

Alterations in Intestinal Micro Flora in Children with Allergic Rhinitis

Khalmatova B.T.,¹Saidkhonova A.M.,²Mirrahimova M.K.³

¹Professor, Head of the Department of Children's Diseases №1,
Tashkent Medical Academy, Uzbekistan.

²Assistant of the Department of Children's Diseases №1,
Tashkent Medical Academy, Uzbekistan

³Associate Professor of the Department of Children's Diseases №1,
Tashkent Medical Academy, Uzbekistan.

Abstract: The article considers the problems to study peculiarities in intestinal micro flora in children with allergic rhinitis (AR). Microbe flora settled in intestine have an active part in the maintenance of local and systemic immunity. It interacts with the cells of lymphoid tissue (physiological structure, performing protective function); and researches consider this interaction to be the basis for the relevance of allergy and intestine. In the article, children with AR were randomized to two groups. In the basic group children received basic therapy for the main disease with addition of probiotic BIFOLAK ACTIVE (BIOTACTDEUTSCHLAND), while in the control group children received only basic therapy. That agent was chosen as it is the only probiotic effecting all parts of gastrointestinal system, including large intestine.

Key words: allergic rhinitis, children, IgE, gastrointestinal dysfunction, probiotic, therapy, BIFOLAK ACTIVE.

Introduction

Since the initial days of life (and before than intrauterine) intestine affects formation of immune response. So, development of protective mechanisms and their activity in the future depend on the stability and balance of micro flora settling on sterile surface of intestinal mucous membrane of a new-born baby [1,3,6]. Thus, prerequisites of disorders in the immune system appear in early childhood. Immature organism of a young child has to adjust to new, sometimes hostile conditions. After birth protection received from mother (antibodies, or special protein complexes transmitted through placenta and breastmilk) helps to overcome certain risks (infection). However, it is valid only for a few months; after that a baby needs his own immunity, even imperfect one. Gastrointestinal tract is a physiological barrier for antigens, in other words alien substances. Every day it catches hundreds and thousands of pathogens such as viruses, bacteria, allergens, parasites, and food proteins [2,4].

When flora is normal and mostly includes "regular" types of microorganisms (bifidobacteria and lactobacilli) immunity responds only to certain antigens, for example infectious agents, while the mechanism of tolerance or immunity to allergens coming with food operates accurately and in harmony [5,6]. At the same time, allergy as a pathologically keen sensitivity to food antigens, wool, animals' saliva, cosmetics, household dust and other media can be linked with alteration in the balance of useful and relatively pathogenic flora or dysbacteriosis.

The last group always lives in intestine, but if "regular" microbes dominate, it is not dangerous. However, in certain circumstances there can be sudden rise in the number of colonies of unfavorable micro organisms with no possibility to suppress their growth, and it can affect the

process of digestion and immune protection. Intestinal allergy has acute or chronic progression, it can cause exhaustion of body and development of anemia (decrease in erythrocyte number and blood hemoglobin) [9,10,11]. Some patients have constipation or congestion of fecal mass in intestine. Due to absence of timely excretion of ballast substances there is intoxication, i.e. absorption of decay products to blood and poisoning of the organism. That intensifies indigestion, dysbacteriosis, and results in individual intolerance forming vicious circle [7,8].

The objective: to study peculiarities in intestinal micro flora in children with allergic rhinitis (AR).

Methods

Forty children, diagnosed with AR at the moment of the first application, were enrolled in the study. Among them 51.7% of the patients had combined allergic lesion of nose and gastrointestinal tract.

Twenty-one children applied with the initial manifestations of AR observed at the age of 3-6 years old (average age 5.09 years old) and nineteen children within the period from 6 to 9 years old (average age 7.8 years old). Maximal number of primary applications due to clinical symptoms of AR was registered among the children under 3 (38.6 %), less among the children of 3-6 years old (36.3 %), and the least from 6 to 9 years old (25.1 %). Comparison group included 20 children from 3 to 9 years old with no hereditary atopic pathologies (average age 7.9 years old).

