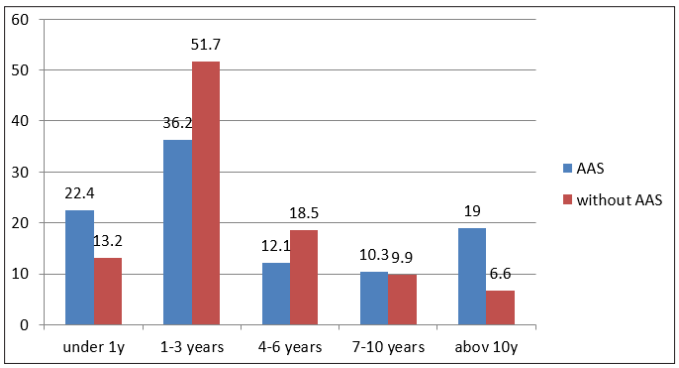

Figure 2: Age Structure of Groups of Patients with an Antibiotic-Associated Syndrome and without, % of patients (*$p<0.05$)

When analyzing the gender structure in groups with and without antibiotic-associated syndrome, it was found that in the first group significantly more women were registered (Figure.3).

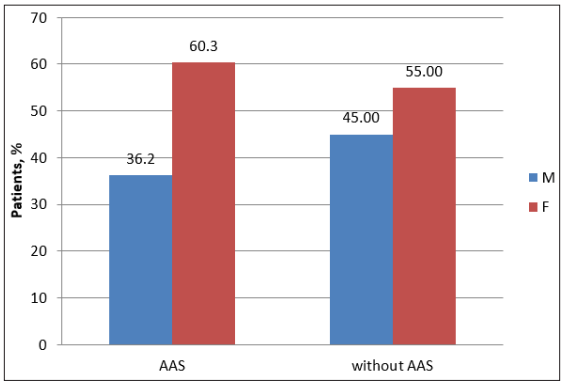

Figure 3: Gender Structure of Groups of Patients with and without Antibiotic-Associated Syndrome, % of patients (*p<0.05)

Within 1 month after antibiotic therapy, symptoms of AAD were diagnosed on 26 patients (13% of the total number of examined patient patients'). In these patients, there was a change in character (from liquefied to liquid, watery) and an increase in the frequency of stool. However, deviations in the condition of patients associated with antibacterial therapy, not limited to violations of the stool. Assessment of the state of digestion organs showed that isolated symptoms of diarrhea which were noted only on 19 patients (32.8% of patients with an established antibiotic-associated syndrome), the other children had different symptoms manifestations of antibiotic-associated syndrome (Figure.4).

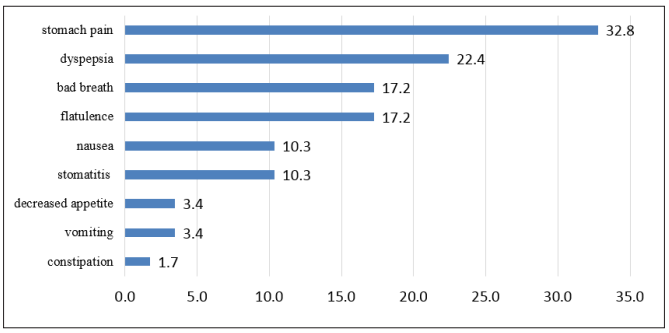

Figure 4: Frequency of Detection of Clinical Manifestations of Digestive Organ Damage in Antibiotic-Associated Syndrome, % of patients

Patients most frequently complained of abdominal pain (19 patients, 32.8%), dyspepsia (13 people, 22.4%), the presence of unpleasant bad breath (10 children-17.2%), flatulence (10 children-17.2%). However, there were also such manifestations of antibiotic-associated syndrome as stomatitis (6 children – 10.3%) and constipation (1 patient-1.7%).

When assessing the condition of the skin and skin appendages for 1a month after antibacterial therapy, it was found that the appearance of dry skin was observed in 15.5% of patients with symptoms of antibiotic-associated syndrome, diaper rash-3.4%, nail fragility-15.5%, skin peeling-3.4% of patients. There were no violations in the condition of hair in these patients.

Among the disorders of the nervous system were diagnosed only deviations in the psycho emotional sphere in the form of increased irritability in 17.2% of patients with antibiotic-associated syndrome.

However, in all patients, these deviations were not isolated character, and combined with pain syndrome (abdominal pain) or diarrhea. Sleep disorders were not detected in these patients. The development of inflammatory changes in the external genitals within 1 month after antibiotic therapy was diagnosed in 1.7% of patients.

