Defensing intestinal dysbiosis in obesity: Exploring the phyla *Bacteroidetes* and *Firmicutes* and the role of LPS endotoxin

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ABSTRACT

Introduction: Obesity is a complex metabolic disorder influenced by genetic and environmental factors. Individuals with a body mass index (BMI) of 30 or greater are considered obese, but even being overweight (BMI between 25 and 29.9) can have adverse consequences. In Brazil, about 60% of adults were overweight in 2020, indicating a growing concern. In addition to physical transformations, obesity is associated with conditions such as insulin resistance, dyslipidemia, and systemic inflammation, increasing the risk of cardiovascular disease and cancer. Dysbiosis in the gut microbiota, an imbalance between bacterial species, plays a crucial role in the etiology of obesity by influencing metabolic homeostasis. LPS endotoxin, when expressed at high levels, contributes to adipose tissue inflammation and the progression of obesity. Thus, the health of the gut microbiota is essential for maintaining metabolic balance and preventing the development of obesity. Objective: The present study investigates how gut dysbiosis, an imbalance in the microbiota, affects obesity and its complications. In addition, it examines the role of LPS endotoxin in gut inflammation and obesity. Methodology: This literature review used the Pubmed database to analyze the role of gut dysbiosis in obesity. Articles published between 2020 and 2024 that addressed the phyla Bacteroidetes and Firmicutes were included, excluding reviews and articles unavailable in full. The central question was about how dysbiosis and LPS endotoxin contribute to inflammation in obesity. Literature review: The gut microbiota, composed mainly of Firmicutes and Bacteroidetes, plays a crucial role in metabolic health. In obese individuals, there is an imbalance in this composition, associated with a predisposition to obesity and metabolic disorders. Factors such as diet, physical activity, and age influence the composition of the microbiota. Certain bacterial strains, such as Bifidobacterium, have varying effects on obesity. Bariatric surgery can remodel the gut microbiota, contributing to weight loss and improved metabolic health. In addition, obesity triggers chronic inflammation, influenced by the presence of Gram-negative gut bacteria that release LPS endotoxin, contributing to pro-inflammatory conditions. A high-fat diet increases the adhesion of these bacteria to the intestinal mucosa, facilitating their passage into the bloodstream and contributing to obesity and insulin resistance. Conclusion: In this study, we investigated the impact of gut microbiota on obesity and metabolic health. Factors such as diet, physical activity, and age influence the imbalance in the composition of the microbiota, with a predominance of Firmicutes over Bacteroidetes in obese individuals. Reduced Bifidobacterium is associated with obesity, while different bacterial strains can affect body weight differently. Bariatric surgery can alter the microbiota, potentially improving metabolism. Obesity triggers chronic inflammation, with Gram-negative gut bacteria and endotoxins contributing to this process, especially with a high-fat diet. These findings underscore the importance of the gut microbiota in metabolic regulation and suggest therapeutic approaches to treat obesity and associated metabolic conditions.

Keywords: Obesity, Microbiota and dysbiosis.

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INTRODUCTION

Obesity, a complex metabolic disorder, is influenced by an intricate interplay of genetic and environmental factors[1]. According to the World Health Organization (WHO) classification, individuals with a body mass index (BMI) equal to or greater than 30 are considered obese, but it is crucial to highlight that those diagnosed with overweight (BMI between 25 and 29.9) may already face adverse consequences associated with excess body adiposity [1].

In Brazil, data from the Ministry of Health reveal that, in 2020, approximately 60% of adults were overweight, which is equivalent to about 96 million people [1]. In other words, for every 4 individuals, 1 is obese. Alarmingly, estimates indicate that by the year 2030, the global number of people with obesity could reach the mark of 1.12 billion[1].

This chronic condition transcends physical transformations, being associated with a series of conditions such as insulin resistance, dyslipidemia, oxidative stress, and a chronic and systemic state of inflammation[2]. These factors significantly increase the risk of developing cardiovascular disease, non-alcoholic steatosis, and certain cancers[2]. In this context, growing evidence indicates that an imbalance in the gut microbiota, known as dysbiosis, may play a crucial role in the etiology of obesity and its complications[2]. The maintenance of systemic metabolic homeostasis is strongly influenced by the balance of the gut microbiota [2]. In the gastrointestinal tract, resides a complex community of approximately 100 trillion microorganisms, represented by more than 35,000 species of bacteria, most of which are anaerobic, such as belonging to the phyla *Bacteroidetes* and *Firmicutes*[23]. *These microorganisms operate synergistically with the host, performing vital functions such as the synthesis of short-chain fatty acids, bile acids, cholesterol and B vitamins and vitamin K*[2]. *In addition, they provide a protective barrier against pathogenic microorganisms*[2].

An increasingly prevalent public health condition worldwide, obesity has aroused great interest in the scientific community. Among the factors implicated in this complex condition, the LPS (lipopolysaccharide) endotoxin, when expressed in high levels, emerges as a critical factor in the etiology of obesity and inflammation of adipose tissue, since it activates a pro-inflammatory intestinal reaction that evidences its role as a trigger of this worrisome scenario [2] [3] [4].

Thus, the gut microbiota plays a crucial role in preserving physiological homeostasis and the integrity of the gastrointestinal tract, promoting the body's energy and metabolic balance[4]. Thus, any disorder in this delicate microenvironment can trigger metabolic changes, induce an increase in central appetite and, consequently, culminate in the development of obesity [2].

