World Journal of Experimental Medicine

Submit a Manuscript: https://www.f6publishing.com

World J Exp Med 2025 December 20; 15(4): 109762

DOI: 10.5493/wjem.v15.i4.109762

ISSN 2220-315x (online)

MINIREVIEWS

Dual incretin analogue tirzepitide - SURMOUNTing the challenge of obesity induced obstructive sleep apnea

Jyoti Bajpai, Mehul Saxena, Utkarsh Agarwal, Akshyaya Pradhan

Specialty type: Medicine, research and experimental

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade C
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade C

P-Reviewer: Cordovil K, PhD, Consultant, Professor, Researcher, Brazil

Received: May 21, 2025
Revised: June 11, 2025
Accepted: October 11, 2025
Published online: December 20, 2025
Processing time: 212 Days and 15.4 Hours

Jyoti Bajpai, Department of Respiratory Medicine, King George's Medical University, Lucknow 226003, Uttar Pradesh, India

Mehul Saxena, Gandhi Memorial Hospital, King George's Medical University, Lucknow 226003, Uttar Pradesh, India

Utkarsh Agarwal, Faculty of Medical Sciences, King George's Medical University, Lucknow 226003, Uttar Pradesh, India

Akshyaya Pradhan, Department of Cardiology, King George's Medical University, Lucknow 226003, Uttar Pradesh, India

Corresponding author: Akshyaya Pradhan, Department of Cardiology, King George's Medical University, Shahmina Road, Chowk, Lucknow 226003, Uttar Pradesh, India.
akshyaya33@gmail.com

Abstract

Obstructive sleep apnea (OSA) is a prevalent and underdiagnosed sleep disorder strongly associated with obesity. Traditional therapies such as continuous positive airway pressure are effective but often limited by poor adherence. Recent evidence suggests that tirzepatide, a dual glucagon like receptor-1 and glucose dependent insulinotropic polypeptide receptor agonist, may offer a pharmacologic approach to OSA management through its weight-reducing and metabolic effects. This narrative review was conducted using a structured search of PubMed, Google Scholar, and Scopus databases for English-language articles published up to May 2024. Keywords included "tirzepatide", "obstructive sleep apnea", "OSA", and "GLP-1 agonist". Clinical trials, systematic reviews, and relevant observational studies focusing on tirzepatide's role in OSA or obesity were included and thematically analyzed. Emerging evidence from the SURMOUNT-OSA and related trials indicates that tirzepatide leads to clinically significant reductions in body weight, apnea-hypopnea index, and systemic inflammation. The drug was found to be effective and also showed additional benefits in sleep quality and cardiovascular risk factors. Tirzepatide represents a promising pharmacologic advancement in the management of obesity-related OSA. By targeting both metabolic and structural contributors to OSA, it may serve as an adjunct or alternative to traditional therapies. Further research is warranted to evaluate long-term outcomes and to define its role in clinical practice guidelines.

Key Words: Apnea hypopnea index; Weight loss; Continuous positive airway pressure; Glucagon like receptor-1; SURMOUNT-1 trial

Core Tip: Obstructive sleep apnea (OSA) is a serious sleep disorder often caused by obesity. Standard treatments like continuous positive airway pressure can help, but many people struggle to use them long term. Tirzepatide, a new medication that targets both glucagon-like peptide-1 and gastric inhibitory polypeptide receptors, offers a different approach. By helping with significant weight loss and improving breathing during sleep, tirzepatide has shown strong results in the SURMOUNT-OSA trial, making it the first approved drug to directly treat obesity-related OSA.

Citation: Bajpai J, Saxena M, Agarwal U, Pradhan A. Dual incretin analogue tirzepitide - SURMOUNTing the challenge of obesity induced obstructive sleep apnea. *World J Exp Med* 2025; 15(4): 109762
URL: https://www.wjgnet.com/2220-315x/full/v15/i4/109762.htm
DOI: https://dx.doi.org/10.5493/wjem.v15.i4.109762

INTRODUCTION

Obesity is a rapidly growing global health issue that contributes significantly to a wide spectrum of chronic diseases. Among these, obstructive sleep apnea (OSA) stands out as both highly prevalent and underdiagnosed. OSA is a sleep-related breathing disorder marked by recurrent episodes of partial or complete obstruction of the upper airway during sleep, resulting in intermittent hypoxia and arousals that disrupt normal sleep architecture[1]. These respiratory events often occur during the rapid eye movement phase of sleep, when muscle tone decreases and pharyngeal collapsibility increases. In obese individuals, adipose deposition around the neck and airway further exacerbates airway narrowing, predisposing them to more frequent and severe obstructive events[2,3]. The relationship between obesity and OSA is well-established. Excess body weight, particularly central adiposity, contributes to compromised airway patency by increasing parapharyngeal fat and decreasing chest wall compliance[4]. While anatomical and neuromuscular factors, such as macroglossia, retrognathia, enlarged tonsils, and impaired pharyngeal dilator muscle responsiveness also play a role, obesity remains the most modifiable and influential risk factor[5,6]. Furthermore, OSA frequently coexists with metabolic conditions such as type 2 diabetes mellitus (T2DM), insulin resistance, dyslipidemia, and systemic inflammation, creating a vicious cycle of cardiometabolic dysfunction[7,8].

Current standard treatments for OSA, such as continuous positive airway pressure (CPAP), effectively reduce apnea-hypopnea index (AHI) and improve sleep quality, but long-term adherence remains suboptimal due to discomfort and inconvenience[9,10]. Weight reduction is consistently associated with improvement in OSA severity, yet durable lifestyle-based solutions remain elusive[11]. While surgical and device-based therapies offer alternatives, none directly target the underlying metabolic drivers of the disease. In this context, pharmacologic approaches that promote significant and sustained weight loss have gained interest. Tirzepatide, a novel dual agonist of glucagon-like peptide-1 (GLP-1) and glucose dependent insulinotropic polypeptide (GIP) receptors, has emerged as a promising therapy for both obesity and T2DM. In recent clinical trials, tirzepatide has demonstrated superior efficacy in weight reduction compared to existing GLP-1 receptor agonists, with additional benefits in glycemic control and cardiometabolic risk reduction[12-15]. The Food and Drug Administration (FDA) has recently approved tirzepatide for use in patients with moderate-to-severe OSA and obesity, based on evidence from the landmark SURMOUNT-OSA trial showing substantial improvements in AHI and metabolic parameters.

This narrative review aims to explore the interrelationship between obesity and OSA, assess limitations of current treatment strategies, and critically evaluate the emerging role of tirzepatide, a dual GLP-1 and GIP receptor agonist and its use as a novel pharmacological intervention for obesity-associated OSA based on recent clinical trial evidence.

METHODOLOGY

This narrative review was conducted to explore the current evidence surrounding the use of tirzepatide in the management of obesity-related OSA. A comprehensive literature search was carried out across multiple databases, including PubMed, Scopus, EMBASE, and Google Scholar, covering publications upto May 2025.

