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Formation of Intestinal Microbiota in Newborns with Maternal Allergy

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Abstract: The results of a clinical and anamnestic examination of 48 newborns with maternal allergies were analyzed. Purpose of the study: to study the nature of changes in the intestinal microbiota in newborns with maternal allergies in order to prevent allergic reactions in newborns. Risk factors for the development of allergies in newborns were identified and optimization of feeding and therapy was recommended. A comparative analysis of the study of intestinal microflora in newborns with and without maternal allergies was carried out.

Key words: newborns, allergies, intestinal microflora, eubiotics.

Relevance. The formation and development of the intestinal microbiota begins in the fetus. It has been established that bacteria are present in the amniotic fluid in utero in healthy newborns due to bacterial translocation, but the number and diversity of microorganisms is still quite low [1]. The infant's intestine is colonized even before birth [2]. Immediately after birth, active colonization of the newborn's gastrointestinal tract by bacteria begins. In the modern world, the formation of intestinal microbiota in newborns is characterized by slow colonization by bifidobacteria; long-term persistence of aerobes (proteobacteria); a small and unstable microbiota, which disrupts immune adaptation and the formation of tolerance, determines the severity of damage to the protective intestinal barrier, maintaining inflammation and atopy [1,2,3,4].

In the first hours and days of postnatal life, the child adapts to enteral feeding, therefore, at this time, the main factor in the formation of the intestinal microbiota is the nature of nutrition [4].

Within a few weeks, bifid flora becomes dominant, with levels twice as high in breastfed infants as in formula-fed infants. In healthy full-term newborns, indigenous bacteria colonize the mucosal surfaces and intestines in a typical sequence.

The factors determining the formation of the intestinal microbiota are diverse.

It has been proven that the dynamics of the formation of the intestinal microbiota of newborns can be disrupted in children infected in utero, with gestosis, with pregnancy pathologies, and if a woman has chronic foci of infection. [5,6].

Placing a newborn on the mother's body and applying it to the breast in the first minutes of life contributes to the normal colonization of various biotopes of his body with maternal microflora. Receiving colostrum, and with it humoral protective factors, contributes to the rapid colonization of the newborn's intestines and the physiological course of the child's postnatal adaptation [7,8]. The most important factor in the formation of intestinal microbiota is feeding a child. The protective effect of breastfeeding in the formation of optimal microbiocenosis in an infant has been revealed. Moreover, differences in the colonization of the intestines of breastfed children are determined by the presence of oligosaccharides in breast milk, which stimulate the growth and activity of Bifidobacterium and Lactobacillus [9,10,11]. During the newborn period, as a result of breastfeeding, when the antigen gains access through mother's milk, sensitization of the child often occurs.

The use of antibiotics when treating a mother or newborn has a negative impact on the colonization of the intestine by commensal microbes. In full-term infants who received ampicillin and gentamicin parenterally during the first 48 hours after birth, there was a significant decrease in the number of bacteria of the phyla Actinobacteria (including Bifidobacterium) and Firmicutes (including Lactobacillus), while an increase in Proteobacteria was noted [4,11]. The dominance of Proteobacteria and the reduction in microbial diversity persisted for 8 weeks after antibiotic exposure. Negative external influences on the microbiota are especially significant in premature infants, especially in children born with very low and extremely low body weight (VLBW) [4]. Targeted correction of the microbiota with the help of probiotics in these children is a significant factor in the prevention and treatment of such dangerous forms of neonatal pathology as sepsis and necrotizing enterocolitis [4,12, 13].

Qualitative disturbances of the microbiota and a decrease in its species diversity in early childhood increase the risk of atopy in children in the first months of life and are of particular importance, since impacts on it during critical periods of ontogenesis create the preconditions for the formation of delayed pathology, associated primarily with disorders of the maturation of the intestinal immune system [9 ,14]. In this case, the composition of the microflora is replaced by mixed polymicrobial biofilms of opportunistic microflora containing multidrug-resistant strains of Staphylococcus, Enterobacter, Klebsiella, Escherichia, Pseudomonas, etc. [15,16]. Even before the development of allergic diseases, the composition of the microbiota in children with atopy has certain features [17]. The presence of pathogenic microflora causes autosensitization of the growing organism with the development of allergic reactions of the IgE-dependent type. In addition, certain strains of S. aureus secrete toxins, which, as superantigens, can enhance sensitization, contributing to the torpid course of allergies [18,19,20.]. Thus, microbiota disturbances contribute to the formation of allergic reactions.

