

GUT MICROBIOTA AND OBESITY: A ROLE FOR PROBIOTICS

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Abstract: Objective: Correlate the intestinal microbiota with obesity and identify the impact of probiotic administration on the treatment strategy for this disease.

Methodology: Narrative bibliographic review and, for this purpose, 567 articles were found in the PubMed database, using the PVO search strategy and the search strategy: (Obesity) AND (Gastrointestinal Microbiota) AND (Probiotics). Among these articles, 22 were selected to compose the present review.

Review: The intestinal microbiota is an extremely dynamic bacterial complex, which, upon receiving the environmental pressure of obesity, undergoes intrinsic changes in its composition. Concomitant to this, dysbiosis can lead to increased insulin resistance, changes in the production of leptin, ghrelin, peptide YY and GLP-1, influencing the global energy metabolism of patients and the pathophysiology of obesity. Adequate diet together with the use of probiotics exert pressure on the intestinal microbiota and restore the balance of the flora, mitigating the progression of obesity. This promising association appears to support the treatment of obesity by reducing body weight, abdominal adipose tissue and other indices.

Final considerations: Intestinal microbiota is linked to obesity and is influenced by several factors while obesity can affect microbial composition and lead to dysbiosis. The use of probiotics is a possible approach for managing obesity, but more studies, especially long-term clinical trials, are needed to direct the clinical applicability of such an approach.

Keywords: obesity; MmicrobiotaIntestinal; probiotics.

INTRODUCTION

The intestinal microbiota represents a complex and dynamic ecosystem of microorganisms that colonize the human gastrointestinal tract. This microbial “organ” plays crucial roles in health and disease, influencing human physiology in ways that have only recently begun to be understood in depth. Accordingly, in recent decades, obesity has become one of the most prominent disorders in the general population, being an important factor contributing to several other lifestyle disorders, such as type 2 diabetes, hypertension and cardiovascular diseases (Benhamed et al. al., 2020).

In humans and mice, more than 90% of the distal gut microbiota comprises species from two bacterial phyla: Bacteroidetes and Firmicutes. The obese phenotype is often cited as being associated with an increased ratio of Firmicutes to Bacteroidetes phyla. This way, it has been demonstrated that dysbiosis of the intestinal microbiota is closely linked to obesity, and many intestinal microorganisms have been identified as related to this pathology by inducing an increase in the host’s energy absorption and central appetite, and an improvement in fat storage., facts that contribute to chronic inflammation and the regulation of circadian rhythms (Santos-Paulo et al., 2021; Cornejo-Pareja, Muñoz-Garach, Clemente-Postigo, Tinahones, 2021).

Randomized clinical trials have shown that probiotics reduce BMI and body weight, but they depend on the strain of bacteria involved, that is, within the same taxon there are beneficial and harmful microorganisms. Furthermore, the composition of the microbiota is connected to the individual’s energy balance and metabolism; obese people have a higher proportion of Proteobacteria, Chloroflexi and Firmicutes and an absence of the Bacteroidetes phylum. This finding established that the Firmicutes/Bacteroidetes

relationship is linked to the pathophysiology of obesity (Benhamed et al., 2020; Cornejo-Pareja, Muñoz-Garach, Clemente-Postigo, Tinahones, 2021; Santos-Paulo et al., 2021).

Thus, probiotics, beneficial bacteria for the body, play a positive role in visceral obesity, reducing BMI and intrahepatic fat fraction, through the production of SCFAs, short-chain fatty acids, which facilitate lipid metabolism and increased insulin sensitivity, resulting in greater benefits to body weight and prevention of obesity (Abenavoli et al.,2019). However, probiotics have their formulations or manufacturing protocols changed over time, which has a dramatic impact on their effectiveness, and there is still a lack of studies that can prove their real effectiveness (Cornejo-Pareja, Muñoz-Garach, Clemente-Postigo, Tinahones, 2021; Hills et al., 2019;

The microbiota plays a fundamental role in preserving the host’s health, through interactions that encompass the immune system and regulate a wide range of metabolic functions. Consequently, changes in the composition of the intestinal microbiota can affect multiple physiological aspects (Benhamed et al., 2020). Therefore, the present review aims to investigate the relationship between the intestinal microbiota and obesity, highlighting the impact of probiotics on the modulation of the microbiota and on obesity treatment and prevention strategies.