Search terms included a combination of keywords and Medical Subject Headings such as: "tirzepatide", "SURMOUNT trials", "obesity", "obstructive sleep apnea", "OSA", "GIP", "GLP-1", "twincretin", "weight loss", and "sleep-disordered breathing". Boolean operators (AND/OR) were used to enhance the search strategy.

Studies were included if they were published in English and comprised clinical trials, randomized controlled trials, narrative reviews, systematic reviews, or meta-analyses that investigated tirzepatide in the context of obesity, OSA, or both. Articles were excluded if they were animal studies, preclinical or *in vitro* investigations, non-peer-reviewed articles,

editorials, or studies that did not focus on tirzepatide or its relationship with either obesity or OSA.

The initial screening was based on titles and abstracts, followed by a full-text review of potentially relevant articles. As this is a narrative review, formal quality appraisal tools were not applied; however, emphasis was placed on including high-quality, peer-reviewed studies, especially recent clinical trials and large cohort studies that provided substantive evidence on the subject.

WHAT IS OSA?

OSA is characterized by repeated interruptions of breathing during sleep[1]. These episodes primarily occur during the rapid eye movement phase of sleep, when muscle tone throughout the body, including the throat muscles, is reduced[2]. This relaxation allows the tongue to partially block the airway. In individuals with obesity, the pharyngeal inlet is already narrowed, and even a slight posterior displacement of the tongue can severely restrict airflow, leading to complete (apnea) or partial (hypopnea) loss of breathing[3]. Such episodes result in reduced oxygen levels (hypoxia) and brief, often unnoticed, arousals from sleep to restore normal breathing.

Common signs and symptoms of OSA include loud, persistent snoring, gasping, choking, or snorting during sleep, pauses in breathing (apneas), and excessive daytime sleepiness (hypersomnia), all indicative of disrupted sleep quality. Additional frequently reported symptoms are morning headaches, difficulty concentrating, memory issues, irritability, and mood swings[4].

Several factors contribute to the risk of developing OSA. Obesity, particularly an increased neck circumference, stands out as a primary risk factor due to its potential to obstruct the airway. Beyond obesity, other factors also play a significant role. These include various anatomical features like enlarged tonsils, a thick neck, hypognathia, a retracted mandible, or a narrow airway[4]. Muscle relaxation can also contribute, as it causes the tongue and soft tissues at the back of the throat to collapse[4]. Age is another important factor, with OSA being more prevalent among middle-aged and older adults[4]. Gender also influences risk, as men are more prone to developing OSA, though postmenopausal women also face an elevated risk[4]. Furthermore, a genetic predisposition, often indicated by a family history of narrow airways or obesity, can increase an individual's susceptibility[4]. Finally, certain lifestyle choices, such as smoking, alcohol consumption, the use of sedatives, and sleeping in the supine position, can worsen airway collapse[4-6]. OSA is associated with several serious health consequences including hypertension, heart disease, stroke, increased risk of left ventricular hypertrophy, irregular heartbeats (arrhythmias), heart failure, T2DM, depression, and anxiety. Furthermore, OSA-related daytime sleepiness can impair reaction time, increasing the risk of workplace errors and motor vehicle crashes[7,8].

CURRENT TREATMENT STRATEGIES FOR OSA

Sleep apnea treatment is broadly categorized into behavioral, medical, and surgical approaches. Treatment decisions should consider the impact on daytime symptoms and cardiopulmonary function, not solely the frequency of apneic episodes. The primary goals are to restore normal nighttime ventilation by preventing upper-airway closure and reducing snoring[1].

Behavioral interventions

Lifestyle modifications are often the first line of behavioral intervention. These include weight loss, avoidance of alcohol and sedatives, and positional therapy. Alcohol consumption exacerbates sleep apnea by relaxing upper-airway muscles, prolonging apneic episodes, and diminishing arousal responses[16]. In individuals with obesity, weight loss significantly improves apnea severity[11]. Positional training, encouraging lateral sleeping, can be beneficial for patients whose upper-airway obstruction primarily occurs in the supine position, though its long-term effectiveness is uncertain[17].

Medical treatments

Positive airway pressure therapy: This is the primary medical intervention for clinically significant sleep apnea[9]. Devices like CPAP and bilevel positive airway pressure (PAP) deliver pressurized air *via* a mask to prevent upper airway collapse. CPAP is highly effective in improving neuropsychiatric function, reducing daytime sleepiness, and alleviating complications such as nocturnal desaturation, cardiac arrhythmias, pulmonary hypertension, and right-sided heart failure[18-20]. However, patient compliance remains a significant challenge, with only about 46% using CPAP for the recommended duration[10]. Side effects, including nasal congestion, dryness, and discomfort, can often be managed with humidification, antihistamines, or corticosteroids[9]. Nasal prongs or bilevel PAP systems may improve comfort for patients experiencing claustrophobia or those needing different pressures during inhalation and exhalation, respectively [21].

Oral appliances: These devices serve as an alternative for patients unable to tolerate PAP therapy. They reposition the jaw or tongue to maintain airway patency and are generally more suitable for individuals with mild sleep apnea. While typically well-tolerated, their effectiveness varies, and close monitoring by both a physician and a dental specialist is recommended to prevent complications like temporomandibular joint discomfort[22,23].

Pharmacological treatments: Medications have shown limited success. Protriptyline and fluoxetine may offer mild benefits but are generally ineffective in severe cases[24]. Thyroxine replacement therapy can improve airway function in

patients with hypothyroidism[22]. Oxygen therapy may benefit patients with severe desaturation who cannot tolerate other treatments, though it does not consistently shorten apneic episode duration[25].

Surgical interventions

Surgical intervention is considered for individuals who cannot tolerate or respond to medical therapy. Tracheostomy, while highly effective, is largely reserved for severe cases due to associated morbidity[26]. Uvulopalatopharyngoplasty is the most commonly performed surgical procedure, but its success rate is less than 50% and it may not address obstructions at other airway sites[27]. Laser-assisted Uvulopalatopharyngoplasty is not recommended for sleep apnea treatment[28]. Maxillofacial surgeries, such as genioglossal advancement and hyoid suspension, can improve airway patency but require specialized surgical teams. Maxillomandibular advancement can be beneficial for patients with craniofacial abnormalities or those who have failed other procedures, but it is typically reserved for those unable to tolerate CPAP therapy[29].

Ultimately, OSA treatment should be individualized based on symptom severity, patient preferences, and response to initial therapy. Notably, prior to tirzepatide's approval, no specific medication was available for OSA, positioning tirzepatide as the first drug for obesity-induced OSA.

TIRZEPATIDE: A NOVEL THERAPEUTIC AGENT

Tirzepatide was approved by the United States FDA in May 2022 for the treatment of T2DM. It operates by simultaneously activating two key receptors: GLP-1 and GIP[12]. This dual mechanism confers greater efficacy compared to single GLP-1 receptor agonists like semaglutide[12]. Tirzepatide is generally prescribed as a second-line treatment for T2DM and is administered as a once-weekly injection, with the dosage gradually increasing over time[13].