The composition of the intestinal microbiota in children with allergies is characterized by a significant decrease in the diversity of symbiont flora and a high frequency ("high pathogenic pressure") of opportunistic and pathogenic flora. Against the background of a decrease in the number of bifidobacteria, the permeability of the intestinal epithelial barrier for food macromolecules increases, There is an increase in food sensitization and IgA deficiency occurs, which also contributes to the development of atopic diseases [5,21]. In addition to the direct effect of disturbances of the intestinal microbiota on the sensitization of the body, in case of allergies, its

influence on the composition of the skin microbiota in patients has also been revealed: a decrease in the number of lactobacilli in the colon leads to an increase in the level of S.epidermidis on the skin, which are an additional source of allergization of the child [7,19, 22].

Currently, the idea has been formed that microbiocenosis controls almost all processes of maintaining homeostasis in our body [21,23]. However, today there are still enough unresolved problems that pediatricians and general practitioners cannot cope with, which was the reason for conducting this study.

Purpose of the study. To identify and study the nature of changes in the intestinal microbiota in newborns with maternal allergies in order to prevent allergic reactions in newborns.

Material and research methods. The medical histories and results of clinical and anamnestic examination of 48 newborns with allergies hospitalized in the neonatal intensive care units and the prematurity care department of the Allergy Medical Center in Samarkand were studied.

Group I consisted of 18 newborns who did not have maternal allergies, Group II included 30 newborns with maternal allergies. Among the newborns there were 28 boys and 20 girls. The diagnosis of atopic dermatitis was established on the basis of a detailed study of anamnestic data and identification of predisposing factors according to the map we developed and clinical manifestations. Intestinal microflora was studied according to the method of R.V. Epstein-Litvak and F.L. Vilshanskaya modified by M.A. Akhtamova et al. (1981).

Research results. A study of the anamnesis of newborns admitted to the neonatology department of the Children's Medical Research Center showed that 21-43.7% of mothers had food allergies, 6-12.5% had urticaria and 3-6.3% had Quincke's edema.

A study of anamnestic data showed that parents of patients in group II were 1.9 times more likely to seek medical help in a hospital late (on the 3rd day or later from the onset of the disease) with severe signs of the disease than mothers of children in group I. According to anamnestic data, the main reason for the development of allergies in the child was the mother's intolerance to cow's milk (20-41.7%).

Allergic reactions in 15-31.3% of mothers were due to the abuse of honey, 8-16.7% - chocolate and 5-10.4% - eggs; in 2 cases the cause was not established. Pregnancy often occurred with complications. 18-37.5% of mothers had chronic somatic diseases during pregnancy and childbirth. Mothers of newborns indicated previous frequent respiratory viral infections in 41-85.4% of cases, bronchopulmonary pathology of bacterial etiology in 21-43.8% of patients, infectious diseases - in 9-18.5% of cases.

Mothers of group II suffered viral-bacterial infections 1.8 times more often than those of group I. 18-37.5% of women received antibiotics for streptococcal infection and maternal hyperthermia, as well as for bacterial vaginosis and mastitis. In group I, bacterial vaginosis was present in 3-6.3% of mothers, complicated pregnancy and childbirth were observed in 4-8.3% of cases, while in group II, in 7-14.6% and 10-20.8%, respectively. mothers. In mothers of group II, more often than in group I there were: dyspepsia (25.0% and 16.7%), indications of anemia (56.2% and 22.9%), allergic reactions (62.5% and 0). %), infectious (12.5% and 6.3%) and somatic diseases (27.1% and 10.4%), frequent respiratory infections (60.4% and 25.0%).

