Dysbiosis of the Intestine in the Genesis of the Immune Failure in Children with Recurrent Bronchitis

Karimdzhanov I.A	Tashkent Medical Academy
Yusupova G.A.	Tashkent Medical Academy
Iskanova G.Kh	Tashkent Medical Academy
Israilova N.A.	Tashkent Medical Academy

ABSTRACT

The immune status of children with recurrent bronchitis complicated by intestinal dysbacteriosis was studied. The role of intestinal dysbacteriosis in the formation of secondary immune deficiency, which mainly causes the development of relapses of bronchitis, has been established. The aim of the study was to study the role of intestinal dysbacteriosis in the formation of secondary immune deficiency in children with recurrent bronchitis. The data obtained showed that children with recurrent bronchitis complicated by intestinal dysbacteriosis have a deficiency of cellular and humoral immunity. In the stage of exacerbation of the disease, there were signs of intestinal dysbiosis II-III severity, in the remission stage of the disease I-II severity. Analysis of the quantitative and qualitative composition of the intestinal microflora in children with recurrent bronchitis showed a pronounced decrease in the content of bifidobacteria and lactobacilli. In children with recurrent bronchitis complicated by intestinal dysbacteriosis, a deficiency of cellular and humoral immunity was revealed.

Keywords: children, immunity, intestinal dysbacteriosis, recurrent bronchitis

Introduction. Violation of intestinal microbiocenosis is one of the urgent problems of modern pediatrics. Intestinal dysbacteriosis in the modern definition of the Industry Standard (2003) is presented as a clinical and laboratory syndrome that occurs in a number of diseases and clinical situations and is characterized by a change in the qualitative and / or quantitative composition of the normoflora, metabolic and immunological disorders [1,3]. The search for the reasons for the deterioration of children's health and the study of the mechanisms of development of diseases made it possible to identify a number of factors that increase the risk of developing many pathological conditions. The main one is a violation of the intestinal microflora [2,4], i.e. dysbacteriosis is not only a consequence of various diseases, but also contributes to the development of the pathological process in the body, further determining the severity and duration of its course. Equally important are the reasons associated with changes in the body's immune response [5].

It is obvious that the violation of the normoflora, the immune status and the manifestations of the disease should be considered in unity, and the role of the trigger in each case may belong to any of these components of the triad: dysbacteriosis, immune status and the pathological process. In some cases, dysbacteriosis gives impetus to the development of the pathological process directly, in others through the development of immunodeficiency, and in others it causes these interrelated processes [6].

In recent years, numerous data have appeared indicating that under physiological

conditions, the intestinal microflora plays a regulatory role, ensuring the maturation of the immune system and its balanced functioning in later life. In a situation of instability of the biocenosis of the gastrointestinal tract, prerequisites are created for the intensity of the processes of the immune response, overcoming the tolerance threshold, and the formation of immune dysfunction [7,8].

In response to changes in the intestinal microbiocenosis, an unfavorable premorbid background is formed in children of the first years of life, which, under the influence of various provoking factors, can transform into a pathological process [9]. Any diseases that occur with intestinal dysbacteriosis, starting in early childhood, can take a protracted, chronic, relapsing course, selectively affecting the respiratory, digestive, urinary and other systems, often leading to serious consequences [2,7].

Recurrent bronchitis is one of the most common forms of respiratory pathology in childhood. They affect 50-100 out of 1000 children under the age of 6 years, and in ecologically unfavorable areas the incidence reaches up to 250 per 1000 children [8]. Considering that most of the territory of Uzbekistan belongs to the zone of "environmental disaster", one can imagine how relevant this problem is for our region. The study of the intestinal microflora of preschool children living in ecologically unfavorable regions made it possible to establish the presence of intestinal dysbacteriosis and susceptibility to bronchopulmonary pathology in the vast majority of children [9, 10]. According to numerous studies, in children of early and preschool age, the development of recurrent bronchitis is provoked by unfavorable environmental factors: pollution of the environment and indoor air, passive smoking, material and living conditions, visits to preschool institutions and crowded places in enclosed spaces [11].

When analyzing the prevalence of immunopathological syndromes in children with colon dysbiosis, it was found that the leading place in their structure is infectious (57.1%), then allergic (47.8%) and in 37% of cases mixed. The infectious syndrome was manifested by the recurrent nature of the course of acute and chronic infectious and inflammatory diseases of various etiology and localization [12]. Despite the large number of studies on the etiology, epidemiology, diagnosis of intestinal dysbacteriosis, many pathogenetic aspects remain insufficiently covered. The mutual dependence of the immune and microecological systems of the child's body determines the scientific and practical interest in studying the state of the immune system in children with recurrent bronchitis against the background of intestinal dysbacteriosis [13].

