

The Gut Microbiota, Obesity and the Effect of Dietary Modulation and Bariatric Surgery on the Microbiome: A Review of the Literature

Shaneeta Johnson¹, Kayellen Umeakunne², Carolyn Moore³, Ayana Worthey⁴, Samy Bendjemil⁵, Ed Childs¹, Larry Hobson¹ and Omar Danner^{1*}

¹*Department of Surgery, Morehouse School of Medicine, Georgia*

²*Clinical Research Center, Morehouse School of Medicine, Georgia*

³*Department of Thoracic Surgery, Brigham and Women's Hospital, Massachusetts, USA*

⁴*Augusta University Medical Center, Georgia*

⁵*Department of Surgery, Rush University, USA*

***Corresponding Author:** Omar Danner, Department of Surgery, Morehouse School of Medicine, Georgia.

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Abstract

The role of the gut microbiome has become the subject of increased interest in the development of chronic metabolic and autoimmune diseases and disorders. Distinctive changes in the gut microbiome have been associated with obesity. Furthermore, dietary modulation and bariatric surgery have been shown to have a significant modulating effect on the constitution of the gut microbiome. The purpose of this review is to explore the importance and relevance of these changes in the gut microbiota and their potential causal relationship with obesity and the development of disease in humans. Further studies are needed to determine the full impact of dietary changes and weight loss after obesity surgery on the gut microbiome and disease development.

Keywords: Gut Microbiota; Gut Microbiome; Obesity; Bariatric Surgery; Dietary Modulation

Introduction

The gut microbiota is a complex community of microbial organisms that live in the gastrointestinal tracts of humans and non-human animals, as well as insects [1]. In man, the gut microbiome has the greatest amount of bacteria and the largest number of species of microbes compared to other areas of the body [2]. In humans, the gut flora is established in the first one to two years of life. It develops in conjunction with the intestinal epithelium in a manner that also provides a barrier to pathogenic microorganisms [3,4]. The composition of the microbiota of the human gut changes over time, particularly when the diet changes, and as the overall health changes [2,5]. Furthermore, the microbial composition of the gut microbiota varies across the digestive tract. In the stomach and small intestine, there are relatively few species of bacteria typically present [6,7]. However, the colon, in contrast, contains a densely-populated microbial bionetwork with over 10¹² cells per gram of intestinal content, which represent between 300 and 1000 different bacterial species [6,7]. Nevertheless, 99% of the bacteria originate from about 30 or 40 species [8].

Based on their abundance in the intestine, up to 60% of the dry mass of feces is made up of bacteria with over 99% of the bacterial microorganisms in the gut being anaerobes [9]. The four dominant bacterial phyla in the human gut are *Firmicutes*, *Bacteroidetes*, *Actinobacteria* and *Proteobacteria* [10]. Most bacteria belong to the genera *Bacteroides*, *Clostridium*, *Faecalibacterium* [6,8], *Eubacterim*, *Rumminococcus*, *Peptococcus*, *Peptostreptococcus* and *Bifidobacterium* [6,8]. Other genera, such as *Escherichia* and *Lactobacillus*, are present to a lesser

extent [6]. Species from the genus *Bacteroides* principally constitute approximately 30% of all bacteria in the gastrointestinal tract, which suggests that this is the most important genus in the proper functioning gut of the healthy host [7]. When a person becomes obese, the composition of the gut flora is in some way gets altered.

Obesity is a state of chronic low-grade inflammation. It is characterized by an increased percentage of total body fat compared to the lean mass above a certain level based on population-based norms. Furthermore, it can be defined as a body mass index greater than or equal to 30 kg/m². Use of 16S rRNA gene sequencing has shown that the gut microbiota in obese individuals is distinctly different from that of lean individuals. Studies in lean and obese twins have been shown to demonstrate that obesity is associated with decreased microbiologic diversity, increased *Firmicutes*: *Bacteroidetes* ratio, and insulin resistance [11,12].

