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Manifestações orais associadas a agonistas de GLP-1/GIP: foco na halitose, microbiota oral e alterações salivares em pacientes que utilizam tirzepatida

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REVISÃO DE LITERATURA

RESUMO

A halitose é uma condição multifatorial com alta prevalência global, que impacta significativamente a qualidade de vida, as interações sociais e o bem-estar psicológico. Sua origem primária é intraoral, especialmente associada ao biofilme da língua, onde bactérias anaeróbias metabolizam aminoácidos sulfurados, produzindo compostos sulfurados voláteis (CSVs). No entanto, condições sistêmicas como distúrbios metabólicos, alterações gastrointestinais e distúrbios do fluxo salivar também desempenham um papel importante em sua fisiopatologia. Nos últimos anos, as terapias baseadas em incretinas, particularmente os agonistas do receptor do peptídeo semelhante ao glucagon-1 (GLP-1) e o agonista duplo tirzepatida, ganharam destaque no tratamento do diabetes tipo 2 e da obesidade devido à sua eficácia no controle glicêmico e na redução de peso. Apesar de seus benefícios clínicos, esses medicamentos estão associados a efeitos adversos gastrointestinais, retardo do esvaziamento gástrico e potenciais alterações na secreção salivar e nos hábitos alimentares, o que pode afetar indiretamente a saúde bucal. Evidências emergentes sugerem que esses medicamentos podem influenciar a composição da microbiota oral, promover hipossalivação e contribuir para condições como xerostomia e alterações no odor do hálito, às vezes descritas como “hálito de Ozempic”. Além disso, a modulação metabólica e possíveis alterações no eixo intestino-oral podem impactar ainda mais a produção de compostos sulfurados voláteis (CSVs). Por outro lado, o melhor controle glicêmico e a redução da inflamação sistêmica podem proporcionar efeitos benéficos à saúde periodontal, destacando o duplo impacto dessas terapias. Esta revisão narrativa teve como objetivo analisar a possível associação entre o uso de tirzepatida e halitose, integrando dados de microbiologia oral, farmacologia e metabolismo sistêmico. Os resultados sugerem que, embora as terapias baseadas em incretinas ofereçam benefícios sistêmicos significativos,

elas também podem criar condições favoráveis à halitose por meio de alterações no fluxo salivar, no equilíbrio da microbiota e na fisiologia gastrointestinal. Permanece uma lacuna significativa na literatura em relação à relação direta entre tirzepatida e halitose. Mais estudos clínicos e experimentais são necessários para melhor compreender esses mecanismos e para apoiar o desenvolvimento de estratégias preventivas e terapêuticas em um contexto clínico interdisciplinar.

Palavras-chave: Halitose; Tirzepatida; Microbiota oral.

Oral manifestations associated with GLP-1/GIP agonists: focus on halitosis oral microbiota and salivary alterations in patients using tirzepatide

ABSTRACT

Halitosis is a multifactorial condition with high global prevalence, significantly impacting quality of life, social interactions, and psychological well-being. Its primary origin is intraoral, especially associated with tongue biofilm, where anaerobic bacteria metabolize sulfur-containing amino acids, producing volatile sulfur compounds (VSCs). However, systemic conditions such as metabolic disorders, gastrointestinal alterations, and salivary flow disturbances also play an important role in its pathophysiology. In recent years, incretin-based therapies, particularly glucagon-like peptide-1 (GLP-1) receptor agonists and the dual agonist tirzepatide, have gained prominence in the treatment of type 2 diabetes and obesity due to their efficacy in glycemic control and weight reduction. Despite their clinical benefits, these drugs are associated with gastrointestinal adverse effects, delayed gastric emptying, and potential alterations in salivary secretion and dietary habits, which may indirectly affect oral health. Emerging evidence suggests that these medications may influence oral microbiota composition, promote hyposalivation, and contribute to conditions such as xerostomia and changes in breath odor, sometimes described as “Ozempic breath.” Additionally, metabolic modulation and possible changes in the gut–oral axis may further impact the production of VSCs. On the other hand, improved glycemic control and reduced systemic inflammation may provide beneficial effects on periodontal health, highlighting a dual impact of these therapies. This narrative review aimed to analyze the potential association between tirzepatide use and halitosis, integrating data from oral microbiology, pharmacology, and systemic metabolism. The findings suggest that while incretin-based therapies offer significant systemic benefits, they may also create conditions favorable to halitosis through alterations in salivary flow, microbiota balance, and gastrointestinal physiology. There remains a significant gap in the literature regarding the direct relationship between tirzepatide and halitosis. Further clinical and experimental studies are needed to better understand these mechanisms and to support the development of preventive and therapeutic strategies in an interdisciplinary clinical context.