The aim of the study was to study the role of intestinal dysbacteriosis in the formation of secondary immune deficiency in children with recurrent bronchitis.

Material and methods

We observed 93 children aged 1 to 7 years with recurrent bronchitis in the acute stage (Group 1), of which 62 were boys and 31 girls, and 30 patients with the same disease were in remission (Group 2).), including 17 boys and 13 girls.

The control group consisted of 20 children with episodic ARVI. The studies were carried out in the first days after admission to the hospital, patients of the 2nd group were examined in the stage of complete clinical and laboratory remission of the underlying disease. The criterion for selecting children in the survey group was the established diagnosis of recurrent bronchitis (bronchitis, episodes of which were repeated 3 or more times within 1-2 years and were characterized by the duration of clinical manifestations).

Research methods:

1. Clinical: a study of the anamnesis of life, illness, analysis of the medical history, assessment of the present somatic status was carried out.

2. Laboratory: study of the general analysis of blood, feces, assessment of the severity of dysbiotic changes in terms of fecal microflora. Bacteriological examination of feces

to establish the type and degree of dysbacteriosis was carried out according to the method according to N.M. Gracheva et al. and V.A. Znamenskaya et al. Bacteriologically, the diagnosis of intestinal dysbacteriosis was established by comparing the obtained data with normal indicators of the composition of the microflora of the large intestine in children. The severity of dysbiotic disorders was determined according to the "Working Classification of Intestinal Microbiocenosis Disorders in Children", proposed by N.M. Gracheva, G.I. Goncharova. The quantitative assessment of the immune system was assessed by the concentration of immunoglobulins G, A and M, the relative content of T-lymphocytes and their regulatory subpopulations - T-helpers, T-suppressors, as well as B-lymphocytes, CD4, CD8, CD16 and immunoregulatory index (II).

Results and discussion

According to the anamnesis, children with recurrent bronchitis have risk factors for the development of dysbacteriosis. The most significant of them were the pathology of the ante- and intranatal periods (82.8%), antibiotic therapy (91.3%), manifestations of dysbacteriosis in the first year of life (62.4%), the presence of frequently ill family members (54.8%). Frequent colds in the first year of life were observed in 58.1% of children, various pathologies of the gastrointestinal tract occurred in 39.7%.

In the formation of intestinal dysbiosis, the nature of the child's nutrition is of great importance. Among the examined children, natural feeding in the first year of life was 24.7%, mixed - 43.1%, artificial - 32.2%. At the time of the survey, 40.8% received food according to their age.

Another important factor is social status. Thus, only 19.4% of the examined patients had good living conditions and sufficient material security, 22.6% of fathers and 10.8% of mothers had higher education.

The bacteriological diagnosis of intestinal dysbacteriosis was confirmed in 100% of patients in the acute stage and in 56.7% in remission. Despite the random sampling of patients with recurrent bronchitis, absolutely all in the stage of exacerbation of the disease showed signs of intestinal dysbiosis. Apparently, this is due to the prevalence of risk factors for the development of dysbacteriosis in the patients we observed, antibiotic therapy that is not always justified, and the environmental conditions of our region. T.O. Daminov (2001) found that 90% of the population of our region suffer from intestinal dysbacteriosis. From the anamnesis of the examined patients, it was found that only 10.7% of them during the period of exacerbation of the disease and then in the period of remission received drugs that correct intestinal dysbiosis.

In the stage of exacerbation of recurrent bronchitis, dysbiotic disorders of the II -III severity were noted, and in children with recurrent bronchitis in remission, dysbacteriosis of I-II severity was detected. Clinical manifestations of intestinal dysbacteriosis in the examined patients were general anxiety, irritability (81.7%), vomiting, regurgitation (64.5%), constipation (52.7%), lag in physical development (54.8%), the presence of pathological impurities in the stool (100%), signs of polyhypovitaminosis (57%).
Indicators of intestinal microflora in children with recurrent bronchitis are presented in Table 1.

