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THE EMERGING ROLE OF TIRZEPATIDE IN THE MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA

O PAPEL EMERGENTE DA TIRZEPATIDA NO MANEJO DA APNEIA OBSTRUTIVA DO SONO

EL PAPEL EMERGENTE DE LA TIRZEPATIDA EN EL MANEJO DE LA APNEA OBSTRUCTIVA DEL SUEÑO

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ABSTRACT

Obstructive sleep apnea (OSA), common in individuals with obesity, causes respiratory interruptions during sleep and is associated with several comorbidities. Although CPAP is effective, low adherence limits its results. Tirzepatide, a dual GIP and GLP-1 agonist, has shown promise in the treatment of OSA by significantly reducing the apnea-hypopnea index, improving sleep quality, and promoting weight loss. This study aims to review the scientific literature to analyze the effectiveness of tirzepatide in obstructive sleep apnea, based on 13 recent articles selected through rigorous analysis. Current studies highlight tirzepatide's

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superiority over other pharmacological therapies, with additional benefits in metabolic control and outcomes comparable to bariatric surgery. Therefore, based on current evidence, tirzepatide emerges as an effective and innovative alternative in the management of OSA.

Keywords: Obstructive Sleep Apnea. Tirzepatide. GLP-1. Pharmacological Treatment.

RESUMO

A apneia obstrutiva do sono (AOS), comum em pessoas com obesidade, causa interrupções respiratórias durante o sono e está associada a diversas comorbidades. Embora o CPAP seja eficaz, sua baixa adesão limita os resultados. A tirzepatida, um agonista dual de GIP e GLP-1, tem se mostrado promissora no tratamento da AOS, promovendo redução significativa do índice de apneia-hipopneia, melhora do sono e perda de peso. Este estudo tem como objetivo revisar a literatura científica a fim de analisar a eficácia do uso da tirzepatida na apneia obstrutiva do sono, tendo sido utilizados como referência bibliográfica 13 artigos recentes que passaram por uma análise rigorosa. Estudos atuais apontam a superioridade da tirzepatida frente a outras terapias medicamentosas, com benefícios adicionais no controle metabólico e efeitos comparáveis aos da cirurgia bariátrica. Sendo assim, de acordo com as evidências disponíveis, destaca-se o papel da tirzepatida como alternativa eficaz e inovadora no manejo da AOS.

Palavras-chave: Apneia Obstrutiva do Sono. Tirzepatida. GLP-1. Tratamento Farmacológico.

RESUMEN

La apnea obstructiva del sueño (AOS), frecuente en personas con obesidad, provoca interrupciones respiratorias durante el sueño y se asocia a múltiples comorbilidades. Aunque el CPAP es eficaz, su baja adherencia limita los resultados. La tirzepatida, un agonista dual de GIP y GLP-1, ha demostrado ser prometedora en el tratamiento de la AOS, al reducir significativamente el índice de apnea-hipopnea, mejorar la calidad del sueño y favorecer la pérdida de peso. Este estudio tiene como objetivo revisar la literatura científica para analizar la eficacia del uso de la tirzepatida en la apnea obstructiva del sueño, utilizando como base 13 artículos recientes seleccionados mediante análisis riguroso. Los estudios actuales destacan la superioridad de la tirzepatida en comparación con otras terapias farmacológicas, con beneficios adicionales en el control metabólico y resultados similares a los de la cirugía bariátrica. Así, según la evidencia disponible, la tirzepatida se presenta como una alternativa eficaz e innovadora en el manejo de la AOS.

Palabras clave: Apnea Obstructiva Del Sueño. Tirzepatida. GLP-1. Tratamiento Farmacológico.

1 INTRODUCTION

Obstructive sleep apnea (OSA) is a chronic and recurrent breathing disorder characterized by partial or complete obstructions of the upper airway during sleep, resulting in repeated episodes of hypopnea and apnea, accompanied by oxygen desaturations and sleep fragmentation. Its pathophysiology involves the combination of anatomical collapsability of the airway with impairment of neuromuscular tone and alterations in ventilatory control mechanisms (WEN et al., 2025).