The role of the gut microbiota in obesity-associated inflammation has become the subject of increasing interest in the study of chronic metabolic conditions as well as autoimmune diseases and disorders. Alterations in the gut microbiota have been attributed to enhanced gut permeability to pathogenic bacteria through loss of mucosal barrier protective microbes, such as *Bifidobacterium* with resultant dysbiosis. Elevated levels of gram-negative gut bacterial derived lipopolysaccharide (LPS) are also associated with inflammation. LPS induces low grade inflammation by triggering innate immune system responses. LPS binds to toll-like receptor 4 (TLR4), leading to a cascade of responses including production of pro-inflammatory mediators that interfere with the modulation of glucose and insulin metabolism [13].

Interestingly, weight loss resulting from a fat or carbohydrate modified or restricted diet has been shown to reduce the *Firmicutes*: *Bacteroidetes* ratio in obese persons [14]. The effect of this reduction in *Firmicutes*: *Bacteroidetes* ratio is just beginning to be better understood. In this review, we explore the sequelae of alterations and manipulation of the gut microbiota and the potential impact of bariatric surgery as a treatment of obesity on the gut microenvironment.

Methods

We researched the major public research databases, including PubMed, Cochrane, Medline, and Ovid for articles related to the study of the gut microbiome and its relationship with obesity. A search was performed using the keywords of obesity and gut micro biome and gut microbiota. Articles were selected and reviewed to determine trends and associations in obesity and gut microbiota.

Results

There were 3019 articles found via Pubmed. There were 54 articles which were excluded that were foreign language articles. Articles were evaluated for relevance to obesity, cardiovascular inflammation, microbiome, and microbiota. We identified the most pertinent 29 articles related to obesity and this subject matter.

Discussion

The role of the diet in gut microbiota profiles has gained increased attention over the last decade. It has been realized that one's diet plays an important part in defining the type of bacteria in the colon of individuals and the effect the microorganisms elicit on the host. Studies of microbiota from high fat fed animals show a decrease in *Bacteroidetes*, for instance, and an increase in *Firmicutes* in response to a high-fat diet.

The resultant increased energy harvest by gut microbiota has been shown to lead to enhanced expression of lipogenic genes in hepatic, muscle and adipose tissue and ultimately obesity [15]. Factors that translate diet into an obese state involve a complex interplay between gut microbiota and host physiological systems, including modulation of the immune system and endocrine system, energy homeostasis and lipid metabolism. One particular interest is dietary fiber, which is known to modulate microbial profiles and fermentation products like short-chain fatty acids (SCFAs) and has a regulatory role in human energy homeostasis.

The SCFAs acetate, propionate and butyrate help to regulate both energy metabolism and body composition. Butyrate is the primary energy source of colonocytes and plays a role in epigenetic control of gene expression through inhibition of histone deacetylase. Thereby, it influences the modification of DNA methylation [16]. Butyrate acts to prevent obesity by promoting energy expenditure and inducing mitochondrial function through molecular mechanisms involving stimulation of peroxisome proliferator-activated receptor (PPAR) coactivator (PGC-1 α) activity. Acetate is the principle substrate used for hepatic cholesterol biosynthesis and the ratio of acetate/propionate produced from carbohydrate fermentation in the colon plays a critical role in the regulation of lipid and cholesterol metabolism.

Oligosaccharides, on the other hand, like those found with an increased legume intake, as well as soluble fibers stimulate the growth of beneficial bacteria which generate SCFAs with anti-inflammatory effects like butyrate, through the binding of SCFAs to SCFA receptors on leukocytes thus promoting a healthy immune system. Recent research suggests that low carbohydrate, animal-based, high protein diets alter the gut microbiota diversity causing a shift from carbohydrate fermentation to protein fermentation, the byproducts of which result in inflammation, increasing chronic disease and cancer risk [17]. Animal protein also contains higher amounts of amino acids, which is associated with increased insulin resistance [18].