Table 1

Indicators of intestinal microflora in children with recurrent bronchitis

Microorganisms	Norm	Patients with recurrent bronchitis		P
		exacerbation stage	remission stage	
Bifidobacteria	9,7±0,14	7,3±0,35	8,1±0,27	< 0,001

Lactobacilli	9,3±0,54	5,6±0,33	7,4±0,36	< 0,001
Total number of aerobes	7,8±0,09	4,2±0,19	5,8±0,21	< 0,001
E. coli L(+)	8,5±0,38	5,5±0,11	6,7±0,22	< 0,001
E. coli L (-)	2,21±0,33	-	1,01±0,19	< 0,001
Enterococci	4,0±0,12	5,7±0,17	4,6±0,20	< 0,001
Staphylococcus aureus	-	2,7±0,43	1,1±0,27	< 0,001
Fungi of the genus Candida	2,0±0,001	4,7±0,9	3,2±0,4	< 0,01

P< 0,001 - reliability of differences in the groups of examined patients

When analyzing the quantitative and qualitative composition of the intestinal microflora in children with recurrent bronchitis, a pronounced decrease in the content of bifidobacteria and lactobacilli was found.

The deficiency of anaerobes also affected the aerobic part of the intestinal microbiocenosis. Thus, there was a decrease in the number of lactose-positive Escherichia coli against the background of an increase in the content of enterobacteria, staphylococci, fungi of the genus Candida. Dysbiotic changes in most cases were accompanied by the isolation of bacteria of the opportunistic pathogenic group.

During the period of exacerbation of recurrent bronchitis, bacteriological examination of feces in 98% of children revealed opportunistic microflora in titers of $10^{-}4$ and above, with Staphylococcus aureus and fungi of the genus Candida being the most common. Statistically significant differences in clinical and immunological parameters in patients with recurrent bronchitis with the inoculation of different types of opportunistic microflora allow us to conclude that the prognosis for health in candidal dysbacteriosis is less favorable, since the severity of intestinal disorders and immune deficiency with it is significantly higher. The main purpose of studying the immune status is to identify causal changes, i.e. those changes that lead to the development of an immunodeficiency state. However, the analysis of investigative changes is also of some interest, since it can be used to evaluate the effectiveness of treatment and predict the course of the disease.

The results of studying the immune status in children with recurrent bronchitis complicated by intestinal dysbacteriosis are presented in Table 2.

Table 2

Indicators of the immune status in patients with recurrent bronchitis complicated by intestinal dysbacteriosis

Indicators	Recurrent bronchitis Рецидивирующий бронхит		Episodically ill children M± m (%)	P
	acute stage M±m, %	stage of remission M±m, %		
Leukocytes, µl Lymphocytes, %	8250±291	6970±207	6430±193	<0,001
Lymphocytes, %	50,7±2,37	41,2 ±2,5	37,5 ±1,3	<0,001
T-lymphocytes, %	55,5±2,85	52,7 ±1,8	63,1 ±1,5	<0,05
B-lymphocytes, µl	851,7±61,2	648±37,1	537±29,0	<0,001
CD4	28,0±1,88	33,1 ±1,4	38,2±1,52	<0,001
CD8	27,1±0,88	24,3±1,33	19,4±0,78	<0,001

CD16	20,3±0,91	11,3 ±0,9	8,3± 1,3	<0,001
IgG, mg%	1161±59	1129 ±35,2	1170±39	>0,05
IgA, mg%	113,2±6,36	127±9,8	142,0±7,0	<0,01
IgM, mg	99,7±5,49	104,8±7,4	119,5±7,41	<0,05
II (SD4/SD8)	1,01±0,07	1,36	1,55±0,07	<0,001

P<0,001- reliability of differences in the groups of examined patients

The data obtained indicate that children with recurrent bronchitis complicated by intestinal dysbacteriosis have a deficiency of cellular and humoral immunity. The immunoregulatory index, which turned out to be reduced to 1.01 in the acute stage of the disease, did not normalize during the remission of the disease. The detected changes in the immune status, being an integral indicator reflecting the unfavorable total effect of a number of factors on the child's body, made it possible to understand the increase in the number of cases of relapse of the disease.

Recurrent bronchitis and intestinal dysbacteriosis in practical terms are the cause and effect of the development of the immunodeficiency state of the body, on the other hand, the immunodeficiency state supports and enhances the inflammatory process in the bronchi and dysbiotic disorders of the intestine due to the development of autoimmune processes.

Recurrent bronchitis leads to the depletion of the entire reserve protective potential of the body as a whole with the formation of a vicious circle of pathological changes, when the cause and effect periodically change places. In clinical terms, these processes manifest themselves as relapses of the disease with the addition of complications, the development of new foci of chronic inflammation, the presence of polyhypovitaminosis and anemia.

Conclusions: The relationship and interdependence of disorders of the intestinal microbiocenosis, immune status and exacerbations of bronchitis has been established, which dictates the need for an integrated approach to the treatment of this category of patients.

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