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Review
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The Effects of Intestinal Microbiota on Newborn

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Abstract

The neonatal period is a critical period for gastrointestinal colonization, affecting the adult intestinal microbiota and the individual's lifelong health. The intestinal microbiota begins to form rapidly within a few hours after the newborn comes into contact with the mother's vagina and the environment and is affected by various factors such as the environment, gestational age, mode of delivery, hospitalization, antibiotic use, and diet. The changes in intestinal microbiota composition are reported to be associated with many conditions such as obesity, hypertension, diabetes, autoimmune diseases, allergy, autism, and gastric cancer. Therefore, the neonatal period is a critical period in terms of factors affecting the development of healthy intestinal microbiota. The aim of this review to evaluate the microbiota and the factors affecting the development of the microbiota in newborns.

Keywords: Microbiota, intestinal microbiota, newborn

Introduction

Humans are confronted with many microorganisms since birth and live with these creatures throughout their lives. During this association, the human body sometimes encounters pathogenic microorganisms and is damaged, sometimes it is not adversely affected in any way, but on the contrary, it benefits from this situation. In many studies conducted to date, the relationship between humans and pathogen-opportunistic microorganisms has been evaluated, and there has not been enough study on the benefits of microorganisms on humans. However, there has been an increase in diseases such as obesity, cancer, and diabetes due to the deterioration of flora, microbiota, and microbiome, which are not harmed by humans.[1]

Microbiota is the ecological structure formed by commensal, symbiotic, and pathogenic microorganisms that share our body.[2] Microbiome refers to all microorganisms living in the body and their genetic material.[3] The microbiota has begun to be accepted as a new organ in line with current research. Studies are being conducted on its effects on diseases and its use for treatment is increasing.[2]

The normal intestinal microbiota consists of approximately 200 common bacterial species and more than 1000 rare species. In healthy humans, the intestinal microbiota can be divided into 6 bacterial classes as *Firmicutes*, *Bacteroidetes*, *Proteobacteria*, *Actinobacteria*, *Fusobacteria*, and *Verrucomicrobia*. *Firmicutes* and *Bacteroidetes* make up 90% of the intestinal microbiota. When examined at the class level, obligate anaerobes *Bacteroidetes*, *Eubacterium*, *Clostridium*, *Ruminococcus*, *Peptococcus*, *Peptostreptococcus*, *Bifidobacterium*, *Fusobacterium* and less frequently facultative anaerobes *Escherichia*, *Enterobacter*, *Enterococcus*, *Klebsiella*, *Lactobacillus*, and *Proteus* were found.[4]

Intestinal microbiota positively affects the normal structural and functional development of the mucosal immune system. It is thought that the altered intestinal flora composition causes frequent infections in the baby and an increase in the incidence of allergic diseases.[5] Intestinal microbiota may contribute therapeutically to the pathogenesis of these diseases in people who are genetically predisposed to intestinal diseases.[6]

Clinical observations and animal experiments have provided lots of evidence of a strong connection between the brain and the gut. This connection is established during the intrauterine period and maintains its effect throughout life.[7] The intestinal microbiota,

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which creates a strong relationship between the brain and the gut, plays an important role in human health. There is strong evidence that the intestinal microbiota is associated with some metabolic and neuropsychiatric diseases. These are obesity, metabolic diseases such as diabetes, and neuropsychiatric disorders such as schizophrenia, autism, anxiety, and depression. It has been reported that beneficial, harmful, and probiotic microorganisms living in the gastrointestinal tract stimulate the immune system, nerve pathways, and central nervous system.[3]

There is growing evidence that microbiomes influence behavior which is supported by the concept of the brain–gut–microbiome axis. Although the specific mechanism underlying this effect is not known, it is known that microbiomes located in the placenta and amnion affect the developing fetus.[8]

Effect of Delivery Type on Newborn Intestinal Microbiota

Intestines are sterile at birth. From birth, the number of bacteria in the intestines increases. Bacteria begin to appear even in the first stool. In the first week after birth, more aerobic bacteria dominate the flora, and then anaerobic bacteria become dominant. In the first 2 years after birth, the intestinal flora shows microbiological changes, and after 2 years of age, it enters the process of transformation into adult-type flora. The intestinal microbiota of the baby is affected by factors such as maternal microbiota, gestational age, mode of delivery, place of delivery, nutrition of mother and baby, and antibiotic use.[9] Newborns born vaginally are initially colonized by the mother's feces and vaginal bacteria, whereas newborns born through cesarean section are initially exposed to microorganisms from the hospital setting and healthcare workers.[10]

