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Brief Communication

Efficacy and safety of GLP-1 receptor agonists in the management of obstructive sleep apnea in individuals without diabetes: A systematic review and meta-analysis of randomized, placebo-controlled trials

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is a common sleep disorder that disrupts breathing during sleep. While continuous positive airway pressure therapy is the standard treatment, poor adherence has led to exploration of alternative treatments. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have been shown to reduce body weight and may help manage OSA. This systematic review and meta-analysis evaluated the efficacy and safety of GLP-1 RAs in individuals with OSA and elevated body weight who are without diabetes.

Methods: A systematic search was conducted in September 2024 across multiple databases. Randomized controlled trials (RCTs) evaluating GLP-1 RAs for OSA in adults with a body mass index (BMI) $\geq$30 kg/m^2 were included. The primary outcomes were changes in the apnea-hypopnea index (AHI) and overall adverse events. Meta-analyses were performed using a random-effects model.

Results: Three RCTs were included in the analysis. Pooled results showed that GLP-1 RA treatment significantly reduced AHI compared to placebo, with a weighted mean difference (WMD) of −16.6 events per hour (95 % confidence interval [CI]: −27.9 to −5.3). However, GLP-1 RAs were associated with a higher frequency of adverse events, with an odds ratio (OR) of 1.62 (95 % CI: 1.16 to 2.24) compared to placebo.

Conclusion: GLP-1 RAs effectively reduce OSA severity, offering a promising alternative for individuals with OSA and elevated body weight. However, the increased risk of side effects must be considered. Further long-term studies are needed to confirm the sustained benefits and safety of GLP-1 RAs in OSA management.

1. Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder characterized by recurrent airway obstruction during sleep, leading to intermittent hypoxemia and disrupted sleep patterns [1]. Affecting 14 % of men and 5 % of women, OSA is linked to daytime sleepiness, cognitive impairment, reduced quality of life, and increased risks of cardiovascular disease, diabetes, and stroke [2–5].

Excess body weight is a major risk factor for OSA, contributing to airway narrowing and impaired respiratory mechanics [6]. OSA and weight gain have a bidirectional relationship, as OSA can also promote weight gain by disrupting sleep [7,8]. While continuous positive airway pressure (CPAP) is the gold standard for treating OSA, poor adherence due to discomfort has spurred interest in alternative treatments, especially for non-diabetic individuals [9]. Although weight loss reduces OSA severity, maintaining it through lifestyle changes is often difficult [10].

Pharmacologic treatments like glucagon-like peptide-1 receptor agonists (GLP-1 RAs), initially developed for blood sugar control, are now being explored for their ability to reduce body weight and improve OSA [11,12]. However, evidence on their efficacy and safety, particularly in populations without diabetes, remains limited.

This systematic review and meta-analysis evaluated the effects of GLP-1 RAs on OSA severity in individuals without diabetes, focusing on changes in Apnea–Hypopnea Index (AHI) and adverse events. By synthesizing data from randomized controlled trials, this study aimed to

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clarify the potential benefits and risks of GLP-1 RAs for managing OSA in those with elevated body weight who are without diabetes.

2. Methods

2.1. Study design

This systematic review and meta-analysis followed the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [13].

2.2. Search strategy

A comprehensive search was conducted to identify relevant randomized controlled trials (RCTs) evaluating the effect of GLP-1 RAs on OSA severity and overall adverse events. The search was performed in September 2024, covering studies published from inception to September 11, 2024. The following electronic databases were searched: PubMed, Embase, Cochrane Central Register of Controlled Trials, and Scopus. Keywords and Medical Subject Headings terms used in the search included: "obstructive sleep apnea," "OSA," "apnea-hypopnea index," "AHI," "glucagon-like peptide-1 receptor agonists," "GLP-1 RAs," "weight loss," "obesity," and "randomized controlled trial." The search was limited to studies published in English within the specified date range.

2.3. Eligibility criteria

Included studies were randomized controlled trials (RCTs) involving adults (≥18 years) with moderate-to-severe obstructive sleep apnea (OSA) and a body mass index (BMI) of ≥30 kg/m^2. The intervention was GLP-1 receptor agonists (GLP-1 RAs) at any dose, compared to placebo. Primary outcomes included changes in apnea-hypopnea index (AHI) and overall adverse events. Studies were excluded if they involved patients with central sleep apnea, type 1 or 2 diabetes, or if they lacked outcome data for AHI or adverse events. Only studies published in English were considered.

