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Nutrition for healthy term infants and the role of gut microbiota

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Abstract

Introduction: Nutrition in the first year of life plays an important role in the child's development, directly through the intake of nutrients, as well as indirectly by influencing the composition of the gut microbiota. Improper diet already at the very beginning can significantly affect the onset of metabolic and other chronic diseases in children and adolescents. Moreover, this period is crucial also for the development of taste and eating habits. *Methods:* A narrative review of the literature in the world databases and currently valid guidelines in the Republic of Slovenia was made. The analysis included studies examining the impact of diet and gut microbiota on health in the first years of life. *Results:* The presence of microorganisms in the placenta and meconium indicates the first contact of the digestive tract with the microbiota already during pregnancy. Extensive colonization occurs during birth and in the first months of life, while the development and maturation of the microbiota is strongly influenced by the factors such as gestational age, mode of delivery, diet, environment, and antibiotic treatment. The composition of the gut microbiota in the first year of life is very uniform and individually specific and develops toward an adult-like structure between the age of three and five. Among the important factors influencing the composition of the gut microbiota is also the introduction of complementary foods (CFs). Current guidelines recommend that CFs should be introduced gradually after the age of six months. The introduction of CFs before the age of 17 weeks can lead to obesity, respiratory disorders and eczema in later childhood. With the later introduction of CFs (five to seven months), there is a risk that the energy value of nutrients in breast milk or infant formula is no longer sufficient for the baby's rapid development. *Discussion and conclusion:* Diet and its indirect influence on the composition and abundance of the gut microbiota are one of the most important factors influencing

metabolism, resistance to infections and development of the immune system. Thus, by choosing an appropriate diet in the early childhood, we can significantly contribute to health later in life.

Keywords: infants, nutrition, gut microbiota, health

Introduction

An increasing amount of scientific evidence shows the importance of diet during early infancy. Fetal development and infancy are life stages that are characterized by rapid growth, development and maturation of organs and systems. Variation in the quality or quantity of nutrients consumed by mothers during pregnancy, or infants during the first year of life, can exert permanent and powerful effects upon developing tissues. These effects are termed 'metabolic programming' and represent an important risk factor for non-communicable diseases of adulthood (Langley-Evans, 2015). Thus, diet in early infancy has a key role on growth pattern and development but is also important for the generation of lifelong flavour preferences and dietary habits that will influence mid- and long-term health (D'Auria et al., 2020). For instance, evolutionary driven preferences for sweet and salty tastes can be modified by repeated early exposure to the taste of some vegetables which enhances liking for those vegetables with effects persisting up to 6 years later (Fewtrell et al., 2017).

Nutrition of infants is divided in three periods: exclusive dairy diet (breast milk or infant formula), introduction of complementary foods (CFs) and transition to modified family diet. Exclusive breast-feeding (EBF) as defined by the World Health Organization (WHO) means that the infant receives only breast milk and no other liquids or solids except for drops or syrups consisting of vitamins, mineral supplements, or medicines (World Health Assembly, 2002). The term complementary feeding (CF) describes a period in which there is a gradual reduction of frequency and volume of breast milk or formula together with the introduction of CFs. This period is important in the transition of the infant from milk feeding to family foods and is necessary for both nutritional and developmental reasons (Dipasquale & Romano, 2020). Available literature data show increasing interest and concerns about the impact of CF timing and modality on the onset of later non-communicable disorders, such as overweight and obesity, allergic diseases, celiac disease, or diabetes (Dipasquale & Romano, 2020). Moreover, nutrition early in life was recognized as a strong determinant of the children gut microbiome assembly and maturation (Lim et al., 2016). This highly modifiable and adaptive system of bacteria, viruses, fungi, protists and other microorganisms reversely affects the host in multiple complex ways (Subramanian et al., 2015). Various epidemiological studies have shown a correlation between factors disrupting the gut microbiota during childhood on the one hand and immune and metabolic disorders in adulthood on the other.

The aim of our study was to present the currently valid guidelines on nutrition for healthy term infants and to review the recent articles regarding the influence of nutrition on gut microbiota and development of diseases later in life.

Methods

A narrative review of scientific and professional literature was performed using the world databases such as PubMed and websites of professional organizations. The keywords used in the search were: infants, nutrition, breast-feeding, complementary feeding, recommendations, gut microbiota, health, and their combinations. Inclusion criteria were English language articles published after 2000, with available full text and the appropriate content. Altogether 30 articles are presented in this narrative review.