In 19-39.6% of cases the birth was physiological, in 29-60.4% of women it was pathological. Surgical delivery by Caesarean section was observed in 8-16.7% of cases. 43-89.6% of children were born full-term, with a birth weight from 2950.0 to 4180.0 grams (3470±312), body length 51.2±0.4 cm. 5-10.4% of children with hypoxic-ischemic damage to the central nervous system and prolonged jaundice.

7-14.6% of children in group I and 31-64.6% of infants in group II had a family history of atopy. Every third child had signs of atopic dermatitis. In the neonatal period, 29-60.4% of newborns were late attached to the mother's breast. In newborns admitted to the hospital with maternal allergies, rash, diaper rash, gneiss were most often recorded, and allergy was the root cause of atopic dermatitis, neurological disorders, enterocolitis and diarrhea.

Such clinical symptoms as diaper rash in skin folds of I - II degree were present in 17-35.4% of patients, gneiss on the scalp - in 26-54.2% of cases, strophulus and miliaria were present in 35-72.9% of patients, crusts on the cheeks - in every second (24-50%) child, vesiculopustulosis and weeping eczema were detected in 13-27.1% of children.

There was irrational use of medications in infants, in particular antibiotics and hormones due to prematurity and the presence of viral and bacterial infections. Parents of children in groups I and II indicated the use of antibiotics for their children (12.5% and 20.8%), NSAIDs (2.1% and 14.6%), and hormone therapy (0% and 6.3%).

A study of the anamnesis showed that 19-39.6% of newborns were on natural and 29-60.4% on mixed or artificial feeding.

Unbalanced maternal nutrition was noted in 14-29.2% of patients; transfer of newborns to early artificial feeding was detected in 27-56.3% of children in group II and in 9-18.7% of patients in group I. Allergies were more common in children on mixed and artificial feeding. Thus, an allergy to cow's milk was noted in 11-22.9% of group II infants who were bottle-fed, and in 9-18.8% of children who received breast milk. The occurrence of “milk” allergies was facilitated by the early transfer of the child to mixed or artificial feeding using various milk formulas, as well as the mother’s excessive consumption of whole cow’s milk and honey during pregnancy and lactation.

In addition to signs of atopic dermatitis, 11-22.9% of newborns had anemia, 6-12.5% of children had thymomegaly, perinatal damage to the central nervous system was detected, and acute bronchial obstruction and acute respiratory infections were recorded in 12-25.0% of cases. The mothers of 31-64.6% of newborns complained of periodic sudden restlessness and causeless crying of the child, 9-18.8% of patients had episodes of increased excitability that ended without reason. Paroxysmal cramping colic associated with nutrition was indicated by mothers of 18-37.5% of patients.

The above factors often, individually and in various combinations, lead to an imbalance of the immune system, enhance the development of dysbiosis and stimulate the atopic reaction.

The research results showed that the intestinal microbiocenosis undergoes noticeable changes in qualitative and quantitative terms. Upon admission to the hospital, the intestinal flora in newborns was poor, both the frequency of detection and the quantitative content of normal intestinal inhabitants were sharply reduced: bifidobacteria were detected in the 3rd dilution in 23-47.9% of children, enzymatically positive Escherichia was sown in 41-85, 41% of cases and non-hemolytic enterococci were isolated from 13-27.1% of children.

Children born by cesarean section had their own microbiota characteristics: there was a lower content of bifidobacteria in the intestines compared to full-term children born naturally.

The intestinal microflora of newborns with maternal allergies in the first weeks of life was characterized by the most frequent decrease in the diversity and richness of microbes. Low microbiota diversity is associated with an increased risk of sensitization to allergens. Qualitative and quantitative shifts in intestinal colonization of infants with maternal allergy compared with infants without maternal allergy were observed.

Thus, in newborns with maternal allergies, compared with children born without maternal allergies, lactose-negative strains of Escherichia were found significantly more often ($P<0.01$) and in significantly greater quantities ($P<0.001$), and the content of enterococci, staphylococci, yeast-like fungi and Proteus bacilli were higher ($P<0.001$) not only in quantity but also in frequency of detection.