EFFICACY IN T2DM AND WEIGHT LOSS

Clinical trials have demonstrated significant therapeutic benefits of tirzepatide. In the SURPASS-5 study, participants receiving 5 mg per week showed a 2.11% reduction in glycated hemoglobin A1c (HbA1c) levels, compared to a 0.86% reduction in the placebo group. At the highest dose of 15 mg per week, HbA1c reduction increased to 2.34%. Significant weight loss was also observed, with average losses of 5.4 kg on the 5 mg dose and 10.5 kg on the 15 mg dose, comparable to semaglutide[14].

Tirzepatide has shown superior results in both blood sugar control and weight loss when compared to other diabetes treatments such as semaglutide, dulaglutide, and long-acting insulins (degludec and glargine). Consequently, the American Diabetes Association recognizes tirzepatide as a highly effective treatment option[15,30]. Beyond its antidiabetic properties, tirzepatide's significant weight-loss effects and lack of liver toxicity suggest potential therapeutic value in managing nonalcoholic fatty liver disease, although further research is needed for official recommendation[31].

Mechanism of action

Tirzepatide, a dual GIP and GLP-1 receptor (GLP-1R) agonist (a "twincretin"), functions by stimulating insulin release, lowering blood sugar levels, increasing adiponectin levels to enhance metabolism, and suppressing appetite, leading to sustained weight loss (Figure 1)[32]. It also improves insulin sensitivity and β-cell function, contributing to effective metabolic control[32].

Incretins, including GIP and GLP-1, are gut-derived hormones released by specialized endocrine cells in the small intestine in response to nutrient intake. Their primary role is to stimulate insulin secretion from pancreatic β-cells[33]. Both GIP and GLP-1 bind to their respective G-protein-coupled receptors, increasing intracellular cyclic adenosine monophosphate levels in pancreatic β-cells, thus enhancing glucose-dependent insulin secretion[34].

Beyond insulinotropic actions, these hormones play significant roles in various tissues and organs expressing their receptors (*e.g.*, pancreas, adipose tissue, bone, brain). In the pancreas, they promote β-cell proliferation and inhibit apoptosis, preserving β-cell mass. GIP facilitates postprandial glucagon response, while GLP-1 suppresses it. In adipose tissue, GIP promotes fat storage, a characteristic not shared by GLP-1. GIP also stimulates bone formation, while GLP-1 reduces bone absorption. Both hormones are implicated in appetite regulation and cognitive functions like memory[35]. GLP-1 receptor agonists mimic natural GLP-1 effects, promoting insulin release, reducing blood sugar, and delaying gastric emptying. Similarly, GIP receptor agonists enhance insulin secretion and regulate blood sugar while potentially reducing appetite and food intake for weight management[34].

PHARMACOKINETICS AND ADMINISTRATION

Tirzepatide exhibits approximately 80% bioavailability, reaching peak serum levels within 8 hours to 72 hours post-administration. It has a volume of distribution of approximately 10.3 L, with 99% binding to plasma albumin. Metabolism occurs in the liver *via* proteolytic cleavage and β-oxidation into amino acids. With a half-life of five days, it is eliminated through urine and feces, enabling convenient weekly dosing. Currently, tirzepatide is administered *via* subcutaneous

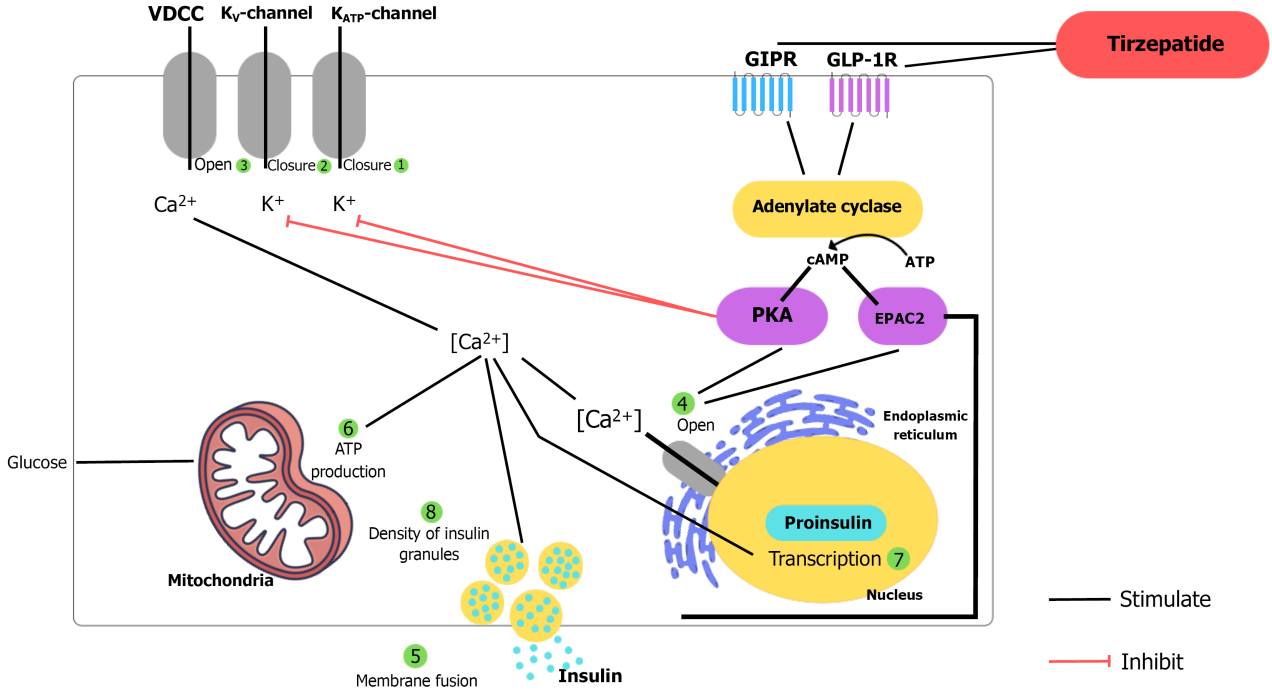

Figure 1 Schematic representation of the mechanism of action of tirzepatide. (1) Closure of K-adenosine triphosphate channels; (2) Closure of K-voltage channels; (3) Opening of voltage-dependent calcium channels; (4) Opening of calcium channels on the endoplasmic reticulum; (5) Fusion of insulin granules with the cell membrane; (6) Increased adenosine triphosphate production; (7) Transcription of proinsulin; and (8) Increased density of insulin granules. VDCC: Voltage-dependent calcium channel; V: Voltage; ATP: Adenosine triphosphate; GIPR: Glucose dependent insulinotropic polypeptide receptor; GLP-1R: Glucagon-like peptide-1 receptor; cAMP: Cyclic adenosine monophosphate.

(SQ) injections in doses ranging from 2.5 mg to 15 mg; no oral formulation is available[35,36].

