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Mini Review

Obesity, Overweight, and the Microbiome

Álvaro Zamudio Tiburcio[1]*, Nydia Ávila Vanzzini[2], Silverio Alonso López[3] and María Magdalena Aguirre-García[4]

[1]Gastroenterologist, Intestinal Microbiota Transplantation, Pennsylvania, Naples Neighborhood, ZIP City Hall Benito Juárez, (Medical Specialties Naples), Mexico City, Mexico

[2]Physician of the Department of Outpatient Care, National Institute of Cardiology Ignacio Chávez, Mexico City, Mexico

[3]Urologist, Chairman Medical Specialties, Naples neighborhood, Mexico City, Mexico

[4]Unidad de Investigación UNAM-INC, División de Investigación, Facultad deMedicina, Instituto Nacional de Cardiología Ignacio Chávez, Ciudad de México, México

***Corresponding Author:** Álvaro Zamudio Tiburcio, Gastroenterologist, Intestinal Microbiota Transplantation, Pennsylvania, Naples neighborhood, ZIP City Hall Benito Juárez, (Medical Specialties Naples), Mexico City, Mexico.

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Abstract

Overweight and obesity, among the most common diseases in the world, contribute to other pathological conditions including cardiovascular disease, cancer, and metabolic syndrome. Excess corporal fat results from an imbalance between energy intake and expenditure, which involves diet and exercise as well as the possible participation of genetics and environmental factors. Overweight and obesity produce changes in the gut microbiota because of altering intestinal permeability (endo-toxemia), stimulating the endocannabinoid system, and increasing the provision of calories. All these alterations must be considered in a treatment strategy to return a patient to homeostasis. The aim of the present study was to analyze the gut microbiota in relation to overweight and obesity in order to explore strategies to reduce excess fat by restoring microbiota homeostasis. Such strategies have the potential not only of improving the health of individuals, but also of enabling enormous savings in the health care system. .

Keywords: *COVID-19 Pandemic; SARS-CoV-2 Infection; Safety Management; Surgery*

Introduction

Mexico assumed second place among all nations in overweight and obesity for adults and fourth place for children in 2015 [1]. In 2016, 39% of adults in the world were overweight or obese [2]. Today, approximately 300 million people are afflicted with morbid obesity, which contributes to other pathological conditions including cardiovascular disease, cancer, and metabolic syndrome [3,4].

Overweight and obesity result from various factors, especially an imbalance between energy intake and expenditure that involves diet and exercise [5]. Genetics and environmental factors may play an important role as well. Such factors must be considered in a treatment strategy to return an individual to homeostasis [6]. The aim of the current contribution was to analyze the gut microbiota in relation to overweight and obesity in order to explore strategies to reduce excess fat by restoring microbiota homeostasis [7].

The human microbiome consists of all the microorganisms in the body [8], including bacteria, viruses, fungi, archaea, eukaryotes, and protozoa. It encompasses more than one hundred trillion microorganisms, thus representing a ten-fold greater quantity than the cells of the human body. The most abundant populations are found in the intestine (colon, rectum, and small intestine), followed by the skin, airways, vagina, oral cavity, urinary tract, ears, nose, and throat. The human intestinal microbiota all microorganisms that coexist symbiotically in the colon, rectum and small intestine, among which are about 1000 bacterial species containing 100 times more genes than the entire human genome [9]. The functions of these species are listed in table 1 [10]. Apart from the diversity of microorganisms and their function, the microbiome has additional complexity due to the oscillations in the composition and functional activity of each microbiota in a 24-hour period [11].

Function number	Specific function
1	Absorbs and produces vitamins
2	Regulates the immune system and metabolism
3	Helps assimilate nutrients
4	Contributes to neurological function through the gut-brain axis, producing serotonin and enzymes
5	Confers resistance during inflammatory processes
6	Digests certain compounds in food
7	Avoids mucosal and skin diseases caused by opportunistic pathogens
8	Participates in endocrine functions
9	Prevents the development of neoplasms
10	Maintains intestinal balance
11	Keeps the gut barrier intact
12	Augments the ability to digest carbohydrates
13	Furnishes resistance to infections
14	Produces substrates and anti-inflammatory agents
15	Provides substrates for enterocytes, preventing opportunistic pathogenic diseases
16	Protects life
17	Regulates energy balance
18	Offers resistance to colonization by pathobionts

***Table 1:** Functions of the microbiome.*

The intestinal microbiota contains the largest number of pathogenic bacteria, some of which are associated with overweight, obesity, arthritis, inflammatory bowel disease, autism spectrum disorder, anxiety, depression, and stress [12]. Over a thousand different species of microorganisms in the intestine [13] play a key role in the maintenance of host homeostasis [14]. The main bacteria in the intestine correspond to the families *Bacteroidetes*, *Firmicutes*, *Proteobacteria*, and *Actinobacteria*. The relative proportion of intestinal bacteria varies from one country to another [15] and is affected by diet, antibiotics, and environmental toxins [16].