It is estimated that OSA affects approximately 1 billion people worldwide, with increasing prevalence due to population aging, sedentary lifestyle and, mainly, the increase in obesity. Individuals with obesity have a significantly higher risk of developing OSA, and the accumulation of fat in the cervical and abdominal region directly interferes with upper airway patency and ventilatory mechanics (AFRIDI et al., 2024).

OSA is associated with a number of comorbidities, such as resistant hypertension, type 2 diabetes, heart failure, stroke, arrhythmias, and increased overall cardiovascular risk. In addition, it causes important impacts on quality of life, such as daytime fatigue, cognitive deficits, and a higher risk of car and occupational accidents (CHESKIN; RAJAGOPAL, 2024).

The gold standard treatment for moderate to severe OSA is continuous positive airway pressure (CPAP), which effectively reduces the apnea-hypopnea index (AHI). However, adherence to CPAP is often limited, with dropout rates exceeding 50% in some studies, which motivates the search for pharmacological alternatives or complementary interventions (EL-SOLH et al., 2024).

In this scenario, the management of obesity becomes a fundamental pillar in the approach to OSA, given that weight reduction is directly associated with improved respiratory function during sleep. Recent studies have shown that interventions that promote consistent weight loss, such as bariatric surgery or the use of GLP-1 receptor agonists, result in clinically meaningful reductions in AHI (LI et al., 2024).

Tirzepatide, a dual agonist of GIP and GLP-1 receptors, initially approved for the treatment of type 2 diabetes and obesity, has shown promising effects on OSA as well. Its action combines glycemic control, appetite suppression, reduction of visceral fat, and improvement of metabolic function, which positions it as a potentially effective therapeutic strategy for patients with OSA associated with obesity (MALHOTRA et al., 2024a).

The FDA's approval of tirzepatide for the treatment of OSA in 2025 marked a significant step in the expansion of the medication's clinical indications. This decision was supported by growing evidence of efficacy in reducing AHI, improving subjective sleep

parameters, and decreasing cardiovascular risk markers in patients with obesity-associated OSA (HASSAN; HASSAN; HASSAN, 2025).

In addition to respiratory benefits, there are indications that tirzepatide may contribute to the reduction of major adverse cardiovascular events (MACE) in patients with OSA and type 2 diabetes, as suggested by observational studies and real-world data, which reinforces its multidimensional therapeutic value (HENNEY et al., 2025).

Given the growing intersection between obesity, sleep-disordered breathing, and cardiometabolic risks, it is essential to understand the real impact of new pharmacological therapies on conditions such as obstructive sleep apnea. In this context, the present study aims to analyze the efficacy of tirzepatide in the treatment of obstructive sleep apnea, considering the mechanisms involved, the potential respiratory benefits and the metabolic factors, as well as the clinical and therapeutic implications observed in the most current scientific evidence

2 METHODOLOGY

This study is a narrative review of the literature, with the objective of consolidating current knowledge about the effects of tirzepatide in the treatment of obstructive sleep apnea, contributing to the advancement of therapeutic strategies aimed at this multifactorial condition of high prevalence. The bibliographic search was carried out in the PubMed, Scielo, LILACS, Scopus, Web of Science and Google Schoolar databases, using the Health Sciences Descriptors (DeCS): "obstructive sleep apnea", "tirzepatide", "GLP-1" and "pharmacological treatment", and their respective correspondents in English and Spanish, combined with Boolean operators "AND" and "OR".

The initial search resulted in 87 scientific articles. After reading titles and abstracts, 35 articles were selected for full reading. Of these, 13 studies fully met the inclusion criteria and made up the final sample of this review.

The inclusion criteria adopted were: studies published between 2022 and 2025, articles available in English, Spanish, or Portuguese, studies with human beings, publications that specifically addressed the use of tirzepatide in patients with obstructive sleep apnea, with or without obesity. The exclusion criteria included: exclusively experimental studies with animals, narrative reviews or letters without empirical basis, duplicate studies in the databases, and studies that addressed tirzepatide without a direct relationship with OSA.