2.4. Data extraction and management

Two independent reviewers (CSK and DSR) screened the titles and abstracts of all studies identified in the search. Full texts of potentially eligible studies were retrieved and assessed for eligibility. Any discrepancies between reviewers were resolved through discussion or consultation with a third reviewer (SSH).

A standardized data extraction form was used to gather study details, including author, year, location, design, sample size, and follow-up duration. Participant information such as age, BMI, baseline AHI, and use of nasal CPAP was recorded. Data on the type, dose, and duration of GLP-1 RA interventions were also collected. The primary outcomes were changes in AHI and the frequency of adverse events.

2.5. Risk of bias assessment

The risk of bias for each study was independently assessed by two reviewers (CSK and SSH) using the Cochrane Risk of Bias Tool [14]. Key domains included random sequence generation, allocation concealment, blinding, completeness of outcome data, selective reporting, and other biases. Disagreements were resolved through discussion or with a third reviewer (KT). Studies were rated as low risk if all domains were low risk, some concerns if one domain raised concerns but none were high risk, and high risk if one or more domains were rated high risk.

2.6. Statistical analysis

Meta-analyses were conducted using MetaXL version 5.3 (EpiGear International Pty Ltd, Queensland, Australia), which employs the inverse variance method to pool data using a random-effects model. This method was chosen to account for variability across studies.

The mean difference in AHI (events per hour) between the GLP-1 RA and control groups was calculated using weighted mean differences (WMD) with 95 % confidence intervals (CIs), ensuring that the estimates account for study-specific variances. The frequency of adverse events was compared between the GLP-1 RA and placebo groups using odds ratios (ORs) with 95 % CIs, providing a measure of the relative likelihood of adverse events across groups.

Heterogeneity was evaluated using the I^2 statistic where values > 50 % indicated substantial heterogeneity, suggesting considerable variation between studies. Heterogeneity was also evaluated using the Cochran's Q test, where a p-value <0.10 suggested significant heterogeneity, indicating non-random variability in study outcomes.

3. Results

3.1. Study selection

Our search was compliant to the PRISMA 2020 statement (Supplementary Materials 1 and 2). The initial search yielded a total of 155 studies. After removing duplicates, 55 titles and abstracts were screened for eligibility. Of these, seven full-text articles were assessed for inclusion based on the predefined criteria. Following full-text review, three RCTs from two studies [15,16] met the eligibility criteria and were included in the systematic review and meta-analysis.

3.2. Study characteristics

The included studies [15,16] consisted of three randomized, double-blind, placebo-controlled trials conducted across multiple countries. The trials involved adults with moderate-to-severe OSA and obesity, with no baseline use of nasal CPAP therapy in two studies. Participants in the GLP-1 RA groups were administered subcutaneous liraglutide or tirzepatide at escalating doses, with liraglutide reaching 3.0 mg/day and tirzepatide titrated up to 10–15 mg weekly, for 32–52 weeks. The average age of participants ranged from 47.3 to 52.7 years, with baseline AHI ranging from 46.1 to 53.1 events per hour, and body mass index (BMI) between 38.6 and 39.7 kg/m^2 across the trials. Table 1 provides a summary of the characteristics of the included studies. All included RCTs were found to have an overall low risk of bias.

Pooled analysis of the included RCTs demonstrated a significant reduction in AHI with GLP-1 RA treatment compared to placebo. The WMD in AHI was −8.00 events per hour (95 % CI, −13.57 to −2.43, indicating a statistically significant improvement in OSA severity with GLP-1 RA therapy (see Fig. 1). Pooled analysis showed that the OR for the occurrence of adverse events in the GLP-1 RA group versus the placebo group was 1.62 (95 % CI, 1.16 to 2.24), indicating a significantly higher frequency of adverse events in the GLP-1 RA group compared to placebo.

4. Discussion

This systematic review and meta-analysis highlight the significant efficacy of GLP-1 RAs in improving OSA severity. The results indicate that GLP-1 RAs effectively reduce the AHI, demonstrating their potential as a viable treatment option for individuals with moderate-to-severe OSA. This reduction in AHI can lead to improved sleep quality, reduced daytime fatigue, and potentially lower the risk of cardiovascular and metabolic complications associated with untreated OSA [17]. These findings suggest that GLP-1 RAs could be particularly beneficial for individuals who may not respond well to or adhere to continuous CPAP therapy.