Sequencing technologies and large-scale sequence-based microbiome projects (e.g., the Human Microbiome Project consortium and the Metagenomics of the Human Intestinal Tract) have facilitated and promoted human microbiome research [17]. Nevertheless, there is as yet no catalogue of all the genomes of microorganisms that make up the intestinal microbiota. Putting together such a catalogue would greatly assist the acquisition of new knowledge in the field. An interesting compilation of a total of 286,997 genome sequences is currently available [18]. Moreover, King., *et al.* proposed a list of 157 microorganisms, plus 863 closely related proteomes [19].

Microbiota function and dysbiosis

Dysbiosis can be generated by host or external factors, the latter including stress, a diet low in residues and high in meat content, the intake of antibiotics and certain oncological drugs, and the lack of metabolism of short chain fatty acids. This disruption of microbiota homeostasis is sometimes capable of triggering disease, as reported in the case of *Helicobacter pylori* and gastric cancer [20].

Microorganisms sent to the fetus by placental circulation play a pivotal role in the later composition of the intestinal microbiota [21], which stabilizes at around three years of age. Subsequently, the microbiota may be involved in the development of cognitive impairment, anxiety, and other alterations through the gut-brain axis [22].

Obesity and the intestinal microbiota

The gut microbiota participates in the pathogenesis of obesity by altering intestinal permeability (endo-toxemia), stimulating the endocannabinoid system, and elevating the provision of calories [23]. Obese individuals have a higher proportion of anaerobic genera, mainly *Veillonella*, *Bulleidia* and *Oribacterium* [24]. They usually exhibit low-grade chronic inflammation, which can be detected by quantifying lipopolysaccharides. Gut Microbiome are capable of altering the level of fasting-induced adipose factor and inhibitors of lipoprotein and lipase activity, thus leading to an accumulation of triglycerides in adipocytes [25].

Besides altering insulin signaling, type 2 diabetes mellitus exacerbates morbid obesity by increasing the level of adipokines, the resistance to insulin, and the synthesis of pro-inflammatory cytokines. Curiously, type 2 diabetes is to a great extent determined by the intestinal microbiota [26].

Next-generation sequencing has demonstrated differences in the intestinal microbiota between non-obese and obese subjects, and a higher ratio of *Firmicutes*/*Bacteroidetes* with obesity [27]. The typical Western diet, with elevated levels of sugar and fat, favors an abundance of the aforementioned organisms [28].

Obesity, diet and surgery

Certain diets are capable of causing a reduction of excess fat in overweight and obese individuals and/or diminishing the symptoms of diabetes. For instance, the 1500 kcal per day diet supplemented with 50g of cheese and *Lactobacillus plantarum* is able to significantly decrease the body mass index of people with obesity and arterial hypertension [29]. However, the regimen for treating the condition of excess fat should not be strictly dietary but rather multidisciplinary. Taking all possible measures into account tends to enhance the effectiveness of the treatment and the duration of the positive outcome.

Following anastomosis-mini gastric bypass, obese patients are reported to show better results when consuming probiotic supplements for 4 weeks prior to surgery and 12 weeks afterwards. This has led to substantially greater efficiency in weight loss, lower levels of body fat, higher levels of vitamin D, and reduced inflammation [30]. Furthermore, there is better composition in the gut microbiota with post-biotics, para-probiotics, a ketogenic diet, and phage therapy, as well as with intestinal microbiota transplantation and the targeting of the complement system [31].

An imbalance in the gut microbiota is associated with inflammatory infections and many diseases [32]. Apart from obesity, they include *Clostridiodes difficile* infection, inflammatory bowel disease, autoimmune disorders, colorectal cancer, celiac disease, and autism spectrum disorder [33]. Among the factors capable of triggering dysbiosis are obesity, stress, and smoking, which are all risk factors for cancer [34]. Probiotics, prebiotics, symbiotics, and intestinal microbiota transplantation are able to reverse intestinal dysbiosis and thus impede or halt the development of various diseases [35].

