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Influence of diet on the gut microbiota

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Abstract

Introduction: Gut microbiota is still a new direction in medicine. The intestinal microbiota contains up to 100 trillion bacteria and around 1000 species. The composition of the intestinal microflora may be affected by external factors, among which eating habits can be considered as one of the most important. There are evidences how gut microbiota may affect the course of diseases, such as autism spectrum disorders, mood disorders, celiac disease, irritable bowel syndrome, diabetes and colorectal cancer

The aim of the study: The purpose of this systemic review was to collect and analyse current and new information on the effect of diet on intestinal microbiota.

Material and method: Standard criteria were used to review the literature data. The search of articles in the PubMed database was carried out using the following keywords: microbiota, gut, diet, gluten-free-diet, ketogenic-diet.

Description of the state of knowledge: There are many studies that show the effect of diet on the intestinal microflora. Changing the amount of plant fiber consumed, ketogenic diet, gluten-free diet can affect the composition of the intestinal microflora in various ways, as shown by the evidence presented by us. For instance ketogenic diet in patients with refractory epilepsy may reduce the symptoms of the disease, which is associated with changes in the composition of gut microbiota.

Summary: Diet is a promising direction of development, due to being a factor which may improve the course of many diseases. However, despite the fact that many new studies have appeared in this field in the last decade, time is still needed to draw specific conclusions.

Keywords: microbiota, gut, diet, gluten-free-diet, ketogenic-diet

1. Introduction

Bacteria have been used for thousands of years in food and fuel production, drug discovery, the chemical industry, and human disease research. Little more than 1% of bacterial organisms can be cultured in laboratory conditions [1]. The intestinal microbiota has several beneficial functions related to host health. The intestinal microbiota contains up to 100 trillion bacteria and around 1000 species [2]. The ratio of host DNA vs. microbiome DNA is 1:10. There were several families of fungi, whose physiological role in the gastrointestinal system is still unclear [3,4]. Commensal bacteria works closely with human body by [5,6]:

- The degradation of nutrients,
- The growth and the differentiation of epithelial cells of the gut barrier,
- The maturation of our immune system,
- First line of defence against luminal antigens and pathogens,
- The colonization resistance and the eradication of pathogens,
- The elimination of xenobiotics,
- The local peristalsism.

Studies have shown that the microbiota influences intestinal barrier architecture, mucus layer and innate immune factors [7]. Intestinal dysbiosis have been associated with chronic inflammatory gastrointestinal conditions, such as inflammatory bowel disease and psychiatric or developmental disorders, such as autism spectrum disorders and mood disorders [8,9,10].

Major intestinal bacteria in the healthy adult gut are Firmicutes and Bacteroidetes, with less the microbiota made up of Actinobacteria, Proteobacteria, and Verrucomicrobia [11]. However, it is also possible to recognize the kingdom of Archaea and eukaryotes, and many viruses and bacteriophages [12,13].

2. Microbiota-gut-brain axis

Microbiota plays significant role in digestion, nutrient assimilation, vitamin production, and metabolism. It also affects host's appetite and food intake [14,15]. Bidirectional relation between gut microbiota and brain exists and is very important. In this complicated relationship the gut microbiota can affect the brain and vice versa [16]. Evidences suggest that there are four ways of communication between the gut microbiota and the brain [17,18]:

- Neuroanatomic pathway (autonomic nervous system),
- Immunological pathway,
- Neuroendocrine-HPA axis pathway,
- Neurotransmitters, neuropeptides, microbial-derived products.

Many studies confirm this. Studies using germ-free mice show that microbiota can positively impact stress responses through the hypothalamus-pituitary-adrenal axis. It includes decreased anxiety and increased exploratory behaviours [19,20]. Other studies show that giving probiotics to mice increase exploratory behaviour in rodents under varied conditions [14,21]. There are also studies which show that early life stress may result in change in composition of intestinal microbiota, which can be an evidence of the existence of a gut-brain axis [22]. Microbiota have a profound influence over the synthesis and metabolism of serotonin and regulating expression of γ -aminobutyric acid (GABA) receptors in hippocampus [23,24,25]. Moreover, it has a huge importance in production of γ -aminobutyric acid (GABA), acetylcholine, dopamine, norepinephrine [26,27,28].

3. Microbiota, diet and short-chain-fatty acids

We know that composition of gut microbiota has a huge impact on our health. Otherwise, our diet has a huge impact on our commensal gut bacteria. In mostly healthy individuals over 90% of diet is absorbed in the small intestine. The rest – carbohydrates (fiber), as well as protein residues and primary bile acids secreted by the liver in response to fat intake enter the colon [29]. The main end products of bacterial fermentation in colon are short-chain-fatty acids (SCFAs) - acetate, propionate, and butyrate and gases (H_2 , CO_2). SCFAs affect gastrointestinal epithelial cell integrity, glucose homeostasis, lipid metabolism, appetite regulation, and immune function. The most important product is butyrate, it acts as a favourable source for colonocytes with mucosal anti-inflammatory and antineoplastic properties through cell metabolism, microbiota homeostasis, anti-proliferation, immunomodulatory and epigenetic regulation [30]. Between 90 and 99% of SCFAs are absorbed in the gut or used by the microbiota [31]. Acetate reaches the highest concentration in plasma of all SCFAs, and it can cross the blood-brain barrier [32]. Acetate has been shown to reduce acute food intake, induce an anorectic neuropeptide expression profile, reduce hypothalamic AMPK catalytic activity [32].