Keywords: Halitosis; Tirzepatide; Microbiota, Oral.

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INTRODUÇÃO

Halitosis, commonly known as bad breath, is a multifactorial condition with high global prevalence, exerting a significant impact on quality of life, interpersonal relationships, and individuals' psychological well-being. Epidemiological studies indicate that a substantial portion of the population presents some degree of halitosis, which is often underdiagnosed and undertreated (Silva et al., 2018). The primary origin of halitosis is intraoral, especially related to the accumulation of biofilm on the dorsal surface of the tongue, where anaerobic microorganisms metabolize proteins and sulfur-containing amino acids, producing volatile sulfur compounds (VSCs), such as hydrogen sulfide, methyl mercaptan, and dimethyl sulfide. Recent advances in metatranscriptomic techniques have enabled the identification of specific metabolic pathways associated with the presence or absence of halitosis, reinforcing the central role of the tongue microbiota in its pathophysiology (Carda-Diéguez et al., 2022; Zhang et al., 2024).

In addition to local factors, systemic conditions also play a relevant role in breath modulation, including metabolic diseases, gastrointestinal disorders, and alterations in salivary flow. Saliva plays an essential role in maintaining oral homeostasis, acting in mechanical cleansing, pH buffering, and microbiological control. Thus, hyposalivation or xerostomia favors the accumulation of protein substrates and the growth of anaerobic bacteria, contributing to the worsening of halitosis. In this context, pharmacological interventions that alter systemic metabolism or gastrointestinal physiology may directly or indirectly impact oral health and the production of oral odors.

In recent years, there has been a significant increase in the use of therapies based on glucagon-like peptide-1 (GLP-1) receptor agonists, initially developed for the treatment of type 2 diabetes mellitus and later widely used in the management of obesity. These drugs act by mimicking the action of endogenous GLP-1, promoting increased glucose-dependent insulin secretion, reduced glucagon secretion, delayed gastric emptying, and enhanced satiety (Anandhakrishnan & Korbonits, 2016; Carvalho et al., 2016; Zheng et al., 2024). More recently, tirzepatide, a dual agonist of GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptors, has stood out due to its high efficacy in reducing body weight and improving glycemic control, representing a

significant advance in metabolic therapy (Del Prato et al., 2021; France & Syed, 2024; Regmi et al., 2024).

Large-scale clinical trials, such as the SURPASS-4 study, have demonstrated that tirzepatide is superior to conventional therapies, such as insulin glargine, in reducing blood glucose levels and body weight, in addition to providing cardiovascular benefits in patients with type 2 diabetes (Del Prato et al., 2021). Comparative studies also show greater efficacy of tirzepatide compared to semaglutide in promoting weight loss in overweight or obese individuals (Rodriguez et al., 2024). These results have contributed to the rapid dissemination of the use of these medications, including in off-label contexts and under strong media influence, raising concerns regarding indiscriminate use and potential adverse effects (Grillo et al., 2025; Rodrigues & Silva, 2024).

Although highly effective, GLP-1 agonists and tirzepatide are associated with side effects, predominantly gastrointestinal, such as nausea, vomiting, diarrhea, and constipation, in addition to delayed gastric emptying (Wharton et al., 2022; Camilleri, 2024). These effects may alter eating habits, meal frequency, and dietary composition, indirectly impacting the oral environment. Furthermore, emerging evidence suggests that these drugs may influence salivary secretion, contributing to hyposalivation, which is directly associated with increased halitosis (Mawardi et al., 2023).

In the context of oral health, recent studies have highlighted possible repercussions of GLP-1 agonist use in the oral cavity, including alterations in microbiota, increased susceptibility to periodontal diseases, and manifestations such as xerostomia and changes in breath odor (Bernardo et al., 2026; Almeida et al., 2026; Lopes et al., 2025). Clinical reports and reviews point to the emergence of conditions described as “Ozempic breath” and “Ozempic tongue,” characterized by sensory alterations and oral odor in patients using semaglutide, suggesting a possible class effect of these medications on the oral environment (Bando et al., 2024).