The intestinal microbiota is close to its mother, both functionally and phylogenetically, when the newborn is 1 month old. When the baby is 11 months old, important phylogenetic differences appear, while the gene functions between mother and baby remain very similar. It has been shown that whether the mode of delivery is vaginal or cesarean section significantly affects the number of Bifidobacteria.[11] It has been stated that Bifidobacteria and all other microbiota types are less common in cesarean deliveries.[12] However, it was stated that the mode of delivery by cesarean or vaginal route did not affect intestinal colonization in preterm newborns.[13]

In the intestinal microbiota of preterm newborns, on the 10th day of life, there are predominantly 3 different bacterial species. Enterobacteria such as *Escherichia coli* and *Klebsiella*, Enterococci such as *Enterococcus faecalis*, and Staphylococci such as *Staphylococcus epidermis*, *Staphylococcus aureus*, and *Staphylococcus haemolyticus* are the most frequently isolated bacteria.[14]

The region of the body with the most bacteria, except the intestines, is the vagina. Lactobacilli are the most important probiotic bacteria in the vaginal flora.[15] According to the results of the research conducted by Dominguez-Bello et al[16] in 9 mothers and 10 babies (1 of them twins), in babies born vaginally, the mother's vaginal flora is inherited to babies and there is lactobacillus colonization within a few hours. In babies born by cesarean section, it was determined that the mother's skin bacteria (Staphylococci) were transmitted to the baby. In their study, Salminen et al[17] examined 60 healthy 7-year-old children in terms of delivery method and intestinal flora and determined that the number of Clostridia detected by the fluorescence in situ hybridization method was higher in those who were born vaginally. They found that the frequency of asthma attack at the age of 7 years was higher in children with low clostridia count. As seen in these studies, the mode of birth and the flora acquired in this way are important in terms of encountering some diseases throughout the individual's life.

The Effect of Newborn Nutrition on Intestinal Microbiota

Another powerful effect that affects the development of the infant's intestinal microbiota is the diet. Comparing formula-fed infants and breast-fed infants, it has been reported that breast-fed infants ingest more Bifidobacteria and Lactobacilli, and less Bacteroides, Clostridium coccoides group, Staphylococci, and *Enterobacter* than formula-fed infants.[18,19] Breast milk is a very important source of oligosaccharides, and its microbiota has a strong prebiotic effect on the developing newborn.[20]

In general, the intestinal microbiota changes more rapidly in the neonatal period than in adults. Even a small amount of formula is added to the diet of a breast-fed infant, causing changes in the intestinal microbiota.[5] The flora distribution of babies born vaginally and fed with breast milk or formula is similar until the 48th hour. While the rate of *Bacteroides fragilis* in breast-fed infants toward the seventh day is only 22%, it affects two-thirds of formula-fed infants.[21]

According to the results of the study by Lee et al[22] in which they compared the intestinal microbiota characteristics of 4-week-old Korean infants fed with breast milk and formula, the density of prebiotic microbiota such as *Bifidobacterium longum* in breast-fed infants was found to be statistically significantly higher than in infants fed with the formula.

It has been reported that periodontal infectious such as *Fusobacterium nucleatum* and some oral pathogens increase the risk of premature birth by settling in the uterus of the pregnant.[23] The intestinal colonization process is both delayed and impaired due to difficulties in the enteral nutrition of preterm newborns and prolonged parenteral nutrition.[24] Breastfeeding of extremely preterm babies may not be possible due to their illness. When the antibiotic use of preterm newborns and their long stay in neonatal intensive care units are added to this, preterm newborns form their intestinal microbiota with the pathological microorganisms they receive from the environment. This situation paves the way for the development of morbidities such as necrotizing enterocolitis and sepsis in preterm newborns.[25]

Conclusion

The intestinal microbiota, which changes and develops with the birth of the newborn, creates a microenvironment necessary for the healthy functioning of the body. Thanks to the beneficial microorganisms in the intestinal microbiota, the newborn is protected against many diseases. Normal vaginal delivery and breastfeeding have significant positive effects on the development of the newborn intestinal microbiota. In this regard, it is important to increase the rates of normal vaginal deliveries and breast milk feeding for the health of newborns and future adults.

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