Fiber and prebiotics intake modulate composition of gut microbiota [33]. Carbohydrates were divided into 3 groups by the Codex Alimentarius Commission in 2009 [34]. “Carbohydrate

polymers with ten or more monomeric units, which are neither digested nor absorbed in the human small intestine and belong to the following categories:

- edible carbohydrate polymers naturally occurring in foods as consumed,
- edible carbohydrate polymers which have been obtained from food raw materials by physical, enzymatic, or chemical means and which have a beneficial physiological effect demonstrated by generally accepted scientific evidence,
- edible synthetic carbohydrate polymers which have a beneficial physiological effect demonstrated by generally accepted scientific evidence.” [34].

However, in Australia, Brazil, Canada, China, Europe and New Zealand, the definitions of fiber includes nondigestible carbohydrates with greater than three monomeric units [35].

Several studies show that human microbion is relatively stable in adults, except in the case of special events such as diet intervention, infectious diarrhea or international immigration [36]. However, there are evidences that switching from a traditional African diet that is high in plant polysaccharides including fiber and low in fat and processed meat to a typical Western diet that is low in plant fiber and high in fat, processed meat and sugar, leads to a rapid shift in the composition and abundance of microbiome along with an increased Ki-67 index in colon tissues [29,37,38,]. The study conducted by Zimmer J, et al. in 2012 in which the effect of vegetarian and vegan diets on the amount of *Bacteroides* spp., *Bifidobacterium* spp., *Escherichia coli* and *Enterobacteriaceae* spp. was examined compared to controls, has shown that total counts of *Bacteroides* spp., *Bifidobacterium* spp., *Escherichia coli* and *Enterobacteriaceae* spp. were significantly lower in vegan samples than in controls, whereas others (*E. coli* biovars, *Klebsiella* spp., *Enterobacter* spp., other *Enterobacteriaceae*, *Enterococcus* spp., *Lactobacillus* spp., *Citrobacter* spp. and *Clostridium* spp.) were not. In this study subjects on a vegetarian diet ranked between vegans and controls [39]. In addition there was observed that subjects on a vegan or vegetarian diet showed lower stool pH than did controls [39]. Statistics induced that consumption of dietary fiber for African children is 14.2 g/d and for European children is 8.4 g/d [40]. De Filippo et al. in 2010 found that children from rural Africa were exclusively colonized by *Treponema* species, *Butyrivibrio*, *Prevotella* and *Xylanibacter* with increased utilization of cellulose and increased synthesis of SCFAs [40]. Another study shows that in rats, the addition of fiber resulted in increased cecal SCFA concentrations compared with control diets. It depends on the type of fiber used and also on the daily fiber intake [41]. Studies on pigs, whose are more similar to human than rats show that increased fiber intake, increased cecal concentration of SCFAs but not as much as in rats [42,43].

Nowadays one of most popular diet is ketogenic diet (KD). For instance, it is used for weight reduction in obesity and related metabolic disorders [44]. This diet permits a very low carbohydrate consumption - 5% to 10% of total caloric intake or below 50 g/d, as a mean to enhance ketones production [45]. This diet is based on increased usage of fat as the main source of energy [46]. In the result there is not enough glucose to both fat oxidation (oxaloacetate in tricarboxylic acid cycle TCA) and energy required for the central nervous system [47]. In one study on mice conducted by Ma, et al. increase level of beneficial bacteria such as *Akkermansia muciniphila* and *Lactobacillus*, SCFA producers, and reduction of pro-inflammatory taxa such as *Desulfovibrio* and *Turicibacter* compared to controls were observed [48]. A study in children with refractory epilepsy after a week of KD showed

increased level of Bacteroidetes and decreased level of Proteobacteria [49]. It also significantly modified symptoms of epilepsy [49]. In another study also in children with refractory epilepsy after 6-months of KD was observed decreased level of Firmicutes and increased level of Bacteroidetes [50]. In addition, reduced intestinal microflora diversity has also been observed. However, not all patients responded by reducing the symptoms of epilepsy. Clostridiales, Ruminococcaceae, Rikenellaceae, Lachnospiraceae and Alistipes were enriched in non-KD responders compared to effective patients [50].

Another popular – gluten free diet (GFD) also may have impact on composition of gut microbiota. This type of diet is usually studied for the effects on celiac disease. In patients with celiac disease on gluten free diet Nistal, et al. found a decrease in Streptococcus and Prevotella levels [51]. However, Di Cagno, et al., reported decrease of healthy bacteria such as Lactobacillus, Enterococcus, and Bifidobacteria and increase of detrimental species such as Bacteroides, Staphylococcus, Salmonella, Shigella, and Klebsiella in 19 children with celiac disease on GFD [52]. Another study conducted by Di Cagno, et al. described that a lower ratio of Bifidobacterium to Bacteroides and Enterobacteria (including E. coli), characteristic of celiac disease patients before diet, still persist under a GFD, which may confirm that GFD only partially restores the imbalance of the intestinal microflora [53].

4. Summary

Nowadays, we are still investigating how the gut microbiota affects our body. There are evidence that using probiotics or prebiotics may have beneficial effect on several psychiatric and developmental disorders, such as autism spectrum disorders or mood disorders. There are also studies, which confirmed that composition of gut microbiota may affect the course of diseases, such as celiac disease, irritable bowel syndrome, diabetes or even colorectal cancer. This is a promising direction of development, but more research is still needed to draw conclusions.

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