However, it is important to note that while our findings highlight the efficacy of GLP-1 RAs in improving OSA severity, these agents are not a

Table 1
Characteristics of included trials.

Study (Year)	Location	Study design	Number of participants	Mean age (years)	Baseline apnea-hypopnea index (events/hour)	Body mass index	Nasal continuous positive airway pressure therapy at baseline	Regimen of GLP-1 RA	Change in apnea-hypopnea index (events/hour)		Any adverse events (n/N; %)		Overall risk of bias
									GLP-1 RA	Placebo	GLP-1 RA	Placebo	
Blackman et al. (2016) [15]	2 countries	Randomized, double-blinded, placebo-controlled trial	GLP-1 RA group: 168 Placebo group: 166	GLP-1 RA group: 48.6 Placebo group: 48.4	GLP-1 RA group: 49.0 Placebo group: 49.3	GLP-1 RA group: 38.9 Placebo group: 39.4	No	Subcutaneous liraglutide started at 0.6 mg/day dose and escalated in weekly 0.6-mg increments to 3.0 mg/day, which was maintained for another 28 weeks	−12.2 ± 1.8	−6.1 ± 2.0	141/176; 80.1	124/179; 69.3	Low
SURMOUNT-OSA 1 (2024) [16]	9 countries	Randomized, double-blinded, placebo-controlled trial	GLP-1 RA group: 114 Placebo group: 120	GLP-1 RA group: 47.3 Placebo group: 48.4	GLP-1 RA group: 52.9 Placebo group: 50.1	GLP-1 RA group: 39.7 Placebo group: 38.6	No	Subcutaneous tirzepatide started at 2.5 mg once weekly dose and increased by 2.5 mg every 4 weeks until the maximum tolerated dose of 10–15 mg in week 20, which was maintained for another 32 weeks	−25.3 ± 2.1	−5.3 ± 2.1	91/114; 79.8	92/120; 76.7	Low
SURMOUNT-OSA 2 (2024) [16]	9 countries	Randomized, double-blinded, placebo-controlled trial	GLP-1 RA group: 120 Placebo group: 115	GLP-1 RA group: 50.8 Placebo group: 52.7	GLP-1 RA group: 46.1 Placebo group: 53.1	GLP-1 RA group: 38.6 Placebo group: 38.7	Yes	Subcutaneous tirzepatide started at 2.5 mg once weekly dose and increased by 2.5 mg every 4 weeks until the maximum tolerated dose of 10–15 mg in week 20, which was maintained for another 32 weeks	−29.3 ± 2.0	−5.5 ± 2.2	99/119; 83.2	83/114; 72.8	Low

substitute for continuous positive airway pressure (CPAP) therapy, which remains the gold standard treatment. Instead, GLP-1 RAs may serve as an adjunct or alternative in cases where CPAP adherence is poor, or in individuals whose OSA severity is primarily weight-related. Additionally, lifestyle changes, including dietary modifications and increased physical activity, are foundational to long-term weight management and OSA improvement. Incorporating GLP-1 RAs into a broader treatment plan that includes lifestyle interventions and CPAP therapy could provide synergistic benefits, addressing both the mechanical and metabolic contributors to OSA. Future studies investigating the combination of these strategies are needed to optimize outcomes for OSA management.

The mechanism behind the efficacy of GLP-1 RAs in reducing OSA severity is likely linked to their ability to promote weight loss. Excess body weight contributes to the narrowing of the upper airway, making airway collapse during sleep more likely [18]. By reducing body fat, particularly in areas such as the neck and upper airway, GLP-1 RAs may help alleviate airway obstruction [19]. Furthermore, GLP-1 RAs improve metabolic health, reducing inflammation and enhancing insulin sensitivity, which may indirectly contribute to better airway function and reduced OSA severity [20].

While GLP-1 RAs are effective in reducing OSA severity, they are associated with an increased frequency of adverse events, primarily gastrointestinal in nature [15,16]. Commonly reported side effects include nausea, vomiting, and diarrhea, which are consistent with the known side effect profile of GLP-1 RAs. Although these adverse events are generally mild to moderate, they can affect patient adherence and overall treatment satisfaction. Clinicians should carefully consider these potential side effects when prescribing GLP-1 RAs for OSA management, especially in patients who may be prone to gastrointestinal discomfort.