Moreover, systemic metabolic modulation promoted by these drugs may influence the composition of microbiota not only in the intestine but also in the oral cavity. Experimental studies indicate that tirzepatide can impact microbiota in animal models, suggesting a possible indirect effect on microbial balance at different sites of the organism (Silva-Veiga et al., 2025). This interaction between metabolism, microbiota, and inflammatory response is particularly relevant in dentistry, as it

reinforces the interconnection between systemic and oral health.

Additionally, recent evidence suggests that GLP-1 agonists may exert beneficial effects on periodontal conditions, possibly due to reduced systemic inflammation and improved glycemic control (Ahmad et al., 2025; Polymeri et al., 2026; Jeong et al., 2025). However, these potential benefits coexist with local adverse effects that are not yet fully understood, particularly regarding the dynamics of tongue biofilm and the production of volatile sulfur compounds.

Another relevant aspect concerns the clinical implications of the use of these medications in dental practice. Changes in gastric emptying and metabolism may influence procedures involving sedation and anesthesia, requiring greater attention from dental professionals in the management of these patients (Dos Santos et al., 2025; Khan, 2025). In addition, oral hygiene habits and dietary behavior may be modified during treatment with these drugs, directly impacting oral health (Jankowska et al., 2025).

Despite the growing body of evidence on the systemic and metabolic effects of tirzepatide and other GLP-1 agonists, there is still a significant gap in understanding their specific repercussions on halitosis. Most available studies address general effects in the oral cavity without deeply exploring the microbiological and biochemical mechanisms involved in bad breath production in these patients. Considering that halitosis is strongly influenced by factors such as salivary flow, microbiota composition, and availability of protein substrates, it is plausible to hypothesize that therapies that alter these parameters may contribute to its development or worsening.

Given this scenario, it becomes essential to investigate the possible association between the use of tirzepatide and the occurrence of halitosis, integrating knowledge from oral microbiology, pharmacology, and systemic metabolism. Understanding these mechanisms may contribute to the development of more effective preventive and therapeutic strategies, as well as guide interdisciplinary clinical practice. Thus, analyzing the relationship between incretin-based therapies and changes in breath represents a promising area of research, with potential impact on both medicine and dentistry.

METODOLOGIA

This study is a narrative literature review. Scientific articles published in indexed databases such as PubMed, Google Scholar, and Bireme were selected, including clinical studies, systematic reviews, meta-analyses, and experimental studies addressing halitosis, GLP-1 agonists, and tirzepatide. The inclusion criteria comprised relevant studies on oral microbiota, metabolism, adverse effects of incretin-based therapies, and dental implications. No restrictions were applied regarding language or year of publication, with priority given to more recent studies and those with greater scientific impact.

REVISÃO DE LITERATURA

Halitosis, defined as the presence of unpleasant odors originating from the oral cavity, is a multifactorial condition with high global prevalence and significant clinical and social relevance. Understanding halitosis in the contemporary clinical setting requires a comprehensive approach that encompasses not only the oral cavity but also the complex mechanisms of systemic metabolism and modern pharmacology.

Epidemiological studies indicate that a significant portion of the population experiences halitosis to some degree, and it is frequently underdiagnosed and neglected in clinical practice (Silva et al., 2018). This condition is closely associated with negative impacts on quality of life, leading to social embarrassment, impaired interpersonal relationships, and psychological consequences.

Advances in the understanding of oral microbiota have significantly progressed with the introduction of high-precision molecular biology techniques. The use of metatranscriptomics has enabled researchers to identify specific metabolic pathways active in the tongue biofilm of individuals affected by halitosis. Carda-Diéguez et al. (2022) demonstrated that bacterial gene expression varies significantly between individuals with normal breath and those with halitosis, emphasizing the importance of microbial functional activity.

From an etiopathogenic perspective, halitosis is predominantly intraoral in origin, especially associated with tongue biofilm. The dorsal surface of the tongue

provides an ideal environment for the accumulation of anaerobic Gram-negative microorganisms, which metabolize sulfur-containing amino acids, generating volatile sulfur compounds (VSCs) such as hydrogen sulfide, methyl mercaptan, and dimethyl sulfide (Zhang et al., 2024).

