EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Review Article

The Development and Importance of the Human Gut Microbiota During the Phases of Life

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Abstract

The development of the intestinal microbial ecosystem is a complex event in human life that is highly variable from individual to individual since it is influenced by multiple factors. Immediately after birth, the intestine begins to populate with a series of microorganisms that vary based on a series of exogenous and endogenous factors. In adult age, some factors that can commonly influence the gut flora are: changes in diet or lifestyle, state of health of the host, presence of metabolic or chronic diseases, antibiotic treatments, and modifications of the immune system. Current scientific literature indicates the Mediterranean diet as the optimal diet for a healthy gut microbiota. In subjects with metabolic diseases or chronic pathologies the identification of a correlation between the prevalence of certain strains of intestinal microbiota, characteristics in the dietary habits, and the presence of specific pathologies/medical conditions could be essential for the creation of personalized diets. It is necessary to fully determine in which ways the microbiota composition can be manipulated in order to achieve specific health benefits. These correlations could also create the grounds for a possible integration with probiotics, prebiotics, macronutrients, and/or micronutrients with the intention of creating an intestinal microbiota in unhealthy subjects that is similar to that of a healthy subject. Further research is necessary to better understand the positive role that some probiotics, prebiotics and micro/macronutrients can play in determining specific health benefits deriving from the intestinal microbiota in humans.

Keywords: *Gut Microbiota; Mediterranean Diet; New-Borns; Probiotics; Prebiotics*

Introduction

The development of the intestinal microbial ecosystem is a complex event in human life that is highly variable from individual to individual since it is influenced by multiple factors. The colonization of the gastrointestinal tract begins at birth and continues through life, forming a gut flora that is peculiar to each individual. Immediately after birth, the intestine begins to populate with a series of microorganisms that vary based on a series of exogenous and endogenous factors. In adult age, some factors that can commonly influence the gut flora are: changes in diet or lifestyle, state of health of the host, presence of metabolic or chronic diseases, antibiotic treatments, and modifications of the immune system. All these factors contribute on an every-day basis to the composition and maintenance of the human gut flora. Furthermore, the external environment and the geographical location in which a person lives also influence the composition of the gut microbiota [1-3].

The microorganisms present in the intestine are crucial for many aspects of human health. Studies show an increasing emphasis on the role played by microbiota in many human diseases and on the mechanisms by which a modification of the composition of the microbiota can determine states of dysbiosis, which negatively impact human health [4].

Alterations in the composition and diversity of gut flora play an important role in the development of metabolic disorders such as obesity and type 2 diabetes mellitus. These metabolic disorders are, in fact, influenced not only by epigenetic and environmental factors but also by behavioural factors such as eating habits [5].

Discussion

Studies found in literature demonstrate that the composition of the intestinal microbiota is different in new-borns born through natural childbirth compared to those born by Caesarean section. In fact, in children born through natural birth the most important factor that influences the microbiota is the composition of the mother's vaginal and faecal microbiota. As a consequence, these infants normally host a gut flora dominated by species of the genera *Lactobacillus, Bifidobacterium, Prevotella,* or *Serratia*. On the other hand, in the case of a caesarean section, the first bacteria encountered by the new-borns are those present on the mother's skin and in the hospital environment. These new-borns, in fact, host a microbiota that is dominated by species belonging to the genera *Corynebacterium, Staphylococcus* and *Propionibacterium*. During the first weeks of life, these new-borns present a gut flora characterized by a lower bacterial count and a smaller diversity compared to those born through natural childbirth [6,7].

Another element that is important in the early development of gut flora is the child's diet. Studies have shown that the gut flora in a breast-fed baby is qualitatively different compared to that of a child who is formula fed. For example, in breast-fed infants the microorganism that normally prevails in the gut flora is *Bifidobacterium*. Furthermore, maternal milk is rich in monosaccharides such as lactose, glycoproteins, glycolipids, sialic acid, fucose, N-acetylglucosamine and oligosaccharides [8,9]. These components are not digested in the intestine but act as a shield against the proliferation of pathogenic bacteria through their role as ligands and substrates for *Bifidobacteria.* Studies have shown in breast-fed children compared to formula-fed ones the presence of a more acidic intestinal environment and of a flora characterized by the prevalence of fermentative bacterial strains compared to putrefactive ones. As a consequence, this determines an improvement of the digestive and absorption functions, a stimulation of the immune system, and a reduction of the risk of developing allergies [10-13]. On the other hand, in new-borns that are fed on formulas the gut flora is complex and- similarly to that of adults- composed mostly by *Bifidobacteria, Enterobacteria, Lactobacilli, Bacteroides, Clostridia, Enterococci* and *Streptococci*. After the first six months of life, with the beginning of the weaning period, characterized by the diversification of the diet and the introduction of solid foods, there is a further differentiation of the micro-organisms and an increase of strains that are typical of adulthood (e.g. *Bacteroidetes* and *Firmicutes*) [14,15].