This review has limitations that may affect the interpretation of results. The small number of included studies limits the generalizability across populations and settings. Additionally, the trials had follow-up periods of up to 52 weeks, leaving uncertainty about the long-term efficacy and safety of GLP-1 RAs in managing OSA. Longer-term studies are needed to assess the durability of AHI improvements and the consistency of the safety profile with extended use. Furthermore, while AHI reduction is a critical marker of OSA improvement, it does not fully encompass treatment efficacy. Effective OSA management ultimately aims to alleviate symptoms such as excessive daytime sleepiness, improve quality of life (QoL), and mitigate long-term health risks. Unfortunately, the included studies did not evaluate these patient-reported outcomes. This represents a gap in the current evidence and highlights the need for future research to explore how GLP-1 RAs impact symptom burden and QoL in OSA patients.

Conclusion

This systematic review and meta-analysis show that GLP-1 RAs significantly reduce the AHI, offering a promising treatment for moderate-to-severe OSA. While effective, GLP-1 RAs are associated with an increased risk of gastrointestinal side effects, which may affect patient adherence. Further long-term studies are needed to confirm the sustained benefits and safety of GLP-1 RAs in OSA management.

CRediT authorship contribution statement

Chia Siang Kow: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Dinesh Sangarran Ramachandram:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Syed Shahzad Hasan:** Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization. **Kaeshaelya Thiruchelvam:** Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization.

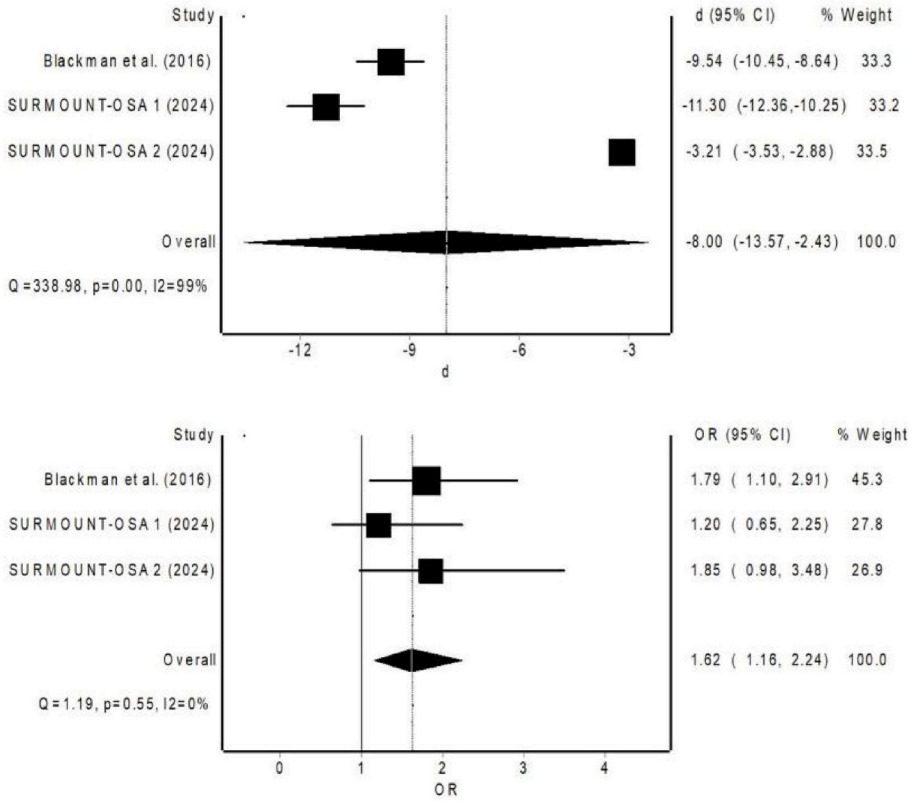

Fig. 1. Pooled weighted mean difference of Apnea–Hypopnea Index and pooled odds ratio of the occurrence of adverse events with GLP-1 RA treatment compared to placebo.

Ethics statement

Not applicable.

Data sharing and data availability

Not applicable.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2025.02.010.

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