Results and discussion

Breastfeeding or formula feeding

Human milk not only provides the perfectly adapted nutritional supply for the infant but also plays a crucial role in promoting healthy growth and development (Mosca & Giannì, 2017). The WHO recommends that infants are exclusively breastfed up to the completion of 6 months, with breastfeeding continuing to be an important part of the diet until the infant is at least 2 years old (World Health Assembly, 2002). EBF by a healthy mother can meet the nutrit ent requirements of healthy-term infants for most nutrients for approximately 6 months, although the lack of evidence from randomized clinical trials suggests that it is not certain whether this applies to all mothers and infants. Some infants may require additional energy or iron before 6 months (Fewtrell et al., 2017). Advances in research have clearly indicated several short and long-term health benefits associated with breastfeeding (Mosca & Giannì, 2017). A systematic review published in 2016 indicates a strong protective effect of EBF during the first 6 months against infectious diseases, with an 88% reduction of mortality in comparison to infants that have never been breastfeed (Victora et al., 2016). Compelling evidence indicates a major protective role of breastfeeding with regard to the risk of gastrointestinal (GI) and respiratory infections, including hospitalization due to these diseases (B. L. Horta et al., 2013). Among the long-term health outcomes, longer exposure to breastfeeding is associated with 35% reduction of the risk of developing diabetes type II (B. L. Horta et al., 2015a). Breastfeeding seems to exert a protective effect against obesity development in later life, while formula feeding seems to favour high weight gain (B. Horta et al., 2013). Furthermore, consistent evidence indicates that breastfeeding is associated with positive cognitive outcome. Specifically, the intelligence quotient in ever breastfed infants has been reported to be 3.4 points higher than that of never breastfed infants (B. L. Horta et al., 2015b).

Complementary feeding

According to the WHO definition, the introduction of CFs is needed to ensure optimal energy and nutrient intake when "breast milk alone is no longer sufficient to meet the nutritional requirements in terms of energy and nutrients of infants" (World Health Assembly, 2002). Based on the available evidence, current guidelines recommend that CFs (solids and liquids other than breast milk or infant formula) should not be introduced before 4 months (17 weeks) but should not be delayed beyond 6 months (26 weeks). GI and renal functions are sufficiently mature by approximately 4 months to enable term infants to process CFs, and by 4 to 6 months they will have attained the necessary motor skills to cope safely with CFs (Fewtrell et al., 2017). The introduction of CF is this time frame is also regarded as the most appropriate in terms of health outcomes. Conversely, the introduction before the age of 17 weeks is associated with greater risk of obesity and adoption of unhealthy eating habits (D'Auria et al., 2020). There may also be an increased risk of allergy if solids are introduced before 3 to 4 months. There is, however, no evidence that delaying the introduction of allergenic foods beyond 4 months reduces the risk of allergy, either for infants in the general population or for those with a family history of atopy (Fewtrell et al., 2017).

Infant's gut microbiota

Until recently, it was widely believed that the microbial colonization of the GI tract begins during and immediately after birth. However, the detection of bacteria in placental tissue and meconium suggests the first contact of the GI tract with the microbiota already during pregnancy (Aagaard et al., 2014). More extensive colonization of the GI tract then occurs during and after birth, while development and maturation of the microbiota are strongly influenced by various factors such as gestational age, mode of delivery (vaginal birth vs. birth by caesarean section), nutrition (breast milk vs. milk formula), environment, and antibiotic treatment (Zhuang et al., 2019). Among these factors, vaginal delivery and breastfeeding were found to positively modulate the composition of the gut microbiota, while both contribute to an enrichment of beneficial bacterial strains such as *Bifidobacterium* (Martin et al., 2016). Moreover, higher abundance of potentially pathogenic and proinflammatory *Klebsiella* and *Enterococcus* in infants born with caesarean section may imply a higher risk of immunological disorders and risk of infections (Reyman et al., 2019). In addition, pregnancy outcome and child development may also be influenced by the microbial compounds and metabolites of the maternal microbiota (Romano-Keeler & Weitkamp, 2015). The gut microbiota of the newborn is therefore characterized by a high inter-individual diversity, which is generally low in the first year of life, changes very rapidly and is shaped toward an adult-like between the age of 3 and 5 (Koenig et al., 2011).