However, plant-based proteins contain a different constitution of amino acids including specific amino acids such as arginine, which are important for antioxidant maintenance. In addition, plant sources of protein contain resistant starch, dietary fiber, flavonoids, phytochemicals, folate and ascorbate which have been shown to promote a healthier gut microbiota by inhibiting the growth of potential pathogens [19]. Plant proteins provide lower intakes of saturated fat and are devoid of cholesterol when compared with animal protein. This may provide protection against the development of coronary artery disease. Finally, plant-based diets have been shown to reverse diabetes and may also reduce hypertension, cholesterol and other diet-related medical conditions [20]. Plant-based protein powders have been improved to contain amino acid profiles that support the retention of muscle mass. The effect of plant-based diets includes prebiotics, fiber, and phytochemicals which we propose would reduce inflammation and improve insulin sensitivity through modulation of the gut microbiota to produce butyrate and other beneficial bioactive compounds compared with an animal-based diet based on the available literature.

The study of the effect of bariatric surgery (BS) on the gut microbiota has similarly gained increased attention over the past few years. Bariatric surgery has emerged as a safe treatment for obese patients with a BMI of ≥ 40 kg/m² or ≥ 35 kg/m² with comorbid diseases. Bariatric surgery has been associated with significant improvements in obesity-related medical conditions including diabetes, hypertension, sleep apnea, and cardiovascular risk factors [21,22]. Current data suggests there are significantly more women than men seeking bariatric surgery nationally as well as in our local community. Prior to embarking upon bariatric surgery, most morbidly obese patients undergo a comprehensive workup, which includes monthly nutrition counseling, periodic psychological counseling, metabolic labs, other medical assessments including endoscopy, completion of a bariatric surgery orientation seminar and attend a bariatric surgery support group. Patients are often expected to lose approximately 5% of their body weight preoperatively to reduce the size of the fat deposits within the liver. To accomplish this, patients are frequently placed on a high-protein, low carbohydrate diet. The typical high protein source is lean animal-based meals supplemented with whey or casein-based protein shakes and powders. In addition, patients are encouraged to adopt an exercise regimen of at least 150 minutes of moderate to high-intensity exercise per week. Studies have shown that patients who demonstrate greater compliance with this type of preoperative diet, behavioral modification, and exercise regimen have greater rates of successful weight loss [23].

Bariatric surgery has been proven to be effective in helping qualified and appropriately selected individuals achieve clinically significant weight loss, reverses metabolic risk factors and improves diabetes in part through its modulation of gut peptides. Changes in gut microbiota following gastric bypass (RYGB) surgery have been revealed to increase *Gamma proteobacteria* and decrease in *Clostridia* in the gut microflora. *Verrucomicrobia* has also been exhibited to be present in obese as well as normal weight individuals following RYGB [24]. Furthermore, in one study comparing the *Bacteroides/Prevotella* group prior to surgery and following bariatric surgery in 30 obese

individuals, analysis showed an increase ratio corresponding to the same level in lean controls. Additionally, levels of *Faecalibacterium prausnitzii* in obese patients increased following RYGB, which negatively correlated with serum concentrations of inflammatory markers, such as C-reactive protein and interleukin-6, suggesting an anti-inflammatory role for these bacteria [25]. These changes suggest the gut microbiota plays an integral role in weight loss, and reduced adiposity following RYGB surgery, which may help to explain the benefit of obesity surgery in the resolution of the multiple chronic metabolic conditions, including type II diabetes, hypertension, and atherosclerotic disease [26-35].

Conclusion

There are distinctive changes in the gut microbiome associated with obesity. Additionally, dietary modulation and bariatric surgery have a significant effect on the constitution of the gut microbiome. Further studies are needed to determine the full significance of these changes and whether there is a causal relationship with obesity.

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