Quantitative fluctuations of microbes had very wide limits: in 1.0 g of feces, bifidobacteria were found in quantities from 102 to 103, lactose-positive strains of Escherichia - from complete absence in 6 newborns to 103, lactose-negative - 102, staphylococci and yeast-like fungi up to 103 microbial bodies.

The fecal microbial composition, metabolites, and pH of infants fed partially hydrolyzed protein formula with added indigestible oligosaccharides were closer to those of breastfed infants than of infants fed formula. In children with maternal allergies, dysbiosis was detected in the form of the development of bacteria of the genera Enterobacteriaceae and Parabacteroides, as well as a decrease in lactate-utilizing bacteria - Eubacterium.

The main areas of complex treatment of newborns with allergies were feeding and care. A special place was occupied by the correction of the mother's diet with the exclusion of identified allergenic products, strengthening of reproductive processes on the skin through local treatment, improvement and normalization of the intestinal flora.

Rational nutrition of the mother was an important part of the comprehensive treatment of allergies in the newborn, since it reduced the drug load on the child's body and contributed to a faster recovery.

Nursing mothers were recommended to have a rational and nutritious diet, a hypoallergenic diet for the entire period of breastfeeding and a dairy-free diet with the complete exclusion of products containing cow's milk proteins, and fermented milk products were also used to expand the dairy-free diet. Taking into account the mother's individual tolerance, the consumption of green and white fruits was allowed. To enrich the mother's diet, products with prebiotic properties were used, contained in corn flakes, cereals, bread, onions, potatoes, artichokes, bananas and other products. Elimination of the allergen product from the diet led to practical recovery or improvement in the condition of the newborn child.

Newborns were prescribed hypoallergenic mixtures for therapeutic purposes: Alfare, Nutrilak, Nutrilon Pepti TCS, with therapeutic and preventive - Nutrilak GA, Humana GA-1 and with preventive - NAN GA 1, Nutrilon GA 1.

For local therapy in the presence of diaper rash, the affected areas were lubricated with hypoallergenic ointment and olive oil. An obligatory component of the treatment of newborns, taking into account the results of a study of the state of intestinal microbiocenosis, was the administration of probiotics in age-appropriate dosages, which, by normalizing the intestinal microflora, prevent the progression of the allergic process, which has a positive effect on the quality of life of the mother and child.

As a result of the administration of probiotics, the number of bifidobacteria increased in all newborns by 1-2 orders of magnitude and the level of opportunistic microorganisms decreased.

Allergies often go away on their own in most children, but their nutritional and social consequences can be significant, requiring regular examination and monitoring by a doctor. There is no product that can completely replace mother's milk in a baby's diet. Each mother, carefully monitoring her sick child, can greatly help doctors in quickly identifying the causes of allergic reactions and the child's recovery.

Organizing nutrition for newborns with maternal allergies is a complex process that requires an individual approach to each child. The intestinal microbiota is a labile system that changes in response to various influences, and therefore its correction in infants at high risk of allergies is of no small importance in the prevention of allergic conditions in the mother and her child.

The mechanism of antenatal transmission of bacteria from mother to child has not been fully deciphered, but it is known that during pregnancy and lactation, bacterial translocation from the intestine to the mother's bloodstream increases, and from there to other systems and organs [23].

Natural birth and breastfeeding provide important benefits for the baby, including stimulation of the immune system and provision of normal gut microbiota.

Despite significant fluctuations in response to external influences, the diversity of a child's microbiota has a linear development trend. Microbial communities in the first months of life are characterized by genes responsible for the absorption of lactate.

The use of probiotics in pregnant women to prevent allergies in the child

Conclusions. Studies have shown that the risk factors for the development of allergic reactions in a newborn are diverse and variable. The main factors that negatively affect the formation of a newborn's biocenosis include perinatal use of antibiotics, operative obstetric care, late breastfeeding and artificial feeding. The use of probiotics seems to be one of the promising areas for protecting newborns.

Newborns with a history of maternal allergies should be monitored at the dispensary, which undoubtedly helps reduce morbidity among children.

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