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THE INFLUENCE OF GUT MICROBIOTA ON TYPE 2 DIABETES MELLITUS: A COMPREHENSIVE REVIEW

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Abstract: INTRODUCTION: Type 2 diabetes (T2DM) is a growing concern globally, related to genetic, environmental and behavioral factors. Recent studies highlight the fundamental role of the intestinal microbiome in the pathophysiology of DM2, affecting energy metabolism and insulin sensitivity. Unbalanced diets can disrupt the gut microbiota, leading to chronic inflammation and insulin resistance. Therapeutic strategies, such as probiotics and prebiotics, have shown potential in improving glucose metabolism. However, there are still significant gaps in understanding this relationship. Therefore, it is essential to synthesize the latest findings to develop more effective approaches to preventing and managing T2DM. **GOAL:** Synthesize recent findings on the relationship between gut microbiota and DM2, identifying gaps in research and directing future investigations to advance knowledge and develop innovative therapeutic approaches. **METHODOLOGY:** A literature review was carried out using the MEDLINE-PubMed database, covering studies published between 2014 and 2024. Of the 850 studies found, 29 were selected after critical analysis. Inclusion criteria were based on the descriptors "Intestinal microbiota" OR "Gut microbiome" AND "diabetes mellitus", excluding animal studies and narrative reviews. **RESULTS:** There was an increase in the abundance of beneficial bacteria in pre-diabetic patients treated with probiotics, potentially improving glucose homeostasis. Disturbances in the circadian rhythms of the microbiota were observed in people with DM2, suggesting possible biomarkers for early identification of the disease. Certain probiotic strains have shown improvements in glycemic control in adults with T2D, while pharmacological treatments such as oral antidiabetics and bariatric surgery have led to significant changes in the microbiota. **DISCUSSION:** The

analysis reveals that changes in the intestinal microbiota are associated with DM2, including a reduction in microbial diversity and an increase in endotoxin-producing bacteria. Dietary interventions, such as probiotics and prebiotics, show potential in the management of DM2, improving body composition and the inflammatory response. However, challenges remain, including interindividual variability and the need to better understand underlying mechanisms. In summary, microbiota modulation may be a promising therapeutic strategy, but requires further research for clinical validation. **CONCLUSION:** The analysis reveals that the intestinal microbiota plays a crucial role in the pathophysiology and treatment of DM2. Changes in microbial composition are associated with the development of the disease, highlighting the importance of personalized therapeutic interventions, such as probiotics and dietary modification, to improve glycemic control and patients' quality of life.
Keywords: Type 2 Diabetes Mellitus; Intestinal microbiota; Probiotics.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) represents a growing challenge for healthcare systems around the world, with a constantly increasing prevalence in developed and developing countries. It is estimated that more than 400 million people worldwide live with T2D, and this number continues to rise, especially in parallel with the rise in obesity and sedentary lifestyles. This complex metabolic disorder is influenced by a multifaceted interaction of host genetic, environmental, and behavioral factors. [3 4.]

Furthermore, it is important to highlight that DM2 is a chronic metabolic condition with an increasing prevalence throughout the world. Recent studies have suggested that changes in the microbiome may play an important role in the pathophysiology of T2D, and understanding these changes may provide valuable insights into the treatment and management of T2D. [4 5].

Understanding the causes and contributing factors of T2DM is crucial for developing effective prevention and treatment strategies. In recent years, research has increasingly focused on the influence of intestinal microbiota on human health. The gut not only plays a vital role in the digestion and absorption of nutrients, but also regulates interactions between the gut microbiome, the immune system, and the host organism.[1 2 3].

Diets high in fat and low in fiber can disrupt the balance of the intestinal microbiota, leading to dysbiosis, chronic inflammation and insulin resistance, associated with the development of DM2. Furthermore, increased consumption of high-calorie foods and decreased physical activity contribute to a positive energy imbalance, increasing the risk of obesity and insulin resistance, a precursor to DM2. [1 2 3].

The gastrointestinal tract is home to a diverse microbial community, playing a crucial role in defense against pathogens and host metabolism. Studies highlight the gastrointestinal microbiome as an endocrine organ capable of modulating hormonal responses and influencing energy metabolism and insulin sensitivity, central aspects in the pathophysiology of DM2. Another important point is that more than 5000 bacterial species reside in the human gastrointestinal tract, and the composition of the gut microbiota has been linked to a wide range of conditions, including allergies, inflammatory bowel diseases, cancer, diabetes, cardiovascular disease, and dyslipidemia.[1 2 3 5].

Despite advances in understanding the relationship between intestinal microbiota and various conditions, including obesity, its specific role in DM2 continues to be the

subject of intense investigation. Innovative therapeutic strategies, such as manipulation of the gut microbiota by probiotics and prebiotics, have demonstrated potential to improve glucose metabolism and insulin resistance [1 2 3].

Modulation of the intestinal microbiota may be a promising strategy to improve glucose metabolism and insulin resistance in T2DM. However, gaps in understanding the interaction between gut microbiota and T2D require further investigations to develop more effective preventive and therapeutic strategies.[6 7]

GOAL

Synthesize the most recent discoveries about this relationship, addressing aspects of the pathophysiology, diagnosis and therapeutic strategies of DM2.