Research methods included definition of qualitative and quantitative composition of intestinal microflora in children, dynamic definition of the number of eosinophiles by means of immersion microscopy of stained smears in compliance with Romanovsky-Gimza's method and definition of total immunoglobulin E (IgE) using enzyme immunoassay according to the recommendations of the manufacturer. Morbidity rates with somatic and infectious origin were assessed with the help of interviewing parent and analysis of children's medical cards (history of physical development № 112). Statistical processing of the result was performed using STATISTICA for WINDOWS 6.1 software.

Results and discussion

All the children with AR had hereditary predisposition to allergy, most often inherited from mothers (67.6%). Among the relatives of the children in both groups we registered high prevalence rates of intestinal pathologies (27.5%) and helminth-protozoa infections (8.9%). Allergic and somatic diseases in the majority of the mothers conditioned the high rates of morbidity within pregnancy. Mother of children with AR had chronic tonsillitis more often, than those from the comparison group (29.2 % versus 7.5 %, $p=0.011$), and four of them (6.7 %) had exacerbation during pregnancy. Pregnancy with chronic pyelonephritis was registered in 18 women out of 40 from the basic group (45 %) and 6 out of 20 in the comparison group (30.0 %), exacerbation was registered only among the women of the basic group ($n=12$, $p=0.017$). The women of the basic group statistically more often had ARVD (69.7 % versus 22% in comparison group, $p=0.001$). Every second woman in the basic group was diagnosed with giardiasis (30 % versus 10 % in comparison group, $p=0.005$), which was not treated during the pregnancy. Women from the basic group significantly more often had a risk of miscarriage (40 % versus 15 %, $p=0.001$) and statistically significant number of diagnoses of CMV (25 % in the basic group versus 10 % in the comparison group, $p=0.001$). Isolation of *Candida albicans* in cervix observed only in 10 women from the basic group ($p=0.001$) was due to administration of antibacterial agents for the therapy of chronic diseases. Fifty percent of the women from the basic group had

preterm birth and 30% had abdominal delivery. In the comparison group these values were equal to 40.0% and 25%, respectively.

Health status of all children at birth was considered to be satisfactory. We revealed no statistically significant differences in mean anthropometric parameters. The work with the mothers of the children with AR started from the maximal preservation of lactation. The leading line in the interaction with the parents was teaching the bases of rational nutrition taking into account atopy. Symptoms of allergic rhinitis in 78.3% of the children under 5 were observed during the whole year.

Within the initial three years 45% of the children had exacerbations of nasal syndrome with running nose due to violation of diet or administration of pharmaceutical agents for the treatment of ARVD. During the next two years exacerbations were registered in 25.0% of the children with stuffy nose due to violation of diet. Exacerbations were stopped by means of prescription of histamine receptor H₁ blockers and topical application of glucocorticosteroids for not more than 7 days. Further follow up in catamnesis till 6 years old did not reveal any exacerbations of AR.

Primary complaints of mothers together with running or stuffy nose were intestinal dysfunctions manifested in colic, pathological inclusions such as green, blood, foam or constipation for several days. Bacterial tests of feces showed no statistically significant differences in the isolation of relatively pathogenic micro flora (RPF) in children of the basic and comparison groups, though *Staphylococcus aureus* and *Klebsiella pneumoniae* titers were higher in the basic group (10^6 - 10^{12}), while in the comparison group these did not exceed 10^4 . Clinical manifestations of debut and therapy of the allergic process dependent on the type of RPF had significant differences. Presence of *Staphylococcus aureus* in the first month of life was displayed by intestinal dysfunction accompanied by intestinal colic, mucous and green feces. Presence of *Klebsiella pneumoniae* conditioned manifestations of various stages of hem colitis (from single blood streaks to excessive amount).