METHODOLOGY

Narrative bibliographic review developed according to the criteria of the PVO strategy, an acronym that represents: population or research problem, variables and outcome. Used to prepare the research through its guiding question: “What is the role of the intestinal microbiota in obesity and how can probiotics contribute to its management?”. The searches were carried out through searches in the PubMed - MEDLINE (Medical

Literature Analysis and Retrieval System Online) database. The search terms were used in combination with the Boolean terms “AND”: (Obesity) AND (Gastrointestinal Microbiota) AND (Probiotics). From this search, 567 articles were found, subsequently submitted to the selection criteria. The inclusion criteria were articles in English and Portuguese, published between 2019 and 2024 and which addressed the themes proposed for this research, including clinical trial-type studies, reviews, systematic, observational studies and other types of studies. The exclusion criteria were: duplicate articles, available only in abstract form, which did not directly address the proposal studied and which did not meet the other inclusion criteria. After applying the inclusion and exclusion criteria, 55 potential articles were selected to form the collection of the present study. After reading and analysis of such articles, a total of 2 were selected for full analysis in the present study.

DISCUSSION

The causes of obesity are multifactorial and include genetic, socioeconomic, hormonal, environmental, and cultural influences (Tokarek et al., 2024). According to Geng et al. (2022), obesity is an epidemic, and as a result, rates of insulin resistance, Type 2 Diabetes Mellitus, non-alcoholic liver diseases, atherosclerosis and cancers have increased significantly. Exposure to endogenous and exogenous factors, such as autoimmune and chronic diseases, medications, smoking, diet and mental stress, leads to a change in the composition of the intestinal microbiota. This microbiota is capable of modulating the host's metabolism through energy balance, low-grade chronic inflammation and intestinal barrier function, and this change is directly associated with obesity, being an environmental modulator of this condition

(Burakova et al., 2022).

Studies show that people who are overweight or obese have dysbiosis and lower microbiota diversity compared to people with a normal BMI. This change leads to a suppressed production of adipose factor induced by fasting, leading to increased triglyceride storage in adipose tissue and decreased secretion of the hormone's peptide YY and glucagon, leading to greater food intake (Kim; Choi; Yim, 2019). However, according to Jian et al. (2022), studies have not identified a substantial correlation between this relationship and Body Mass Index (BMI) or obesity. This suggests that this ratio, or specific microbial traits, do not differ between the gut microbiota of normal weight and obese individuals.

According to Liu et al. (2024), randomized studies demonstrate that there are distinct microbes among the study population in relation to different types of obesity. The intestinal microbiota comprises a complex of eighty trillion bacteria, which act in the homeostasis of the human organism, including the regulation of the host's metabolism, the maintenance of the intestinal barrier function and the modulation of the immune system. Since diet is the main factor in maintaining the intestinal microbiota, dysbiosis can cause profound changes in intestinal dynamics (Geng et al., 2022).

Gut microbial diversity is incredibly dynamic, with permanent and transient resident members that depend on the host's diet and environmental resources (Cornejo-Pareja; Muñoz-Garach; Clemente-Postigo; Tinahones, 2021). Among the changes that obesity entails, the change in the exogenous dietary substrate stands out, short-chain fatty acids that activate defense cells, such as neutrophils, macrophages and dendritic cells, activating interleukins (IL) IL-18, IL-22 and IgA and causing metabolic disorders (Geng et al., 2022).

The intestinal microbiota is characterized by the great diversity of bacteria, including *Lactobacillus* spp., *Bifidobacterium* spp., *Bacteroides* spp., *Enterococcus* spp., *Clostridium leptum*, *Enterobacter* spp., Ruminococcaceae UCG010, *Butyricimonas* and Pasteurellaceae (Geng et al., 2022). Obesity puts environmental pressure on these bacteria, with an upregulation for *Lactobacillus* spp., *Bifidobacterium* spp., *Bacteroides* spp. and *Enterococcus* spp., while negatively for *Clostridium leptum* and *Enterobacter* spp. (Geng et al., 2022; Kou et al., 2023). *Clostridium bifermentans* or its metabolites may be the main microbial factors affecting lipid absorption (Jian et al., 2022).

According to Liu et al. (2024), the bacteria Ruminococcaceae UCG 010, *Butyricimonas* and Pasteurellaceae are related to the development of different types of obesity, and studies such as those by Tokarek et al. (2024) demonstrate that both in human and animal models, obesity is related to the Bacteroidetes/Firmicutes ratio, with obese individuals showing a predominance of Firmicutes and a lower proportion of Bacteroidetes when compared to non-obese individuals.