Tirzepatide is supplied in strengths of 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, and 15 mg per 0.5 mL. The medication is taken once a week, with dosage adjustments based on treatment efficacy (HbA1c levels, body weight changes, patient tolerability). The starting dose is 2.5 mg SQ once weekly, primarily for physiological adaptation. After four weeks, the dose increases to 5 mg SQ once weekly. Further increases occur in 2.5 mg increments at intervals of at least four weeks, up to a maximum of 15 mg per week. A missed dose should be taken within four days (96 hours); otherwise, it should be skipped, and the regular weekly schedule resumed[37].

SIDE EFFECTS AND CONTRAINDICATIONS

Tirzepatide generally has a favorable safety profile, with most individuals not experiencing major adverse effects. The most common issues are reduced appetite, nausea, and diarrhea (around 10% of patients), along with occasional vomiting, acid reflux, and constipation[12]. Sinus tachycardia has been documented[38]. Infrequent acute kidney injury cases are linked to dehydration from gastrointestinal side effects, highlighting the need for adequate hydration[35]. Hypersensitivity reactions at the injection site, similar to GLP-1R agonists, have been reported[39].

Like other GLP-1R agonists, tirzepatide carries a potential risk of acute pancreatitis; patients should seek immediate medical care for severe abdominal pain. Elevated pancreatic enzymes (lipase, amylase) may occur without symptoms[39]. Gallstones and gallbladder inflammation have been reported, possibly due to rapid weight loss[35]. Patients with diabetic retinopathy may experience temporary worsening if blood sugar levels improve too quickly; vision changes should be reported[40]. Tirzepatide may induce hypoglycemia, especially with insulin or sulfonylurea use, necessitating proper symptom recognition and management[41]. A review of nine clinical trials found tirzepatide's safety profile comparable to GLP-1R agonists, though gastrointestinal and injection-site reactions are more pronounced at higher doses[42].

DRUG INTERACTIONS AND CONTRAINDICATIONS

Tirzepatide should not be co-administered with other GLP-1 medications (*e.g.*, semaglutide, liraglutide). Patients on insulin may start tirzepatide, but insulin dosages should be gradually reduced to minimize hypoglycemia risk. It may reduce the effectiveness of oral contraceptives, requiring alternative or additional birth control for four weeks after initiation or dose escalation. As it slows gastric emptying, tirzepatide may interfere with the absorption of orally administered medications, particularly those requiring stable blood levels or with a narrow therapeutic index. This effect may be more pronounced in patients with preexisting delayed gastric emptying[43,44].

Tirzepatide is contraindicated in individuals with a history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type-2. Its use is also not advised in patients with known hypersensitivity reactions, including anaphylaxis or angioedema. Caution is warranted in patients with a history of severe reactions to GLP-1R agonists[43,45].

CLINICAL EVIDENCE: TIRZEPATIDE IN OSA AND RELATED CONDITIONS

SURMOUNT-OSA trials

Malhotra *et al*[45] conducted two phase 3, double-blind, randomized controlled trials on adults with moderate-to-severe OSA and obesity. Trial 1 enrolled participants not on PAP therapy, while trial 2 included individuals already receiving PAP therapy. Participants were randomly assigned to receive the highest tolerated dose of tirzepatide (10 mg or 15 mg) or a placebo for 52 weeks (Figure 2)[46].

The primary endpoint was the change from baseline in the AHI. Key secondary endpoints included percentage change in AHI and body weight, changes in hypoxic burden, sleep impairment, C-reactive protein, and systolic blood pressure [45].

At baseline, mean AHI was 51.5 events/hour in trial 1 and 49.5 events/hour in trial 2; mean body mass index was 39.1 and 38.7, respectively. Trial 1 results showed a mean AHI reduction after 52 weeks was -25.3 events/hour [95% confidence interval (CI): -29.3 to -21.2] with tirzepatide *vs* -5.3 events/hour (95%CI: -9.4 to -1.1) with placebo, resulting in an estimated treatment difference of -20.0 events/hour (95%CI: -25.8 to -14.2; $P < 0.001$)[47]. While, in trial 2, mean AHI change at week 52 was -29.3 events/hour (95%CI: -33.2 to -25.4) with tirzepatide *vs* -5.5 events/hour (95%CI: -9.9 to -1.2) with placebo, yielding an estimated treatment difference of -23.8 events/hour (95%CI: -29.6 to -17.9; $P < 0.001$)[47]. Tirzepatide demonstrated significant improvements across all key secondary endpoints compared to placebo. The most common adverse events were mild to moderate gastrointestinal issues[45,46]. These results have been summarized in Table 1.

Other relevant trials

SURMOUNT-1 trial (weight loss in OSA and obesity): A 72-week, phase 3 study evaluated tirzepatide's effect on weight loss in 197 participants with both OSA and obesity or overweight. Doses of 5 mg, 10 mg, and 15 mg were tested against a placebo. At week 72, tirzepatide led to significant reductions in body weight: -11.2% (5 mg), -18.2% (10 mg), and -20.7% (15 mg) relative to placebo. A significantly higher proportion of tirzepatide recipients achieved ≥ 5%, ≥ 10%, and ≥ 20% weight loss compared to placebo (all $P < 0.001$). Waist circumference also reduced significantly (-10.6 cm to -18.9 cm)[47].

SURPASS-1 trial (T2DM management): This 40-week, phase 3 study tested tirzepatide against placebo in 478 adults with T2DM managed through diet and exercise. Tirzepatide (5 mg, 10 mg, 15 mg) significantly reduced HbA1c levels compared to placebo (-1.87% to -2.07% *vs* 0.04%, $P < 0.0001$). More participants achieved HbA1c targets, and significant weight loss (7-9.5 kg) was observed. Side effects were mostly mild gastrointestinal issues, with no severe hypoglycemia reported[48].

COMPARISON WITH OTHER TREATMENT OPTIONS

Anti-obesity medications and OSA risk

Baser *et al*[49] conducted a retrospective analysis using Kaythera Lab data (November 2022 to June 2024) to investigate the link between anti-obesity medications (AOMs) (tirzepatide/zepbound or semaglutide/wegovy) and OSA[49]. The study compared 20384 AOM users (17859 on semaglutide, 2525 on tirzepatide) with 85018 non-AOM users over a minimum 6-month follow-up period. A higher percentage of AOM users had a Chronic Disease Score of ≥ 2 (52.25% *vs* 8.44%, $P < 0.001$). However, the incidence of OSA was significantly lower among AOM users (3.12%) than non-users (12.56%, $P < 0.001$)[50]. Among AOM users, tirzepatide users showed a slightly lower OSA incidence than semaglutide users (2.65% *vs* 3.18%, $P = 0.0303$), though this difference was not statistically significant after adjustment for demographic and clinical variables ($P = 0.1664$)[50]. Overall, AOM use was associated with a 40% lower likelihood of developing OSA (hazard ratio = 0.60, $P < 0.0001$)[50]. These findings suggest a strong association between AOM use and reduced OSA risk[50]. Liraglutide, another GLP-1R agonist, is also approved for weight management[50].