Total immunoglobulin E was tested at the primary application and by the end of the second year of follow-up. First test of IgE showed average 465.50 ± 121.71 IU, while the next showed 99.14 ± 23.6 IU ($p=0.001$), which testifies decrease in the allergic process intensity ($p=0.001$). Number of eosinophiles in the children of the basic group reached 4.9 ± 0.21 %, and in the comparison group 1.4 ± 0.2 % ($p=0.001$). Statistically significant prevalence of eosinophiles in children of the basic group was preserved until 6 months. Later there was no notable difference, while the level of eosinophiles was higher in the comparison group due to greater prevalence of worm infestation.

Useful properties of BIFOLAK ACTIVE are conditioned by alive sublimated probiotic bacteria possessing antagonist activity against a wide range of pathogenic and relatively pathogenic micro organisms. Great quantity of bifidobacteria and lactobacilli promotes fast recovery of physiological balance of intestinal micro flora and activate protective mechanisms in body improving activity of gastrointestinal tract, exchange processes and parietal digestion. BIFOLAK ACTIVE diminishes the risk of allergens manifestation due to good digestion of the consumed food; bacteria synthesize proteolytic enzymes splitting protein (and other toxins and allergens) and decrease development of allergy. Probiotic bacteria synthesize proteolytic enzymes, which split proteins (and allergens). Probiotic bacteria also stimulate production of protease enzymes, which intensify splitting of proteins (and allergens) in cells of intestine. Micro

crystal cellulose (MCC) adsorbs toxins, allergens and other slags in intestine and cleans the body. In all cases it is recommended to consult a doctor. Early diagnosis of intestinal allergy in AR the most important direction in the work of practicing doctor is to eliminate significant causing allergens from the diet and to choose therapy [5,11].

Table 1.

Dynamics of gastrointestinal symptoms in the follow-up of the children before the therapy

Symptoms	Basic group		Control group	
	n=17	%	n=24	%
	First examination			
Stomachache	17	100	11	46.0
Discomfort in abdomen	17	100	21	87.5
Nausea	14	82.3	7	29.1
Vomiting	10	58.9	4	16.7
Heartburn	6	35.2	3	12.5
Diarrhea	8	47.0	5	21.0
Constipation	4	23.5	4	16.7
Flatulence	12	70.5	14	58.3
Rumbling	13	76.4	17	71.0

Children were examined again at the end of the first hospitalization and at the next hospitalization in 7-9 months. The basic group included 17 children with AR and the control group included 24 children. Performed therapy caused decrease in the expression of gastrointestinal complaints (Table 1). In the basic group we observed a positive dynamics in all studied symptoms of digestion.

The most explicit positive dynamics was observed in stomachache. In the majority of the children symptoms disappeared within initial weeks of the therapy, but in some part of them, insignificant one, the symptoms were revealed in several months. It was mostly relevant to heartburn and rumbling in stomach. Reappearance of heartburn in some children with AR allows us to think that $\frac{1}{4}$ of the patients had gastro esophageal reflux requiring additional tests and therapy. Reappearance of a symptom such as rumbling in stomach seemingly indicates the necessity of a longer therapy with probiotics (Table 2).

Table 2.

Dynamic of gastrointestinal symptoms before and after the therapy

Symptoms	Basic group n=17		Control group n=24	
	before (%)	after (%)	before (%)	after (%)
Stomachache	17(100)	1 (5.8)	11(46.0)	5 (20.8)
Discomfort in abdomen	17 (100)	2 (11.7)	21 (87.5)	7 (29.1)
Nausea	14 (82.3)	4 (23.5)	7 (29.1)	2 (8.3)

Vomiting	10 (58.9)	-	4 (16.7)	-
Heartburn	6 (35.2)	-	3 (12.5)	1(4.1)
Diarrhea	8 (47.0)	-	5 (21.0)	1 (4.1)
Constipation	4 (23.5)	-	4 (16.7)	1 (4.1)
Flatulence	12 (70.5)	1 (5.8)	14 (58.3)	5 (20.8)
Rumbling	13 (76.4)	2 (11.7)	17 (71.0)	8 (33.3)