OBJECTIVE

The present study aims to investigate the impact of gut dysbiosis, characterized by an imbalance in the gut microbiota, especially in relation to the phyla Bacteroidetes and Firmicutes, on

the etiology and complications associated with obesity. In addition, it aims to understand the role of LPS endotoxin in the activation of intestinal pro-inflammatory processes and its contribution to obesity and adipose tissue inflammation. In addition, to provide fundamental knowledge for understanding and coping with obesity as a public health challenge of global reach.

METHODOLOGY

To compose this literature review, a bibliographic survey was carried out in the Pubmed databases, using the following keywords: obesity, microbiota and dysbiosis. Articles published between 2020 and 2024, focusing on the identification of factors related to obesity, were included, and review articles were excluded, not available in full and that did not answer the guiding question, in addition to having more than 4 years of publications. In addition, a database on the Ministry of Health website on obesity data was used.

Guiding question: What is the specific role of gut dysbiosis, including the imbalance between the phyla Bacteroidetes and Firmicutes, in the pathogenesis of obesity and its metabolic complications, and how does the LPS endotoxin contribute to these inflammatory processes?

LITERATURE REVIEW

The gut microbiota, composed mainly of Firmicutes and Bacteroidetes, plays a key role in metabolic health[2]. In obese individuals, there is often an imbalance in this composition, characterized by an increase in the Firmicutes:Bacteroidetes (F:B) ratio, which is associated with a predisposition to obesity and metabolic disorders[2]. This was shown through a study with rats fed a high-fat diet that shows that the composition of the microbiome is altered, with a decrease in Bacteroidetes and an increase in Firmicutes, evidencing the direct impact of diet on the microbiota[1]. In humans, a similar association is observed between obesity and the predominance of Firmicutes over Bacteroidetes[1].

In another approach, the composition of the gut microbiota is influenced by a variety of factors, including diet, physical activity levels, age, antibiotic use, and other environmental factors[2]. Studies show divergent results regarding the F:B ratio in different populations and contexts, reflecting the complexity of the interaction between microbiota and obesity [2]. In addition, sleep disturbances can also contribute to obesity by affecting circadian rhythms and, consequently, the gut microbiome[1].

It is a fact that *Bifidobacterium*, an important probiotic, plays an intrinsic role in the balance of the gut microbiota, and studies show varying effects on obesity, depending on the strain used[1]. In this context, the reduction in the abundance of *Bifidobacterium* is associated with obesity, while specific species such as *M. smithii* and *B. animalis* are linked to normal weight, and *L. reuteri* to

obesity[1]. Thus, these findings highlight the specificity of microorganisms in the metabolic regulation of obesity[1].

Recent research has explored the potential of bariatric surgery as an intervention to remodel the gut microbiota in patients with obesity[2]. As a result, this surgery may increase microbial diversity and reduce the ratio of *Firmicutes* to *Bacteroidetes*, which may contribute to the benefits seen in weight loss and improved metabolic health after bariatric surgery[2]. Thus, these findings highlight the importance of the gut microbiota in the regulation of metabolism and suggest new therapeutic strategies for the treatment of obesity and its metabolic comorbidities [2].

From another perspective, obesity triggers chronic low-grade inflammation, driven by pro-inflammatory mediators released by adipocytes, such as TNF-α, IL-1 and IL-6[3]. In this way, the intestine, crucial in the modulation of the immune response, is affected by the increased presence of Gram-negative intestinal bacteria in obese individuals, which constantly release LPS, activating receptors such as Toll-Like 4 (TLR4) and CD14 and causing pro-inflammatory conditions such as metabolic bacteremia and endotoxemia[3].

Finally, a high-fat diet increases the adhesion of these bacteria to the intestinal mucosa, facilitating their passage into the bloodstream and mesenteric lymph [3]. Thus, LPS, absorbed by enterocytes, contributes to obesity and insulin resistance by stimulating inflammation in adipose and hepatic tissues[3]. Experiments in mice have shown that LPS infusion results in weight gain similar to the high-fat diet[3]. In this way, the reduced presence of certain bacteria, such as *Bacteroides* and *Bifidobacterium*, associated with a high-fat diet, decreases intestinal LPS levels and improves mucosal barrier function [3].

CONCLUSION

This study investigated the role of the gut microbiota in metabolic health and obesity. It has been observed that obese individuals often have an imbalance in the composition of the microbiota, with an increased ratio of *Firmicutes* to *Bacteroidetes*. Factors such as diet, physical activity, and age influence this composition. Reduction in *Bifidobacterium abundance* is associated with obesity, while some specific strains may have varying effects on body weight. Bariatric surgery can remodel the microbiota, increasing its diversity and reducing the proportion of *Firmicutes,* with potential metabolic benefits.

In addition, obesity triggers chronic inflammation, mediated by pro-inflammatory mediators released by adipocytes and the elevated presence of Gram-negative bacteria in the gut, resulting in the constant release of LPS and pro-inflammatory conditions. The high-fat diet increases this bacterial adhesion to the intestinal mucosa, contributing to obesity and insulin resistance. These findings highlight the importance of the gut microbiota in metabolic regulation and suggest

therapeutic interventions aimed at modulating the microbiota for the treatment of obesity and its metabolic comorbidities. Research is being conducted to better understand how the composition and function of the gut microbiota influence obesity and associated metabolic conditions.

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