MINIREVIEWS

Effects of a high fat diet on intestinal microbiota and gastrointestinal diseases

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Abstract

Along with the rapid development of society, lifestyles and diets have gradually changed. Due to overwhelming material abundance, high fat, high sugar and high protein diets are common. Numerous studies have determined that diet and its impact on gut microbiota are closely related to obesity and metabolic diseases. Different dietary components affect gut microbiota, thus impacting gastrointestinal disease occurrence and development. A large number of related studies are progressing rapidly. Gut microbiota may be an important intermediate link, causing gastrointestinal diseases under the influence of changes in diet and genetic predisposition. To promote healthy gut microbiota and to prevent and cure gastrointestinal diseases, diets should be improved and supplemented with probiotics.

Key words: Intestinal microbiota; Gastrointestinal diseases; High fat diet

Core tip: Along with the rapid development of society, lifestyles and diets have gradually changed. Due to overwhelming material abundance, high fat, high sugar and high protein diets are common. Numerous studies have determined that diet and its impact on gut microbiota are closely related to obesity and metabolic diseases. Different dietary components affect gut microbiota, thus impacting gastrointestinal disease occurrence and development. A large number of related studies are progressing rapidly. In this review, we summarize the relationship between a high fat diet, gut microbiota and gastrointestinal diseases.

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INTRODUCTION

Along with the rapid development of society, lifestyles and diets have gradually changed. Due to overwhelming material abundance, high fat, high sugar and high protein diets are common. Numerous studies have determined that diet and its impact on gut microbiota are closely related to obesity and metabolic diseases[1]. Different dietary components affect gut microbiota, thus impacting gastrointestinal disease occurrence and development. A large number of related studies are progressing rapidly. In this review, we summarize the relationship between a high fat diet, gut microbiota and gastrointestinal diseases.

BASIC COMPOSITION OF INTESTINAL MICROBIOTA

The intestinal tract is the primary site of bacterial colonization in the human body. These complex and diverse bacteria form the gut flora. There are more than 1000 bacterial species in the human gut and this number can reach as high as 1×10^8 species. The intestinal flora is primarily composed of anaerobes, facultative anaerobes and aerobes. Anaerobes comprise more than 99% of gut microbes. The intestinal flora of the human body primarily includes Firmicutes, Bacteroidetes, Actinomycetes, Proteobacteria, Verrucomicrobia and Archaebacteria. More than 90% are Firmicutes or Bacteroidetes. The Firmicutes, Bacteroidetes, Proteobacteria and Actinomycetes comprise 64%, 23%, 8% and 3% of the gut microbiota, respectively[2]. The intestinal flora of the human body is established in infancy and gradually stabilizes with age. By approximately 2 years of age, it is similar to the adult intestinal flora[3]. The intestinal flora composition differs by age group. The proportion of Firmicutes and Bacteroidetes in infants, adults and the elderly is 0.4, 0.9 and 0.6, respectively[4].

EFFECT OF A HIGH FAT DIET ON INTESTINAL MICROBIOTA

Diet is an important factor determining intestinal flora composition. It plays a critical role in the colonization, maturation and stability of the intestinal flora. Both animal and human experiments have demonstrated that dietary changes can rapidly affect intestinal flora structure. Within 4 d of eating a specific dietary component, the human intestinal flora composition will change significantly[1,5].

Animal experiments have indicated that dietary structure affects intestinal flora. The proportion of Bacteroidetes decreased and the proportion of Firmicutes increased, which increased the proportion of Mollicutes in the intestinal tracts of mice fed a high fat and high sugar diet compared with mice fed a low fat and high sugar diet[6]. Intestinal flora diversity is reduced in mice fed a high fat and high sugar diet. However, control diet consumption gradually reversed these changes. Furthermore, one study investigated varying proportions of dietary fatty acids in mice for 8 wk. A diet high in saturated fatty acids led to an increased proportion of intestinal Firmicutes and decreased intestinal flora diversity[7]. This study suggests that dietary fats and saturated fatty acid intake may affect intestinal flora composition. One study found that converting a low sugar, low fat diet to a high sugar, high fat diet caused a rapid decline in the number of Bacteroidetes in the intestines[8]. Another study also suggested that the number of *Bacillus bifidus* was reduced in mice fed a high fat diet[9]. Animal studies have demonstrated a significant reduction in the number of lactic acid bacteria, *Bacillus bifidus* and *Enterococcus* in the intestinal tract of the group fed a high fat diet. Furthermore, the phylum Bacteroidetes displayed a decreasing trend, while the *Bacillus fusiformis* displayed an increasing trend[10,11].