Development of repeated episodes of acute respiratory infections (ARVI) within a month after antibiotic therapy significantly more often it was observed in patients with symptoms of antibiotic-associated syndrome than without them (Figure.5).

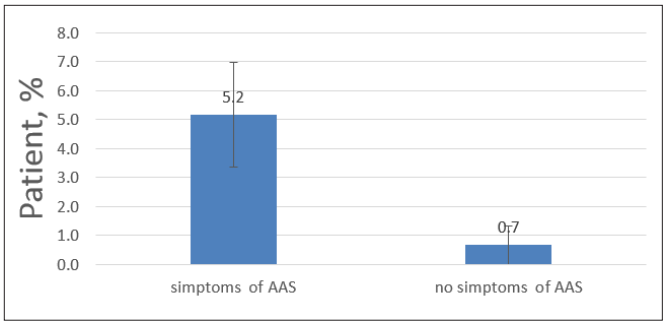

Figure 5: Percentage of Patients with Repeated ORI in Groups of Patients with and without Antibiotic-Associated Syndrome, % of patients (*p<0.05)

The frequency of development of clinical manifestations of antibiotic-associated syndrome during different probiotic therapy was different. Stomatitis was significantly more common in group 1 of patients (p<0.01) and the appearance of dry skin (p<0.05) than in patients 2 groups. There was also a slight increase in the share of this group patients with complaints of bad breath (# 0,1>p>0,05). At the same time in the second group of patients, there was a slight increase in the proportion of patients with dyspeptic complaints (# 0.1>p>0.05) (Figure.6).

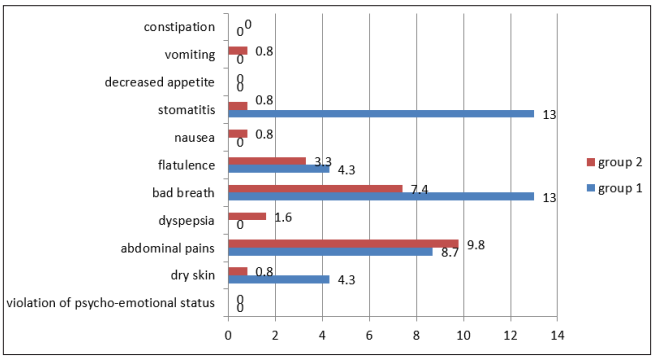

Figure 6: Frequency of Detection of Clinical Manifestations of an Antibiotic-Associated Syndrome in Comparison Groups, % of patients (#0.1>p>0.05, *p<0.05, * * p<0.01)

Thus, the data obtained during the study allow introduce the new term "antibiotic-associated syndrome", which implies the development of a wider range of clinical manifestations, associated with the use of antibacterial agents than the development of only antibiotic-associated diarrhea.

Prophylactic use of probioticы does not exclude the development of antibiotic-associated syndrome, but in comparison of two probiotics in preventive therapy (containing Lactobacillus acidophilus +polysaccharide of kefir fungus and which includes Lactobacillus acidophilus + Bifidobacterium infantis + Enterococcus faecium), showed the advantages of the second.

References

1. Gorelov AV, Usenko DV (2005) Modern approaches to the prevention of antibiotic-associated diarrhea in children. Consilium Medicum 2.
2. McFarland LV (1998) Epidemiology, risk factors and treatments for antibiotic-associated diarrhea. Dig Dis 16: 292-307.
3. Elstner CL, Lindsay AN, Book LS, Matsen JM (1983) Lack of relationship of Clostridium difficile to antibiotic-associated diarrhea in children. Pediatr Inf Dis 2: 364-366.
4. Turck D, Bernet JP, Marx J, Kempf H, Giard P, et al. (2003) Incidence and risk factors of oral antibiotic-associated diarrhea in an outpatient pediatric population. J Pediatr Gastroenterol Nutr 37: 22-26.
5. Beaugerie L, Petit JC (2004) Microbial-gut interactions in health and disease. Antibiotic-associated diarrhea. Best Pract Res Clin Gastroenterol 18: 337-352.
6. Clausen MR, Bonnen H, Tvede M, Mortensen PB (1991) Colonic fermentation to short-chain fatty acids is decreased in antibiotic- associated diarrhea. Gastroenterology 101: 1497-1504.
7. D'Argenio V (2015) The role of the gut microbiome in the healthy adult status / D'Argenio V., Salvatore F. // Clin Chim Acta 451: 97-102.
8. Petri A (2010) Visual medical statistics / A. Petri, K. Sabin. - Moscow: GEOTAR-MED 169.