METHODOLOGY

A literature review was carried out through the selection of studies in the MEDLINE-PubMed database (National Library of Medicine, National Institutes of Health) published between the years 2014 and 2024. 850 studies were found, of which 29 were selected by a critical analysis. Articles published in English and/or Portuguese that addressed the relationship between intestinal microbiota and the development of type 2 Diabetes Mellitus and available in full were included in this review. The descriptors used were "Intestinal microbiota" OR "Gut microbiome" AND "diabetes mellitus". Through the analysis, articles that did not meet the inclusion criteria, such as animal studies and narrative reviews, were excluded.

RESULTS

The results of the analysis revealed several important findings about the relationship between the gut microbiota and T2D. Firstly, an increase in the abundance of beneficial bacteria, such as Bifidobacterium breve, Akkermansia muciniphila and Clostridium hathewayi, associated with the production of short-chain fatty acids (SCFA), was observed in pre-diabetic patients who received probiotics. Although there was no overall effect on microbiota diversity, this improvement suggests a potential to facilitate glucose homeostasis and improve T2D treatment outcomes. [8 7.]

Furthermore, a disruption of the circadian rhythms of the microbiota was observed in people with DM2, with the identification of an arrhythmic pattern strongly associated with the disease. These arrhythmic bacterial taxa have been proposed as useful biomarkers for early identification and monitoring of T2D progression.

In another study, 11 microbiota taxa were identified as new predictive factors for the risk of DM2, including several bacterial orders and families. The decrease in the genus *Roseburia* and the increase in the *Lactobacillaceae* family in patients with DM2 were also observed, reinforcing their relevance as potential biomarkers of the disease [4 5 7.]

Furthermore, individuals with DM2 showed a reduction in blood cell counts. *Bifidobacterium* and *Faecalibacterium prausnitzii*, both with anti-inflammatory properties, and a decrease in levels of *Clostridium and Firmicutes* in the intestinal microbiota. The reduction in the frequency of butyrate-producing bacteria was one of the most significant changes associated with DM2[8].

Supplementing with certain probiotic strains, such as: *Bifidobacterium lactis, Streptococcus thermophilus, Lactobacillus*

bulgaricus and Lactobacillus acidophilus, showed promising results in improving glycemic control in adults with DM2. Furthermore, transferring fecal samples from DM2 patients treated with metformin to mice lacking microbiota demonstrated improved glucose tolerance in recipient mice. [6 8].

It was also identified that pharmacological treatments, such as oral antidiabetic therapy and bariatric surgery, led to significant changes in the intestinal microbiome in patients with DM2. This included an increase in the abundance of Firmicutes and Proteobacteria, as well as a decrease in microbiome diversity following treatment, associated with an improvement in glycemic control.[1 6 8]

DISCUSSION

Initially, it was observed that overweight, moderate obesity, insulin resistance and DM2 itself are associated with changes in microbial composition, characterized by a decrease in the abundance and diversity of microorganisms. These modifications appear to be related to metabolic deficiencies and may play a crucial role in chronic systemic inflammation. [1 6 8]

Furthermore, studies highlighted that T2D status correlated with a decrease in the abundance of short-chain fatty acid (SCFA)-producing bacterial genera and an increase in the abundance of gram-negative endotoxin-producing bacteria. These findings suggest that changes in the gut microbiome may contribute to the pathogenesis of T2D, possibly through bacterial translocation and inflammation. [6 8].

Dietary intervention, including the use of probiotics, prebiotics and dietary patterns such as the Mediterranean and high-fiber diet, has emerged as a promising strategy in the management of T2DM. Studies have shown that probiotic supplementation can improve body composition, insulin sensitivity and inflammatory response in patients with DM2. Additionally, taking prebiotics such as berberine has been linked to improved insulin sensitivity and reduced inflammatory markers. [4 6 8]

However, it is important to recognize that there are still challenges and gaps to be addressed. Interindividual variability in microbial composition, influenced by factors such as diet, lifestyle and health status, represents a significant limitation. Furthermore, the need to replicate results in different populations and contexts, as well as understand the mechanisms underlying the observed associations, highlights the continued importance of research in this area.

CONCLUSION

Thus, the relationship between intestinal microbiota and DM2 highlights its importance in the pathophysiology, diagnosis and treatment of the disease. Studies show that the imbalance in the composition of the microbiota is strongly linked to the development of DM2, from pre-diabetic stages to the established condition. This suggests an early role of the microbiota in disease progression.

Understanding the microbiota as a modifiable determinant of T2DM offers a new perspective on treatment, highlighting the importance of therapeutic interventions aimed at restoring microbiota balance. Strategies such as supplementation with probiotics, prebiotics and dietary modification show potential in improving glycemic control and reducing systemic inflammation.

However, challenges such as individual variability in response to these interventions and gaps in research, such as replication of results in different populations, point to the need for more personalized approaches and ongoing investigations.

Despite the limitations, promising results indicate an encouraging direction in the treatment of T2DM. The identification of

specific microbiota patterns suggests the potential development of more effective biomarkers and therapeutic strategies. Therefore, it is crucial to continue exploring this complex relationship to improve the management and clinical outcomes of T2DM.

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