At the same time dynamics of flatulence was clearly positive. In the control group at the time of therapy in most of the children stomachache, discomfort in stomach, nausea, vomiting, heartburn, diarrhea, flatulence disappeared with complete absence of any changes in constipation. However, at the next hospitalization in fact many symptoms (stomachache, discomfort in abdomen, vomiting) were observed again, while the prevalence of heartburn even increased. There were few children with nausea, flatulence and rumbling in stomach. The obtained data testify that, though the therapy of the basic disease has a positive effect on GIT, in long-term follow-up disorders in digestive system are preserved and require specialized testing and therapy.

Treatment in clinic led to a significant improvement of coprogram parameters and results of ultrasound imaging of digestive organs. Inclusion of BIFOLAK ACTIVE probiotic into the therapy mostly effects intestinal micro flora recovering its imbalance in patients with AR.

Conclusion

1. Thus, recently intestinal microbiota is considered to be a leading etiological factor in the development of allergic immune pathological states, including AR in children. Data indicate the necessity of further study of both the whole microbe community and its separate representatives.
2. The basic marker controlling allergic process in children with hereditary predisposition within initial months of life is the level of eosinophiles and total IgE.
3. Inclusion of BIFOLAK ACTIVE probiotic into the therapy mostly effects intestinal micro flora recovering its imbalance in patients with AR.

References

1. A.M. Saidkhonova, M. Kh. Mirraximova, M.B. Kasimova. Use of montelukast in the treatment of allergic rhinitis in children. Journal of biomedicine and practice 2020, vol. 6, issue 5, pp.205-210
2. Childhood allergic rhinitis, traffic-related air pollution, and variability in the GSTP1, TNF, TLR2, and TLR4 genes: results from the TAG Study. Fuertes E. et al. // J Allergy Clin Immunol. 2013 Aug; 132(2):342-52.e2.
3. D.R. Kurbanova, M.K. Mirrakhimova, Improving diagnostic methods for detecting allergic diseases in children, Journal of Biomedicine and Practice 2020, Special issue, pp.522-530
4. Disparate geographic prevalences of asthma, allergic rhinoconjunctivitis and atopic eczema among adolescents in five Canadian cities. Wang HY. et al. // Zhongguo Dang Dai ErKeZaZhi. 2014 Jan; 16(1):16-9.
5. Khabibullayevna M. M., Murotkhonovna S. A. Optimization of Allergic Rhinitis Therapy in Children // The American Journal of Medical Sciences and Pharmaceutical Research. –

Received 15 December 2020; Accepted 05 January 2021.

2020. – T. 2. – №. 08. – C. 119-125.
6. Kim SW., Han D.H., Lee SJ. Bronchial hyperresponsiveness in pediatric rhinitis patients: the difference between allergic and nonallergic rhinitis. // Am J Rhinol Allergy] 2013 May-Jun; Vol. 27 (3), pp. e63-8.
 7. M. K. Mirrakhimova et al.: Characteristics of Allergic Pathologies Progression in Young Children. American Journal of Medicine and Medical Sciences 2020, 10(9): 652-656
 8. Mirrakhimova M. X. et al /Antileukotriene Drugs in The Treatment of Atopic Dermatitis in Children. International Journal of Pharmaceutical Research |Jan - Mar 2021|Vol 13 | Issue 1: 2117-212
 9. Nishonboyeva Nilufar Yunusjanovna et al. Digestive organs status in children with atopic dermatitis /Journal of Critical Reviews, 2020.7/5. 678-679
 10. S.A. Ibragimova et al /Comordid course of atopic dermatitis with bronchial asthma in children: frequency, clinical and allergological characteristics - Journal of Critical Reviews, 2020.7/17.2317-2321
 11. Zakirova U. I. et al /Analysis Of The Prevalence Of Bronchial Asthma In Children In Outpatient Clinics. International Journal of Pharmaceutical Research | Oct - Dec 2020 | Vol 12 | Issue 4: 759-765