Human experiments have also demonstrated that dietary composition affects intestinal flora. Compared with Italian children who consume a large amount of plant protein, fat, sugar and starch, the proportion of Bacteroidetes in the intestinal flora of African children was high, while the proportion of Firmicutes was low[12] (Table 1).

RELATIONSHIP BETWEEN INTESTINAL MICROBIOTA AND GASTROINTESTINAL DISEASES

The composition and proportion of gut microbiota are closely related to human health. Upsetting the gut microbiota equilibrium can cause enteric dysbacteriosis and a variety of gastrointestinal and systemic diseases[13].

Intestinal microbiota and inflammatory bowel disease

Inflammatory bowel disease (IBD) comprises a group of inflammatory conditions of the colon and small intestine, including Crohn's disease (CD) and ulcerative colitis (UC), the cause and pathogeny of which are not completely understood. Gut microbiota are closely related to IBD occurrence and development. Although the specific bacteria involved in IBD have not been identified, the gut microbiota in patients with IBD differs from those of healthy individuals. One study[14] determined that the total number of mucosa-associated bacteria in the IBD group was higher than that in the control group. In the CD group, *Streptococcus* was dominant in the inflammatory mucosal region, while in the UC group, lactic acid *Bacillus* was dominant. Studies have demonstrated that the number of *Faecalibacterium prausnitzii* decreased in patients with CD[15]. Their secretory products have immune regulatory activity *in vitro*[16]. IBD pathogenesis includes intestinal flora imbalance,

Table 1 Effect of a high fat diet on intestinal microbiota

Diet	Intestinal flora	Animal experiments	Human experiments
High fat diet	Bacteroidetes	Decreased	Decreased
	Firmicutes	Increased	Increased
Low fat diet	Bacteroidetes	Increased	Increased
	Firmicutes	Decreased	Decreased

increased pathogenic bacteria, toxin damage to the intestinal epithelium, immune function abnormalities and immune tolerance imbalance. Intestinal bacteria can induce epithelial endoplasmic reticulum stress, leading to intestinal mucosal barrier damage and increased intestinal permeability. Probiotic supplements in patients with IBD can effectively alleviate symptoms and delay disease progress[17,18].

Intestinal microbiota and irritable bowel syndrome

Irritable bowel syndrome (IBS), affecting approximately 5%-25% of the population, comprises a group of symptoms, including abdominal pain and changes in bowel movement patterns, without any evidence of underlying damage. The mechanisms of IBS are unclear. One study found that 3%-36% of intestinal infections can cause persistent symptoms of IBS, which suggests that gut microbiota play an important role in IBS onset[19]. Intestinal flora may affect gastrointestinal motility, visceral sensitivity, the inflammatory response and the brain-gut axis, which leads to IBS. A number of studies have confirmed that the intestinal flora of patients with IBS differs from that of healthy individuals[20,21]. At present, however, intestinal flora composition results in patients with IBS have been inconsistent and some have been contradictory. These inconsistencies may be owing to differences in specimen collection, molecular detection methods or definitions of IBS[22]. The majority of studies have found that the Bacteroidetes are reduced, while the Firmicutes are increased in the intestinal flora of patients with IBS. However, it is not yet determined whether the changes in intestinal flora directly cause or are secondary to IBS. In the future, treatment of the intestinal flora imbalance may become an option for patients with IBS[23].