Tirzepatide vs semaglutide (SURMOUNT-5)

The SURMOUNT-5 trial, conducted by Aronne *et al*[51], compared tirzepatide and semaglutide in 750 adults with obesity but without diabetes over 72 weeks. Participants were randomized to receive tirzepatide (10 mg or 15 mg) or semaglutide (1.7 mg or 2.4 mg) once weekly (Table 2).

Weight loss: Tirzepatide led to greater weight loss (average 20.2% reduction or 22.8 kg) compared to semaglutide (13.7% reduction or 15 kg)[51].

Waist circumference: Waist sizes shrank more with tirzepatide (18.4 cm) than semaglutide (13 cm).

Weight loss targets: More participants in the tirzepatide group achieved ≥ 10%, ≥ 15%, ≥ 20%, and ≥ 25% weight loss goals. Nearly 20% on tirzepatide lost over 30% of body weight, compared to 6.9% on semaglutide.

Table 1 Summary of main results from the SURMOUNT-obstructive sleep apnoea trials

Group	Tirzepatide	Placebo	Treatment difference
Mean change in AHI			
Trial 1	-25.3 (-29.3 to -21.2)	-5.3 (-9.4 to -1.1)	-20.0 (-25.8 to -14.2)
Trial 2	-29.3 (-33.2 to -25.4)	-5.5 (-9.9 to -1.2)	-23.8 (-29.6 to -17.9)
Change in AHI (%)			
Trial 1	-50.7 (-62.3 to -39.1)	-3.0 (-16.9 to 10.9)	-47.7 (-65.8 to -29.6)
Trial 2	-58.7 (-69.1 to -48.4)	-2.5 (-16.2 to 11.2)	-56.2 (-73.7 to -38.7)
Change in body weight (%)			
Trial 1	-17.7 (-19.0 to -16.3)	-1.6 (-2.9 to -0.2)	-16.1 (-18.0 to -14.2)
Trial 2	-19.6 (-21.0 to -18.2)	-2.3 (-3.8 to -0.9)	-17.3 (-19.3 to -15.3)
Change in systolic blood pressure			
Trial 1	-9.5 (-11.5 to -7.5)	-1.8 (-3.9 to 0.2)	-7.6 (-10.5 to -4.8)
Trial 2	-7.6 (-9.7 to -5.6)	-3.9 (-6.3 to -1.6)	-3.7 (-6.8 to -0.7)
Change in diastolic blood pressure			
Trial 1	-4.9 (-6.4 to -3.5)	-2.1 (-3.6 to -0.6)	-2.8 (-5.0 to -0.7)
Trial 2	-3.3 (-4.7 to -1.9)	-2.2 (-3.8 to -0.6)	-1.1 (-3.2 to 1.0)

There were two parts of the study: Trial 1 was done on patients without background continuous positive airway pressure therapy while trial 2 enrolled patients on background continuous positive airway pressure therapy. AHI: Apnoea hypopnea index.

Table 2 Comparison of the two major parenteral incretin analogues - semaglutide and tirzepatide

Parameters	Semaglutide	Tirzepatide
Drug class	GLP-1 receptor agonist	Dual GIP and GLP-1 receptor agonist (twincretin)
Mechanism of action	Mimics GLP-1: Suppresses appetite, slows gastric emptying, regulates insulin and glucagon	Activates both GIP and GLP-1 receptors: Synergistically reduces appetite, enhances insulin sensitivity
Receptor targets	GLP-1 only	GLP-1 and GIP
Dosing frequency	Once weekly (subcutaneous)	Once weekly (subcutaneous)
FDA approval for obesity	Approved (as Wegovy)	Approved for Obesity/OSA (as Zepbound)
Additional benefits	Cardiovascular risk reduction	Potentially better metabolic and cardiovascular profile
Effect on appetite	Reduces appetite *via* central GLP-1 pathways	Stronger appetite suppression *via* dual hormone action
Effect on gastric emptying	Slows gastric emptying	Slows gastric emptying
Insulin sensitivity	Improves glucose-dependent insulin secretion	Further improves insulin sensitivity through GIP action
Weight loss efficacy	High (average about 10%-15% body weight reduction)	Higher (average about 15%-22% body weight reduction)

GLP: Glucagon like peeptide; GIP: Glucose dependent insulinotropic polypeptide.

Health markers: Both medications improved blood pressure, cholesterol, and blood sugar levels, particularly with greater weight loss[51].

Side effects: Most side effects were mild to moderate gastrointestinal issues (nausea, vomiting), with semaglutide causing more dropouts due to these issues[51].

Tirzepatide (SURMOUNT-OSA) *vs* lifestyle intervention: While CPAP remains the most common treatment for OSA [52], the lifestyle intervention (INTERAPNEA) trial investigated the effectiveness of weight reduction through lifestyle intervention in reducing reliance on CPAP[53]. Both SURMOUNT-OSA and INTERAPNEA evaluated OSA treatments in

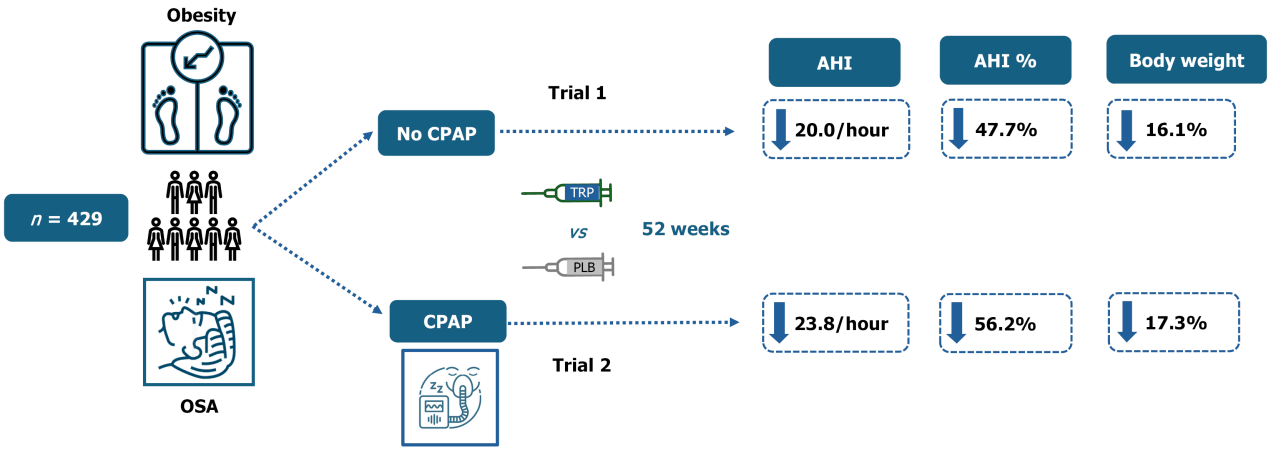

Figure 2 The design and conduct of the SURMOUNT-obstructive sleep apnoea study. There were two parts of the study - part 1 was done on patients without background continuous positive airway pressure therapy while part 2 enrolled patients on background continuous positive airway pressure therapy. Tirzepatide was administered as once weekly injections in doses of 10 mg or 15 mg. AHI: Apnoea hypopnea index; CPAP: Continuous positive airway pressure; OSA: Obstructive sleep apnoea; TRP: Tirzepatide; PLB: Placebo.

individuals with obesity but differed in approach, study population, and outcomes.