Effects of nutrition on infant's microbiota

Breast milk is widely accepted as the nutritional gold standard for infants, with recommended EBF for the first 6 months (World Health Assembly, 2002). In addition to the essential nutrients, the breast milk contains complex microbial community, that is not aleatory assembled (Drago et al., 2017). As shown by Biagi et al. (2018), different types of microbial communities in milk are ask sociated with features in the infant's gut and mouth ecosystems, such as high relative abundance of the most important probiotic group of bifidobacteria. Additionally to the intrinsic health-promoting effects of milk itself, feeding directly from the breast can contribute to the preterm infant's microbiome assembly (Biagi et al., 2018). However, the breastmilk composition is adjusted to the needs of the new-born and is changing over time e.g., colostrum is rich in human milk oligosaccharides (HMOs), while mature milk contains greater amounts of proteins (Bode, 2012). HMOs represent one of the most abundant bioactive molecules in human milk known to stimulate the growth and colonization of beneficial gut microbiota species and suppress the growth of opportunistic pathogenic species (Newburg et al., 2005). While the gut microbiota of breastfed infants is characterized by the higher counts of bifidobacteria and lactobacilli and lower levels of potential pathogens, the gut microbiota of formula-fed infants is associated with a more diverse gut microbiota that is dominated by *Staphylococcus*, *Enterococcus*, *Bacteroides*, *Clostridium*, enterobacteria, and the genus *Atopobium* (Martin et al., 2016). It was also shown that breast milk in the case of EBF infants may provide the gut microbiome with a greater plasticity that eases the transition into CF (Thompson et al., 2015). The last induces the development of a mature microbiota with genes responsible for complex carbohydrate, starch, and xenobiotic degradation as well as vitamin production (Koenig et al., 2011). Although the introduction of solid foods is a major event in the first year of life, it is little known to what extent the choice of specific foods or the diversity of introduced foods influence microbial community diversity, structure, and taxonomy in the gut (Homann et al., 2021). Mainly the introduction of solid foods has been associated with changes in phyla abundances, especially an increase in *Bacteroidetes* (Koenig et al., 2011). However, some study results suggest that the introduction of solid food does not appear to result in a profound shift in microbial community structure as long as breastfeeding is continued (Galazzo et al., 2020).

The role of gut microbiota in infant's health

Gut microbiota was recognized as an important determinant of the GI, immune and central nervous system (CNS) development. Therefore, an early life as a critical period for microbial colonization can affect not only the infant's health but is also profound for wellbeing further in life (Yao et al., 2021). While an early life is a period of fast brain development, the gut microbiota metabolites (e.g., short-chain fatty acids and lipopolysaccharides) are one of the most important components that pass directly through epithelial cells and can regulate the development of the brain and CNS. Therefore, the disturbances in the assembly and maturation of the gut microbiota may impact development of motor, social, and cognitive function (Diaz Heijtz, 2016). Furthermore, after birth infant microbiota shape innate and acquired immunity and may have a profound impact on the structure and function of the immune system e.g. (i) low diversity and bacterial density may cause an impaired stimulation of secretory IgA that can result in a reduced mucosal barrier function; (ii) bacterial diversity was inversely associated with allergic sensitization; fecal microbiota transplant from normal weight infant to germfree mice showed greater villus height and crypt depth, as well as higher proliferating cells in the ileum than recipients of low-weight infant microbiota (Ximenez & Torres, 2017). Based on the data supporting the correlation between microbiota colonization and disease onset, there is also a great overall impact on long-term health. However, the specific influencing factors and mechanisms need to be further explored.

Conclusions

Nutrition in the first years of life is one of the most important factors that can significantly affect the wellbeing, development and health of the child. The first years of children's life are also recognized as an important factor in the development of a healthy gut microbiota. Based on this literature review the protective role of breastmilk against numerous diseases such as diabetes and obesity, was noted. Moreover, there are different microbial colonization patterns of the gut between breastfed and formula-fed infants, with the latter achieving an early divergence toward an adult-like microbiota composition. However, findings support the current WHO recommendation for exclusive breastfeeding during the first 6 months with continued breastfeeding until at least 12 months. To sum up, while the infants gut microbiota effects both infant health and long-term health, it is important to follow the nutritional guidelines in order to establish its favourable composition.

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