All included studies were critically analyzed regarding their methodological design, population evaluated, type of intervention, primary and secondary outcomes, as well as limitations and clinical applicability. The evidence was organized into thematic categories,

according to the main focuses addressed: clinical efficacy, impact on OSA severity, comparisons with other therapies, and associated metabolic and cardiovascular effects.

3 RESULTS AND DISCUSSION

Tirzepatide is a drug for weekly subcutaneous use, belonging to the class of double agonists of GIP (gastric inhibitor polypeptide) and GLP-1 (glucagon-like peptide type 1) receptors. This innovative combination potentiates metabolic effects, such as increased insulin secretion in a glucose-dependent manner, inhibition of insulin secretion, and inhibition of insulin secretion glucagon, delayed gastric emptying and promotion of satiety. These mechanisms contribute synergistically to weight loss and improved glycemic control, and are fundamental in the treatment of obesity and, more recently, obstructive sleep apnea (AFRIDI et al., 2024).

In 2025, tirzepatide was approved by the FDA for the treatment of obstructive sleep apnea (OSA) in adults with obesity, after demonstrating clinical efficacy in phase 3 trials. This approval expanded the therapeutic scope of the molecule, previously restricted to the management of obesity and type 2 diabetes, and positioned tirzepatide as the first non-respiratory drug to obtain a formal indication for OSA (HASSAN; HASSAN; HASSAN, 2025).

The pathophysiological rationale for the use of tirzepatide in OSA is directly related to the reduction of visceral and cervical fat, the improvement of ventilatory mechanics, and the reduction of systemic inflammation, all factors that contribute to upper airway collapse during sleep. Studies in humans also suggest possible positive effects on autonomic control and pharyngeal muscle tone, although these mechanisms are still being investigated (EL-SOLH et al., 2024).

The SURMOUNT-OSA study, conducted by Malhotra et al. (2024a), is a randomized, double-blind, placebo-controlled, phase 3 clinical trial designed to evaluate the efficacy of tirzepatide in adults with obesity (BMI ≥ 30 kg/m²) and moderate to severe obstructive sleep apnea (OSA). The sample consisted of 469 participants, of whom 234 were allocated to receive tirzepatide in increasing doses up to 10 mg or 15 mg weekly, while the others received placebo, for a period of 52 weeks. The primary outcome was change in the apnea-hypopnea index (AHI) as measured by polysomnography, while secondary endpoints included weight loss, minimal oxygen saturation, daytime sleepiness (assessed by the Epworth scale), and metabolic markers. The results showed an average reduction of 55% in AHI in the tirzepatide group, compared to a 12% reduction in the placebo group, a statistically significant difference. In addition, patients who used tirzepatide had a mean reduction of 17.7% in body weight, significant improvement in nocturnal oxygen saturation, and a decrease in daytime

sleepiness scores, with positive implications for quality of life and cardiovascular outcomes associated with OSA (MALHOTRA et al., 2024a; MALHOTRA et al., 2024b).

In addition to the reduction in AHI, the study demonstrated important improvements in minimum nocturnal oxygen saturation, Epworth sleepiness score, and self-reported sleep quality. Participants also showed significant reduction in body weight and waist circumference, indicating that the respiratory effects were accompanied by an improvement in the metabolic profile (CHESKIN; RAJAGOPAL, 2024).

In the same vein, Ebell (2025) highlighted in a clinical article that tirzepatide promoted multidimensional benefits in patients with OSA, including improved sleep-related quality of life, reduced daytime fatigue, and less need for therapeutic escalation with positive pressure devices (EBELL, 2025).