SURMOUNT-OSA: A randomized, placebo-controlled trial evaluating tirzepatide (pharmacological intervention) for weight loss and AHI reduction over 52 weeks. It included 469 adults with obesity and moderate-to-severe OSA, with separate cohorts for PAP users and non-users[45]. Results showed tirzepatide led to a 27.4-30.4 events/hour reduction in AHI and an 18%-20% decrease in body weight, positioning it as a promising pharmacologic treatment for OSA, leading to its FDA approval[45].

INTERAPNEA: Assessed an 8-week lifestyle intervention (dietary changes, aerobic exercise, sleep hygiene, substance cessation) followed by a 6-month follow-up in 89 overweight or obese men (body mass index ≥ 25) with moderate-to-severe OSA, all already undergoing CPAP therapy[53]. This trial focused on AHI improvement and CPAP discontinuation. It reported that 45% of participants discontinued CPAP after 8 weeks, increasing to 62% at 6 months. Significant improvements in dietary habits, mental health, and quality of life were also observed[53].

Clinically, SURMOUNT-OSA highlights tirzepatide as a weight-loss-driven pharmacological treatment for OSA, offering a medication-based approach. INTERAPNEA reinforces the power of structured lifestyle changes, particularly for reducing or discontinuing CPAP therapy. Both studies emphasize the strong connection between obesity and OSA; however, SURMOUNT-OSA provides evidence for a drug-centered intervention, while INTERAPNEA demonstrates that behavioral modifications can lead to meaningful and sustained improvements in OSA severity and overall well-being[46, 53].

CONCLUSION

OSA is a multifaceted disorder with significant health implications, strongly linked to obesity and a range of anatomical and lifestyle factors. While traditional management strategies, including CPAP therapy, oral appliances, and surgical interventions, remain cornerstones of treatment, adherence and variable efficacy present ongoing challenges. The emergence of tirzepatide represents a pivotal advancement in the treatment landscape, particularly for obesity-induced OSA. Clinical trials like SURMOUNT-OSA demonstrate its remarkable ability to significantly reduce AHI and promote substantial weight loss, offering a novel pharmacological pathway to disease improvement. This dual GIP/GLP-1 receptor agonist not only addresses the metabolic underpinnings of OSA but also provides a promising alternative or adjunct to existing therapies. As research continues to unfold, tirzepatide is poised to redefine OSA management, highlighting the crucial link between obesity and sleep apnea while paving the way for more personalized and effective treatment options.

FOOTNOTES

Author contributions: Bajpai J and Pradhan A conceived the project; Saxena M and Agarwal U performed the literature search and prepared the first draft; Bajpai J and Saxena M finalised the draft and prepared the revision; Pradhan A critically reviewed the first draft and submitted the final version; and all authors thoroughly reviewed and endorsed the final manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Country of origin: India

ORCID number: Jyoti Bajpai 0000-0001-6337-856X; Akshyaya Pradhan 0000-0002-2360-7580.

S-Editor: Bai Y
L-Editor: A
P-Editor: Zheng XM

REFERENCES

1 **Strollo PJ Jr**, Rogers RM. Obstructive sleep apnea. *N Engl J Med* 1996; **334**: 99-104 [*RCA*] [PMID: 8531966 DOI: 10.1056/NEJM199601113340207] [FullText]
2 **Sullivan CE**, Issa FG. Obstructive sleep apnea. *Clin Chest Med* 1985; **6**: 633-650 [*RCA*] [PMID: 3936665] [FullText]
3 **Horner RL**, Mohiaddin RH, Lowell DG, Shea SA, Burman ED, Longmore DB, Guz A. Sites and sizes of fat deposits around the pharynx in obese patients with obstructive sleep apnoea and weight matched controls. *Eur Respir J* 1989; **2**: 613-622 [*RCA*] [PMID: 2776867] [FullText]
4 **Flemons WW**, Whitelaw WA, Brant R, Remmers JE. Likelihood ratios for a sleep apnea clinical prediction rule. *Am J Respir Crit Care Med* 1994; **150**: 1279-1285 [*RCA*] [PMID: 7952553 DOI: 10.1164/ajrccm.150.5.7952553] [FullText]
5 **Shepard JW Jr**, Gefter WB, Guilleminault C, Hoffman EA, Hoffstein V, Hudgel DW, Suratt PM, White DP. Evaluation of the upper airway in patients with obstructive sleep apnea. *Sleep* 1991; **14**: 361-371 [*RCA*] [PMID: 1947602 DOI: 10.1093/sleep/14.4.361] [FullText]
6 **Young T**, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med* 1993; **328**: 1230-1235 [*RCA*] [PMID: 8464434 DOI: 10.1056/NEJM199304293281704] [FullText]
7 **Guilleminault C**, Stoohs R, Clerk A, Cetel M, Maistros P. A cause of excessive daytime sleepiness. The upper airway resistance syndrome. *Chest* 1993; **104**: 781-787 [*RCA*] [PMID: 8365289 DOI: 10.1378/chest.104.3.781] [FullText]
8 **Bonsignore MR**, Marrone O, Insalaco G, Bonsignore G. The cardiovascular effects of obstructive sleep apnoeas: analysis of pathogenic mechanisms. *Eur Respir J* 1994; **7**: 786-805 [*RCA*] [PMID: 8005263 DOI: 10.1183/09031936.94.07040786] [FullText]
9 Indications and standards for use of nasal continuous positive airway pressure (CPAP) in sleep apnea syndromes. American Thoracic Society. Official statement adopted March 1944. *Am J Respir Crit Care Med* 1994; **150**: 1738-1745 [*RCA*] [PMID: 7952642 DOI: 10.1164/ajrccm.150.6.7952642] [FullText]
10 **Kribbs NB**, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, Redline S, Henry JN, Getsy JE, Dinges DF. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis* 1993; **147**: 887-895 [*RCA*] [PMID: 8466125 DOI: 10.1164/ajrccm/147.4.887] [FullText]
11 **Smith PL**, Gold AR, Meyers DA, Haponik EF, Bleecker ER. Weight loss in mildly to moderately obese patients with obstructive sleep apnea. *Ann Intern Med* 1985; **103**: 850-855 [*RCA*] [PMID: 3933396 DOI: 10.7326/0003-4819-103-6-850] [FullText]
12 Tirzepatide (Mounjaro) for type 2 diabetes. *Med Lett Drugs Ther* 2022; **64**: 105-107 [*RCA*] [PMID: 35802842] [FullText]
13 **Collins L**, Costello RA. Glucagon-Like Peptide-1 Receptor Agonists. 2024 Feb 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan- [PMID: 31855395] [FullText]
14 **Dahl D**, Onishi Y, Norwood P, Huh R, Bray R, Patel H, Rodríguez Á. Effect of Subcutaneous Tirzepatide vs Placebo Added to Titrated Insulin Glargine on Glycemic Control in Patients With Type 2 Diabetes: The SURPASS-5 Randomized Clinical Trial. *JAMA* 2022; **327**: 534-545 [*RCA*] [PMID: 35133415 DOI: 10.1001/jama.2022.0078] [FullText]
15 **Gao L**, Lee BW, Chawla M, Kim J, Huo L, Du L, Huang Y, Ji L. Tirzepatide versus insulin glargine as second-line or third-line therapy in type 2 diabetes in the Asia-Pacific region: the SURPASS-AP-Combo trial. *Nat Med* 2023; **29**: 1500-1510 [*RCA*] [PMID: 37231074 DOI: 10.1038/s41591-023-02344-1] [FullText]
16 **Bonora M**, Shields GI, Knuth SL, Bartlett D Jr, St John WM. Selective depression by ethanol of upper airway respiratory motor activity in cats. *Am Rev Respir Dis* 1984; **130**: 156-161 [*RCA*] [PMID: 6465668 DOI: 10.1164/arrd.1984.130.2.156] [FullText]
17 **Cartwright R**, Ristanovic R, Diaz F, Caldarelli D, Alder G. A comparative study of treatments for positional sleep apnea. *Sleep* 1991; **14**: 546-552 [*RCA*] [PMID: 1798889 DOI: 10.1093/sleep/14.6.546] [FullText]
18 **Sanders MH**, Kern NB, Stiller RA, Strollo PJ Jr, Martin TJ, Atwood CW Jr. CPAP therapy *via* oronasal mask for obstructive sleep apnea. *Chest* 1994; **106**: 774-779 [*RCA*] [PMID: 8082358 DOI: 10.1378/chest.106.3.774] [FullText]
19 **Prosise GL**, Berry RB. Oral-nasal continuous positive airway pressure as a treatment for obstructive sleep apnea. *Chest* 1994; **106**: 180-186 [*RCA*] [PMID: 8020269 DOI: 10.1378/chest.106.1.180] [FullText]
20 **Derderian SS**, Bridenbaugh RH, Rajagopal KR. Neuropsychologic symptoms in obstructive sleep apnea improve after treatment with nasal continuous positive airway pressure. *Chest* 1988; **94**: 1023-1027 [*RCA*] [PMID: 3053055 DOI: 10.1378/chest.94.5.1023] [FullText]
21 **Edinger JD**, Radtke RA. Use of in vivo desensitization to treat a patient's claustrophobic response to nasal CPAP. *Sleep* 1993; **16**: 678-680 [*RCA*] [PMID: 7904770] [FullText]
22 **Rajagopal KR**, Abbrecht PH, Derderian SS, Pickett C, Hofeldt F, Tellis CJ, Zwillich CW. Obstructive sleep apnea in hypothyroidism. *Ann Intern Med* 1984; **101**: 491-494 [*RCA*] [PMID: 6476635 DOI: 10.7326/0003-4819-101-4-491] [FullText]
23 **Eveloff SE**, Rosenberg CL, Carlisle CC, Millman RP. Efficacy of a Herbst mandibular advancement device in obstructive sleep apnea. *Am J Respir Crit Care Med* 1994; **149**: 905-909 [*RCA*] [PMID: 8143054 DOI: 10.1164/ajrccm.149.4.8143054] [FullText]
24 **Hanzel DA**, Proia NG, Hudgel DW. Response of obstructive sleep apnea to fluoxetine and protriptyline. *Chest* 1991; **100**: 416-421 [*RCA*] [PMID: 1864117 DOI: 10.1378/chest.100.2.416] [FullText]