Intestinal microbiota and tumors

Colorectal cancer is a common gastrointestinal tumor, the incidence and mortality rates of which are increasing each year. Most colorectal cancers are due to old age, lifestyle factors and underlying genetic disorders. Additionally, changes in the gut microbiota are closely related to colorectal cancer occurrence and development[24]. Many studies have detected imbalances in the gut microbiota of patients with colorectal cancer, while those of healthy individuals are in equilibrium. Furthermore, some reports have suggested that changes in the gut microbiota can cause cancer directly. However, it is unclear which species of bacteria play a primary role in causing cancer[25-27]. There are two theories regarding the pathogenesis of colorectal cancer associated with intestinal flora. First, some intestinal bacteria may either directly or indirectly affect intestinal epithelial cells, causing genetic mutations. These bacteria are defined as "Alpha-bugs"[28]. Their direct effects include secreting toxic proteins and the indirect effects include changes in intestinal flora that are more likely to cause mucosal immune responses and changes in colonic epithelial cells. When gene mutations accumulate, it can lead to colorectal cancer. The second theory is named the "driver-passenger" model[29]. Following colorectal cancer incidence, primary pathogens (defined as "drivers") are replaced by opportunistic pathogens (defined as "passengers"), which are more viable in the intestinal tumor microenvironment. Possible mechanisms of intestinal flora-induced colon cancer are summarized as follows: (1) the carcinogen precursor is absorbed by the stomach, then secreted into the intestinal cavity by the liver and the active ingredient is released by intestinal flora activity; (2) the carcinogen precursor in food is released by intestinal flora activity; and (3) metabolites produced by intestinal flora induce carcinogenic effects. Many studies have explored the role of probiotics in colon cancer prevention[30]; however, there is not yet a consensus.

Intestinal microbiota and liver disease

The intestinal blood flows through the portal vein system to return to the liver. The liver affects intestinal function by secreting bile into the enterohepatic circulation. The physiological link between the two organ systems is called the "intestine-liver axis". Studies have indicated that changes in intestinal flora play an important role in liver disease incidence and progression[31]. Intestinal probiotics can improve liver disease and are now widely used in its clinical treatment[32]. Nonalcoholic fatty liver disease (NFALD) is one of the most rapidly growing chronic liver diseases. A number of studies have indicated that intestinal flora play an important role in NFALD development[33]. Bacterial overgrowth and intestinal permeability are the primary mechanisms underlying endotoxemia and inflammatory reaction-initiated liver disease. One study confirmed the relationship between intestinal bacterial overgrowth and NFALD[34]. In another study, the relationship between intestinal permeability and NFALD was demonstrated in animal experiments[35]. Alcoholic fatty liver was also associated with gut-derived endotoxemia. Specifically, ethanol intake in the intestinal tract may cause intestinal mucosal injury and intestinal flora disorder, resulting in increased endotoxin-induced intestinal epithelial permeability, bacterial translocation and endotoxemia[36]. The intestinal flora in patients with liver cirrhosis is dramatically disordered. One study demonstrated

a significant decrease in *Bacillus bifidus* and lactic acid *Bacillus* in the intestinal tract of patients with liver cirrhosis, suggesting the possibility of intestinal bacterial translocation and increased infection[37]. The occurrence of primary hepatocellular carcinoma is also associated with intestinal flora imbalance[38].

CONCLUSION

In summary, gut microbiota may be an important intermediate link, causing gastrointestinal diseases under the influence of changes in diet and genetic predisposition. A diet that is high in fat, especially high in saturated and trans fat, is closely related to obesity, metabolic syndrome and gastrointestinal diseases; polyunsaturated fats such as omega-3, omega-6 and omega-9 in right proportions are suggested as substitutes. To promote healthy gut microbiota and to prevent and cure gastrointestinal diseases, diets should be improved with low fat, low sugar, high fruit and vegetable intake and complex fibers and supplemented with probiotics or increased fermented dairy product consumption, such as yogurt and buttermilk. It is essential for patients with GI diseases to not only change their dietary composition, but also to establish a healthy eating habit and pattern to promote healthy microbiota as well as to alleviate disease-associated syndromes. Maintenance of normal gut microbiota may be a potentially key means of preventing GI diseases in the future.

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