The early microbial colonization of the intestine is certainly a very important factor in determining the gut flora present also in adulthood. In fact, once constituted the gut flora remains largely stable except for variations due to some factors such as changes in eating habits or the onset of a disease [16]. However, the most important factor involved in altering the composition of gut microbiota has been shown to be the use of broad-spectrum antibiotics. These, in fact, reduce the presence particularly of anaerobic microorganisms determining a qualitative and quantitative change in the flora and a reduction of its fermentative and metabolic capacity [17]. An alteration in the composition of the gut microbiota can determine the prevalence of some bacteria such as S*taphylococcus, Clostridium, Pseudomonas* that can exert a harmful action over other species such as *Lactobacillus, Bifidobacterium, Eubacterium* that instead tend to have a protective action [18].

While many studies underline the fundamental effects of diet on the composition of microbial flora in the first months of life, other studies observed the impact of different eating habits in the adult life on the long-term composition of the gut microbiota. Many studies have demonstrated that a variation in intestinal microbiota can derive from a variation in the eating habits of an individual. Subjects who prefer a diet rich in fats and sugars (similar to the Western diet) have a composition of the intestinal microbiota that is different from those who follow a more balanced diet or even a vegetarian diet [19].

As mentioned above, dietary habits and their modifications both influence the equilibrium of the gut flora. Epidemiological studies found in literature have associated the increase of chronic inflammatory diseases and cancer with the diffusion of the “Western diet”, characterized by large quantities of red meat, simple carbohydrates (e.g. sugars), refined vegetable fats and by small quantities of vegetables, fruit and fish [20]. The “Western diet”, however, also has the capacity of influencing the composition of the gut microbiota. Low quantities of dietary fiber alter the flora, resulting in a reduced production by part of the flora of compounds including certain Short-Chain Fatty Acids (SCFA) such as butyrate, polysaccharide A, peptidoglycans that have the effect of modulating the response of the immune system. Saturated fatty acids are considered pro-inflammatory, while the unsaturated ones can have both anti-inflammatory and pro-inflammatory properties [21]. Omega-3 and omega-6 polyunsaturated fatty acids are not only essential components of cell membranes but also the precursors of prostaglandins, powerful regulators of inflammation. Omega-3 performs an anti-inflammatory action by replacing omega-6 in several metabolic pathways. An increase in the omega-3/omega-6 ratio can be achieved by increasing the consumption of fish and reducing the consumption of vegetable oils. A good dietary omega-3/omega-6 ratio has protective effects against many diseases, including cardiovascular and atherosclerotic diseases [22]. A low production of SCFA, resulting from a diet low in fiber and complex starches not only slows down the growth of intestinal epithelial cells but also inhibits their proliferation and differentiation. The microflora’s anaerobic metabolism of peptides and proteins determines the production of SCFA while generating also a series of potentially toxic substances including polyamines, phenols, thiols and indoles. A balanced diet is essential in order to preserve the health of the gastrointestinal tract since a correct intake of nutrients provides to the individual not only sustenance and energy but also influences and promotes the diversity of the composition of the microbiota. In fact, based on scientific data found in literature, the Mediterranean diet can be considered an important reference point for human health. This diet is rich in olive oil, fresh fruit and vegetables, whole grains, nuts and dried fruit, with a modest consumption of fish and poultry, and a low consumption of red meat and of simple carbohydrates. It is the ensemble of these nutritional characteristics of the Mediterranean diet and not the single macronutrients and micronutrients that play an important role in the protective effect of this diet [23].

Conclusion

The composition of the gut microbiota has effects not only on digestion but also on the health of the intestine in general, on the immune system and even on brain functions [24]. In fact, studies show that a balanced diet promotes the formation and maintenance of a well-composed bacterial community. The starting point in correcting a state of dysbiosis and in positively modulating the equilibrium of an intestinal microbiota is certainly that of acting upon the dietary habits. Current scientific literature indicates the Mediterranean diet as the optimal diet for a healthy gut microbiota. It would be advisable to educate the population towards a correct diet which favours foods that provide: an adequate fibre content (e.g. cellulose, hemicellulose, pectin, lignin) that is essential for maintaining a positive intestinal microbiota composition; a correct dietary ratio of 0mega 3-6; a sufficient dietary intake of vitamins through the consumption of food of both animal and vegetable origin [25].

If the equilibrium of the microbiota is altered various health conditions may result including inflammatory, chronic and/or metabolic diseases. In subjects with metabolic diseases or chronic pathologies the identification of a correlation between the prevalence of certain strains of intestinal microbiota, characteristics in the dietary habits, and the presence of specific pathologies/medical conditions could be essential for the creation of personalized diets. It is necessary to fully determine in which ways the microbiota composition can be manipulated in order to achieve specific health benefits. These correlations could also create the grounds for a possible integration with probiotics, prebiotics, macronutrients, and/or micronutrients with the intention of creating an intestinal microbiota in unhealthy subjects that is similar to that of a healthy subject. This could, in fact, prove to be a winning strategy in reducing or even solving many inflammatory, chronic and/or metabolic diseases with consequent improvement of patient symptomatology [26]. Further research is necessary to better understand the positive role that some probiotics, prebiotics and micro/macronutrients can play in determining specific health benefits deriving from the intestinal microbiota in humans.

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