In addition to local factors, halitosis is also influenced by systemic conditions. Saliva plays an essential role in oral homeostasis, and alterations such as hyposalivation or xerostomia favor the proliferation of anaerobic bacteria and increased VSC production. In recent years, there has been an increase in the use of glucagon-like peptide-1 (GLP-1) receptor agonists. These drugs have gained prominence in the treatment of type 2 diabetes mellitus and obesity due to their effects on glycemic control and satiety (Anandhakrishnan & Korbonits, 2016; Carvalho et al., 2016; Zheng et al., 2024). Tirzepatide, a dual agonist of GLP-1 and GIP receptors, has demonstrated superior efficacy in weight reduction and glycemic control (Frías et al., 2021; Rodriguez et al., 2024), with confirmation in large clinical trials such as SURPASS-4 (Del Prato et al., 2021).

These therapies act, among other mechanisms, by delaying gastric emptying, which contributes to satiety and weight loss (Camilleri, 2024). However, they are also associated with gastrointestinal adverse effects such as nausea, vomiting, diarrhea, and constipation (Wharton et al., 2022; Sillassen et al., 2024).

RESULTADOS E DISCUSSÃO

The effects of GLP-1 and GIP agonists extend beyond metabolic control and may significantly impact oral health. Delayed gastric emptying can lead to prolonged fermentation processes, potentially influencing breath odor. Additionally, gastrointestinal discomfort may result in reduced fluid intake and dehydration, contributing to decreased salivary flow (Holst, 2024).

Changes in dietary habits and metabolism associated with these therapies may alter oral microbiota and the production of volatile sulfur compounds. Experimental evidence suggests that tirzepatide may modulate gut microbiota, with possible

implications for oral microbiota (Silva-Veiga et al., 2025). Clinical reports also indicate hyposalivation in patients using semaglutide (Mawardi et al., 2023), suggesting a similar effect may occur with tirzepatide.

Thus, halitosis in these patients may result from a combination of reduced salivary flow, metabolic alterations, and microbiota imbalance. The interaction between systemic metabolism and oral microbiota reinforces the relevance of the gut–oral axis.

Despite these adverse effects, GLP-1 agonists may also provide benefits to periodontal health by reducing systemic inflammation and improving glycemic control (Ahmad et al., 2025; Polymeri et al., 2026; Almohammad et al., 2025; Jeong et al., 2025), demonstrating a dual impact.

Studies have reported oral manifestations such as xerostomia, dysgeusia, and microbiota alterations (Bernardo et al., 2026; Almeida et al., 2026; Lopes et al., 2025). Additionally, phenomena described as “Ozempic breath” and “Ozempic tongue” highlight changes in breath odor and oral sensitivity (Bando et al., 2024).

In dental practice, these medications require special attention, as delayed gastric emptying may increase the risk of aspiration during sedation procedures (Dos Santos et al., 2025; Khan, 2025). Changes in oral hygiene habits have also been observed (Jankowska et al., 2025).

Despite advances, there is still a significant gap in the literature regarding the direct relationship between tirzepatide and halitosis. Most studies focus on systemic and periodontal effects, with limited exploration of microbiological mechanisms involved in oral odor production.

The relationship between tirzepatide and halitosis is complex and multifactorial. Reduced salivary flow, alterations in tongue microbiota, and delayed gastric emptying contribute to a distinct oral profile. Early identification of symptoms such as xerostomia and halitosis is essential for guiding preventive and therapeutic strategies.

Future perspectives highlight the importance of integrating metabolic and oral health management, ensuring that systemic benefits are not accompanied by negative impacts on oral health and quality of life.

CONSIDERAÇÕES FINAIS

Halitosis is a multifactorial condition strongly associated with oral microbiota, salivary flow, and systemic factors. Incretin-based therapies, particularly tirzepatide, represent a significant advancement in the treatment of obesity and diabetes; however, they may indirectly impact oral health.

The main findings of this review indicate that Halitosis is directly associated with bacterial metabolic activity in tongue biofilm. Tirzepatide may influence factors related to halitosis, such as microbiotas, metabolism, and salivary flow. There is evidence of oral adverse effects, including xerostomia and changes in breath. On the other hand, these drugs may provide periodontal benefits due to improved metabolic control. There is a lack of specific studies on halitosis and tirzepatide, representing an important scientific gap.

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