In a comprehensive systematic review, several clinical studies investigating the effects of tirzepatide in patients with obstructive sleep apnea (OSA) were analyzed, with an emphasis on additional mechanisms beyond weight loss. The authors highlight that, although weight reduction contributes significantly to the improvement of OSA severity, tirzepatide has pleiotropic effects that go beyond the simple reduction of BMI. Among the mechanisms pointed out are the reduction of systemic inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), which are implicated in the pathogenesis of OSA and upper airway stiffness. The review also cites experimental data suggesting that tirzepatide may improve pharyngeal muscle tone and modulate neural pathways involved in respiratory control, resulting in improvement of nocturnal airway collapse. These findings support the hypothesis that the respiratory benefits observed with the use of tirzepatide do not derive exclusively from the loss of body fat, but also from an inflammatory and neuromuscular modulation that can act independently or complementarily (WEN et al., 2025).

A robust meta-analysis evaluated the effects of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) on obstructive sleep apnea (OSA), including studies with tirzepatide. The analysis covered 14 randomized controlled trials, totaling more than 1,800 adult participants diagnosed with OSA and obesity, most of whom had grade II or III obesity. The main outcomes evaluated were variation in the apnea-hypopnea index (AHI), sleep efficiency, nocturnal oxygen saturation, and weight loss. The results showed that all GLP-1 RAs promoted significant improvement in the AHI, however, the dual agonists – especially tirzepatide – showed superiority both in the magnitude of the AHI reduction and in the improvement of sleep architecture. This superiority was even more pronounced among patients with severe obesity, suggesting that tirzepatide may offer more robust clinical benefits for subgroups with greater respiratory impairment (LI et al., 2024).

Another retrospective multicenter study based on data from electronic medical records of hospital institutions in the United States aimed to compare the efficacy of tirzepatide with bariatric surgery in adults with severe obstructive sleep apnea (OSA) and grade II or III obesity.

1,212 patients, of whom 606 were treated with tirzepatide and 606 with bariatric surgery. The main outcomes analyzed included the variation in the apnea-hypopnea index (AHI), quality of life markers, complication rates, and associated costs. Tirzepatide has been shown to be non-inferior to bariatric surgery in reducing AHI, with comparable clinical efficacy in improving sleep quality and overall well-being. In addition, the tirzepatide group had a lower rate of post-treatment adverse events (6.2% versus 14.8%) and a lower mean cost of treatment per patient, suggesting an effective and more affordable therapeutic alternative for the management of severe OSA in patients with severe obesity (WU et al., 2025).

In turn, Henney et al. (2025), conducted a real-world analysis using data from large-scale clinical registries in the United States, focusing on patients with OSA and type 2 diabetes. The study compared the efficacy of tirzepatide, semaglutide and liraglutide in reducing major adverse cardiovascular events (MACE) and clinically relevant weight loss. The cohort analyzed included more than 8,000 patients divided between the three therapeutic groups, followed for up to 18 months. Tirzepatide demonstrated the greatest reduction in MACE, including acute myocardial infarction, stroke, and cardiovascular death, and had the highest percentage of patients who achieved weight loss ≥15% (43% with tirzepatide versus 31% with semaglutide and 22% with liraglutide). These findings reinforce the superior profile of tirzepatide in the combined management of OSA, obesity, and elevated cardiovascular risk (HENNEY et al., 2025).

The use of tirzepatide in perioperative settings of patients with severe OSA is also noteworthy, reaching the conclusion that the drug contributes to better preoperative preparation, lower anesthetic risk and reduced need for intensive CPAP in the immediate postoperative period (KUKANTI; CHOWDHURY; SINGH, 2025).

In this same context, a mathematical modeling analysis was performed based on SURMOUNT-OSA data, in which it was estimated that the use of tirzepatide can lead to a reduction of up to 30% in overall cardiovascular risk in patients with OSA and obesity, especially when continuous use of the medication is maintained for 12 months or more (BECCUTI et al., 2024).

Compared to other pharmacological therapies, such as liraglutide and semaglutide, tirzepatide has greater efficacy in reducing AHI, greater impact on weight loss, and lower

discontinuation rate due to adverse effects, as discussed by El-Solh et al. (2024) in a narrative review on the topic (EL-SOLH et al., 2024).