Morbid obesity can be treated with intestinal microbiota transplantation at a lower cost and with less morbidity than bypasses. For a patient that has already undergone a bypass, probiotics, prebiotics, or symbiotics along with exercise is recommended to continue to control weight by modulating the intestinal microbiota. Of course, the indications of the FDA must be considered when performing intestinal microbiota transplantation [36].

Probiotics

According to the World Health Organization, probiotics are "live microorganisms that, when administered in adequate amounts, confer a benefit to the health of the host". The most commonly used probiotics are normal components of the intestinal microbiota: *Lactobacilli*, *Bifidobacteria* and *Streptococci* [37]. While yogurt is the most common carrier of probiotics, cheese, juices, fermented and unfermented milk, and infant formula may potentially contain probiotics. With the intake of probiotics, a decrease in polyunsaturated fatty acids has been observed, which is usually beneficial for people with overweight or obesity. Probiotics lessen the symptoms of type 1 diabetes in obese mice [38].

In one study, overweight adults received *Bifidobacterium breve* B-3 (5 x 1010 CFU per day) for 12 weeks. The measurement of metabolic parameters and adiposity showed a reduction in fat mass and inflammation and an improvement in liver function. A similar outcome was found with *Lactobacillus rhamnosus* DSMZ 21690 and *L. acidophillus*. A meta-analysis revealed that the use of Vivomixx® led to significantly lower weight. The administration of *L. gasseri* SBT2055 to experimental animals resulted in the prevention of influenza and weight loss [39]. In short, numerous reports refer to beneficial effects of probiotics in overweight or obese individuals.

Prebiotics

Prebiotics are compounds in food not digested by the host that are capable of selectively favoring the generation of microorganisms in the intestinal microbiota. In addition to indigestible oligosaccharides, inulin, lactulose and resistant starch can act as prebiotics. Although inulin is present in many foods, it is necessary to consume at least 4 - 8 grams per day of fructo-oligosaccharides to enhance the amount of *Bifidobacteria* [40].

Symbiotic

The combination of a probiotic and prebiotic, denominated a symbiotic, induces better effects on the intestinal microbiota than probiotics or prebiotics alone. Yogurt with *Streptococcus thermophiles* and *Lactobacillus bulgaricus* plus inulin decreases abdominal girth. The level of *Lactobacillus* and *Bifidobacterium* (beneficial in obesity) increases and that of *Clostridium perfringens* decreases when using symbiotic [41].

If symbiotic are recommended by the physician attending an overweight or obese patient, they should be taken frequently. If the ketogenic diet (reduced fat and carbohydrates) is suitable for an overweight or obese individual, it will be more helpful (accompanied by exercise in accordance with age) than probiotics, prebiotics or symbiotic. The intake of postbiotic and para-probiotics also improves the condition of excess body fat.

Fecal microbiota transplantation

A clinical trial found a significant improvement in insulin sensitivity after fecal microbiota transplantation. The same occurs in the presence of a greater diversity of intestinal bacteria. Obesity-resistant, germ-free mice increase energy and calorie absorption upon undergoing fecal microbiota transplantation [42], as evidenced by multiple studies.

The recent advances in the analysis of bacteriophages (viruses) has afforded new opportunities in the application of intestinal microbiota transplantation, which provides a notable improvement in the modulation of immune homeostasis by the regulation of the intestinal microbiota. Sequencing of bacteria has been an integral part of efforts to counter the effects of antibiotic resistance and endotoxins. Of course, the technical difficulties of virome sequencing will have to be resolved. A large gap still exists in the sequencing technology for eukaryotes versus viruses and the phage community. Finally, further research is needed to better understand the mechanism of action as well as the therapeutic and adverse effects of intestinal microbiota transplantation [43].

Conclusion

Dysbiosis is caused by many factors such as stress, diet, medications, and metabolic disorders. Overweight and obesity is linked to an imbalance in the intestinal microbiota. Different treatments are capable of positively or negatively affecting the microbiota and therefore of generating disease or recovery of homeostasis in the human organism. Many studies have found that diet, probiotics, prebiotics, symbionts, intestinal microbiota transplantation, and fecal microbiota transplantation can help overweight and obese patients significantly reduce excess body fat.

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Conflicts of Interest

The authors declare that they do not have any affiliation or participation in organizations with financial interests.

Ethical Approval

This project did not imply any experimentation with human or animal subjects carried out by the authors.

Informed Consent

The authors obtained informed written consent from the patients in order to develop this article.

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