According to Díez-Sainz, Milagro, Riezu-Boj and Lorente-Cebrián (2022), the microbiota and mammalian kingdoms communicate through extracellular vesicles (EVS), which transport genetic material, including microRNA, in an autocrine or paracrine manner, being able to regulate the immune system and suppress cancer cells. Such vesicles have a variable function depending on the bacteria in question, such as *Pediococcus pentosaceus*, which produces immunosuppressive EVS, while *E. coli* Nissle strengthens the epithelial barrier, positively regulating zonula occludens-1, having a protective response. In dysbiosis, *Pseudomonas* EVS can act on glucose metabolism, consequently increasing insulin

resistance in skeletal muscle and adipose tissue (Díez-Sainz et al., 2022).

The intestinal microbial community can influence the production of hormones such as leptin, peptide YY (PYY), ghrelin, insulin and glucagon-like peptide-1 (GLP-1), which are hormones related to obesity (Liu et al., 2024). According to Silva, Casarotti, Oliveira and Penna (2020), changes in the intestinal microbiota occur mainly through the ingestion of probiotics, prebiotics and synbiotics, which are regulated by numerous systems such as the enteric nervous system, central nervous system and sympathetic and parasympathetic branches, in line with Tokarek et al. (2024), who demonstrate that diet, lifestyle and the use of antibiotics alter and exert pressure on these complexes.

The clearest biomarker observed in the obesity-related study appears to be the ratio of Firmicutes to Bacteroidetes. A higher ratio was observed in obese populations or those with metabolic syndrome compared to healthy ones (López-Moreno et al., 2021). Despite these considerations, the discovery of the use of probiotics can contribute to reestablishing the balance of the intestinal flora. The risk of a chronic disease such as obesity increasing microbiota dysregulation can cause dysbiosis, generating chronic inflammation. The use of probiotics has many beneficial functions and can be used as a potential therapeutic to alleviate obesity and obesity-related chronic diseases. Various dead probiotics, which also have anti-obesity properties, expand the applications of probiotics in the food industry, since anaerobic probiotics are difficult to utilize in the food process (Tang et al., 2021). Therefore, the association of the use of probiotics with a good dietary intake, which helps to modulate the microbiota, has become beneficial for obese patients (Abenavoli et al., 2019).

The chronic inflammation to which obese patients are susceptible, due to excess body fat and poor diet, has been shown to have a strong relationship with negative effects on the intestinal microbiota. Furthermore, gut microbiota dysbiosis promotes the development of obesity-related non-alcoholic fatty liver disease (NAFLD) as a result of bacterial overgrowth in the small intestine and an increase in intestinal permeability.

Gut microbiota dysbiosis promotes obesity and related diseases, and the gut microbiota is changing during the progression of obesity, profoundly affected by diets. Probiotic intake effectively reduces body weight, abdominal adipose tissue, and other obesity indices in humans and animals (Wang et al., 2021). Therefore, we can see the importance of associating the use of probiotics in treatment strategies for obese patients.

Stool samples were obtained before and after the study to evaluate the intestinal microbiota. After use, it was concluded that supplementation with synbiotics induced statistically significant changes in the composition of the intestinal microbiota at the end of the trial, compared to the placebo group. Bifidobacterium has been found to be beneficial in the intestinal microbiota

and has also been associated with anti-obesity effects (Sergeev et al., 2020). The use of the strains obtained in the study, which were Bifidobacterium and Lactobacillus, demonstrated beneficial actions on the microbiota, causing changes in body metabolism and obesity (Alard et al., 2021).

FINAL CONSIDERATIONS

The intestinal microbiota has an intimate relationship with obesity. Endogenous and exogenous factors influence the dynamic composition of this microbiome, which directly impacts the host, whether via energy metabolism, low-grade chronic inflammation or alteration of the intestinal epithelial barrier, contributing to the pathophysiological mechanism of obesity. On the other hand, the progression of obesity can lead to intestinal dysbiosis, resulting in a lower diversity of microorganisms. This important retroactive cycle opens the way for promising research into the use of probiotics as a tool for managing obesity, via rebalancing the flora. Despite the growing number of new studies, research, especially long-term randomized clinical trials, is necessary to further elucidate the substantial impact of the use of probiotics in obese patients.

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