In addition to the direct effects on OSA, tirzepatide also promotes clinical improvements in associated conditions, such as insulin resistance, hypertension, and dyslipidemia, composing a multisystem treatment profile that benefits OSA patients globally (HENNEY et al., 2025).

From a safety point of view, the most common adverse events were mild gastrointestinal events, such as nausea and diarrhea, which were usually self-limiting and did not require treatment discontinuation. The discontinuation rate was less than 10% in the main clinical trials (MALHOTRA et al., 2024b).

The introduction of tirzepatide as a therapeutic approach for obstructive sleep apnea (OSA) has been shown to be especially relevant for patients who have poor adherence or intolerance to the use of continuous positive airway pressure (CPAP) devices. The medication promotes not only a significant reduction in the apnea-hypopnea index (AHI), but also improves metabolic parameters, such as fasting glucose, lipid profile, and blood pressure, aspects that are frequently altered in patients with OSA and obesity. It is noteworthy that the ease of weekly subcutaneous administration and the multisystem impact of the medication represent a practical and promising alternative for individuals who do not adhere to CPAP. In addition, an analysis of adult patients with moderate to severe OSA showed that tirzepatide reduced the number of respiratory events per hour compared to placebo, even in individuals who were not on ventilatory support. The authors suggest that the effect of the medication may extend beyond weight loss, considering the potential anti-inflammatory effects and improvement of upper airway neuromuscular function. Thus, tirzepatide emerges as a viable pharmacological intervention, capable of benefiting patients with multiple metabolic and respiratory comorbidities who face barriers with conventional treatment (EBELL, 2025; CHESKIN; RAJAGOPAL, 2024).

Tirzepatide represents a significant break in the traditional paradigms of the treatment of obstructive sleep apnea (OSA) associated with obesity, because, unlike mechanical approaches such as the use of CPAP, which only attenuate symptoms by keeping the airways open during sleep, tirzepatide acts at the root of the pathophysiological problem. Its mechanism of action promotes substantial weight loss, reduction of central adiposity and improvement of insulin sensitivity, elements directly related to the genesis and worsening of OSA in obese individuals. In addition, its anti-inflammatory and metabolic effects contribute to systemic modulation that can reduce upper airway collapsibility. This systemic pharmacological approach proposes not only nocturnal symptom relief but also a positive

impact on the factors underlying the pathology, offering a potentially longer-lasting and more comprehensive solution than exclusively symptomatic treatments (AFRIDI et al., 2024).

The implications of the approval of the drug for oral health professionals and interdisciplinary teams are also highlighted, highlighting the need to update protocols and greater integration of care in OSA (HASSAN; HASSAN; HASSAN, 2025).

Therefore, based on the evidence gathered, it is possible to affirm that tirzepatide represents an effective and safe therapeutic strategy in the treatment of obstructive sleep apnea, especially in patients with moderate to severe obesity, bringing together respiratory, metabolic, and cardiovascular benefits with a good tolerability profile.

4 CONCLUSION

Tirzepatide has stood out as one of the most promising approaches in the management of obstructive sleep apnea (OSA) associated with obesity, demonstrating superior clinical efficacy both in reducing the apnea-hypopnea index and in improving several metabolic and cardiovascular parameters. By acting directly on the etiology of the disorder, especially through significant weight loss, this medication inaugurates a new era in the treatment of OSA, going beyond purely mechanical strategies.

High-quality clinical studies and comparative analyses reinforce the superiority of tirzepatide over other pharmacological options and even over bariatric surgery in certain contexts. The additional benefits on systemic inflammation, lipid profile, and treatment adherence make its use especially relevant in patients with multiple comorbidities.

Thus, tirzepatide is consolidated as an effective, safe, and broad-spectrum therapeutic option, contributing not only to the control of OSA, but also to a comprehensive approach to the metabolic health of these patients. The advance represents an important milestone in the care of a population that is often neglected and refractory to conventional therapies.

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