25 **Fletcher EC**, Munafo DA. Role of nocturnal oxygen therapy in obstructive sleep apnea. When should it be used? *Chest* 1990; **98**: 1497-1504 [*RCA*] [PMID: 2245694 DOI: 10.1378/chest.98.6.1497] [FullText]

26 **Guilleminault C**, Simmons FB, Motta J, Cummiskey J, Rosekind M, Schroeder JS, Dement WC. Obstructive sleep apnea syndrome and tracheostomy. Long-term follow-up experience. *Arch Intern Med* 1981; **141**: 985-988 [*RCA*] [PMID: 7247605] [FullText]

27 **Shepard JW Jr**, Olsen KD. Uvulopalatopharyngoplasty for treatment of obstructive sleep apnea. *Mayo Clin Proc* 1990; **65**: 1260-1267 [*RCA*] [PMID: 2205764 DOI: 10.1016/s0025-6196(12)62750-5] [FullText]

28 Practice parameters for the use of laser-assisted uvulopalatoplasty. Standards of Practice Committee of the American Sleep Disorders Association. *Sleep* 1994; **17**: 744-748 [*RCA*] [PMID: 7701187] [FullText]

29 **Johnson NT**, Chinn J. Uvulopalatopharyngoplasty and inferior sagittal mandibular osteotomy with genioglossus advancement for treatment of obstructive sleep apnea. *Chest* 1994; **105**: 278-283 [*RCA*] [PMID: 8275747 DOI: 10.1378/chest.105.1.278] [FullText]

30 **Davies MJ**, Aroda VR, Collins BS, Gabbay RA, Green J, Maruthur NM, Rosas SE, Del Prato S, Mathieu C, Mingrone G, Rossing P, Tankova T, Tsapas A, Buse JB. Management of Hyperglycemia in Type 2 Diabetes, 2022. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2022; **45**: 2753-2786 [*RCA*] [PMID: 36148880 DOI: 10.2337/dci22-0034] [FullText]

31 **Valenzuela-Vallejo L**, Guatibonza-García V, Mantzoros CS. Recent guidelines for Non-Alcoholic Fatty Liver disease (NAFLD)/ Fatty Liver Disease (FLD): Are they already outdated and in need of supplementation? *Metabolism* 2022; **136**: 155248 [*RCA*] [PMID: 35803320 DOI: 10.1016/j.metabol.2022.155248] [FullText]

32 **Dutta D**, Surana V, Singla R, Aggarwal S, Sharma M. Efficacy and safety of novel twincretin tirzepatide a dual GIP and GLP-1 receptor agonist in the management of type-2 diabetes: A Cochrane meta-analysis. *Indian J Endocrinol Metab* 2021; **25**: 475-489 [*RCA*] [PMID: 35355921 DOI: 10.4103/ijem.ijem_423_21] [FullText] [Full Text(PDF)]

33 **Thomas MK**, Nikooienejad A, Bray R, Cui X, Wilson J, Duffin K, Milicevic Z, Haupt A, Robins DA. Dual GIP and GLP-1 Receptor Agonist Tirzepatide Improves Beta-cell Function and Insulin Sensitivity in Type 2 Diabetes. *J Clin Endocrinol Metab* 2021; **106**: 388-396 [*RCA*] [PMID: 33236115 DOI: 10.1210/clinem/dgaa863] [FullText]

34 **Sun B**, Willard FS, Feng D, Alsina-Fernandez J, Chen Q, Vieth M, Ho JD, Showalter AD, Stutsman C, Ding L, Suter TM, Dunbar JD, Carpenter JW, Mohammed FA, Aihara E, Brown RA, Bueno AB, Emmerson PJ, Moyers JS, Kobilka TS, Coghlan MP, Kobilka BK, Sloop KW. Structural determinants of dual incretin receptor agonism by tirzepatide. *Proc Natl Acad Sci U S A* 2022; **119**: e2116506119 [*RCA*] [PMID: 35333651 DOI: 10.1073/pnas.2116506119] [FullText] [Full Text(PDF)]

35 LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012– [PMID: 31643176] [FullText]

36 **Bucheit J**, Ayers J, Pamulapati L, Browning A, Sisson E. A Novel Dual Incretin Agent, Tirzepatide (LY3298176), for the Treatment of Type 2 Diabetes Mellitus and Cardiometabolic Health. *J Cardiovasc Pharmacol* 2022; **80**: 171-179 [*RCA*] [PMID: 35767712 DOI: 10.1097/FJC.0000000000001299] [FullText]

37 **Farzam K**, Patel P. Tirzepatide. 2024 Feb 20. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan- [PMID: 36251836] [FullText]

38 **Farzam K**, Jan A. Beta Blockers. 2023 Aug 22. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan- [PMID: 30422501] [FullText]

39 **Trujillo J**. Safety and tolerability of once-weekly GLP-1 receptor agonists in type 2 diabetes. *J Clin Pharm Ther* 2020; **45** Suppl 1: 43-60 [*RCA*] [PMID: 32910487 DOI: 10.1111/jcpt.13225] [FullText] [Full Text(PDF)]

40 **Bethel MA**, Diaz R, Castellana N, Bhattacharya I, Gerstein HC, Lakshmanan MC. HbA(1c) Change and Diabetic Retinopathy During GLP-1 Receptor Agonist Cardiovascular Outcome Trials: A Meta-analysis and Meta-regression. *Diabetes Care* 2021; **44**: 290-296 [*RCA*] [PMID: 33444163 DOI: 10.2337/dc20-1815] [FullText] [Full Text(PDF)]

41 **Chavda VP**, Ajabiya J, Teli D, Bojarska J, Apostolopoulos V. Tirzepatide, a New Era of Dual-Targeted Treatment for Diabetes and Obesity: A Mini-Review. *Molecules* 2022; **27**: 4315 [*RCA*] [PMID: 35807558 DOI: 10.3390/molecules27134315] [FullText] [Full Text(PDF)]

42 **Meng Z**, Yang M, Wen H, Zhou S, Xiong C, Wang Y. A systematic review of the safety of tirzepatide-a new dual GLP1 and GIP agonist - is its safety profile acceptable? *Front Endocrinol (Lausanne)* 2023; **14**: 1121387 [*RCA*] [PMID: 37051199 DOI: 10.3389/fendo.2023.1121387] [FullText]

43 **Krauss Z**, Hintz A, Fisk R. Tirzepatide: Clinical review of the "twincretin" injectable. *Am J Health Syst Pharm* 2023; **80**: 879-888 [*RCA*] [PMID: 37070418 DOI: 10.1093/ajhp/zxad080] [FullText]

44 **Feingold KR**. Oral and Injectable (Non-Insulin) Pharmacological Agents for the Treatment of Type 2 Diabetes. 2024 Sep 11. In: Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000– [PMID: 25905364] [FullText]

45 **Malhotra A**, Grunstein RR, Fietze I, Weaver TE, Redline S, Azarbarzin A, Sands SA, Schwab RJ, Dunn JP, Chakladar S, Bunck MC, Bednarik J; SURMOUNT-OSA Investigators. Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity. *N Engl J Med* 2024; **391**: 1193-1205 [*RCA*] [PMID: 38912654 DOI: 10.1056/NEJMoa2404881] [FullText] [Full Text(PDF)]

46 **Malhotra A**, Bednarik J, Chakladar S, Dunn JP, Weaver T, Grunstein R, Fietze I, Redline S, Azarbarzin A, Sands SA, Schwab RJ, Bunck MC. Tirzepatide for the treatment of obstructive sleep apnea: Rationale, design, and sample baseline characteristics of the SURMOUNT -OSA phase 3 trial. *Contemp Clin Trials* 2024; **141**: 107516 [*RCA*] [PMID: 38547961 DOI: 10.1016/j.cct.2024.107516] [FullText]

47 **Jastreboff AM**, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, Kiyosue A, Zhang S, Liu B, Bunck MC, Stefanski A; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. *N Engl J Med* 2022; **387**: 205-216 [*RCA*] [PMID: 35658024 DOI: 10.1056/NEJMoa2206038] [FullText]

48 **Rosenstock J**, Wysham C, Frías JP, Kaneko S, Lee CJ, Fernández Landó L, Mao H, Cui X, Karanikas CA, Thieu VT. Efficacy and safety of a novel dual GIP and GLP-1 receptor agonist tirzepatide in patients with type 2 diabetes (SURPASS-1): a double-blind, randomised, phase 3 trial. *Lancet* 2021; **398**: 143-155 [*RCA*] [PMID: 34186022 DOI: 10.1016/S0140-6736(21)01324-6] [FullText]

49 **Baser O**, Lu Y, Chen S, Chen S, Baser E. Tirzepatide and Semaglutide for the Treatment of Obstructive Sleep Apnea and Obesity: A Retrospective Analysis. *Med Res Arch* 2025; **13** [DOI: 10.18103/mra.v13i1.6236] [FullText]

50 **Popoviciu MS**, Păduraru L, Yahya G, Metwally K, Cavalu S. Emerging Role of GLP-1 Agonists in Obesity: A Comprehensive Review of Randomised Controlled Trials. *Int J Mol Sci* 2023; **24**: 10449 [*RCA*] [PMID: 37445623 DOI: 10.3390/ijms241310449] [FullText]

51 **Aronne LJ**, Horn DB, le Roux CW, Ho W, Falcon BL, Gomez Valderas E, Das S, Lee CJ, Glass LC, Senyucel C, Dunn JP; SURMOUNT-5 Trial Investigators. Tirzepatide as Compared with Semaglutide for the Treatment of Obesity. *N Engl J Med* 2025; **393**: 26-36 [*RCA*] [PMID:

40353578 DOI: 10.1056/NEJMoa2416394] [FullText]

52 Interventions for the Treatment of Obstructive Sleep Apnea in Adults: Recommendations [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2017 Mar- [PMID: 29517883] [FullText]

53 **Carneiro-Barrera A**, Amaro-Gahete FJ, Guillén-Riquelme A, Jurado-Fasoli L, Sáez-Roca G, Martín-Carrasco C, Buela-Casal G, Ruiz JR. Effect of an Interdisciplinary Weight Loss and Lifestyle Intervention on Obstructive Sleep Apnea Severity: The INTERAPNEA Randomized Clinical Trial. *JAMA Netw Open* 2022; **5**: e228212 [*RCA*] [PMID: 35452108 DOI: 10.1001/jamanetworkopen.2022.8212] [FullText] [Full Text (PDF)]