Tirzepatide in OSA: What SURMOUNT-OSA means for management

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Obstructive sleep apnea (OSA) remains a significant public health challenge, characterized by recurrent episodes of upper airway collapse during sleep, leading to intermittent hypoxia and sleep fragmentation. Current management strategies, while effective for many, often face issues with adherence and do not address the underlying metabolic drivers frequently observed in this patient population. The emergence of novel pharmacotherapies, particularly those targeting metabolic pathways, presents a compelling shift in how clinicians might approach OSA.

KEY TAKEAWAYS

- The Pivot: Tirzepatide, a dual GIP and GLP-1 receptor agonist, offers a pharmacological approach to OSA management, moving beyond traditional mechanical or surgical interventions.
- The Data: Clinical studies indicate a reduction in the apnea-hypopnea index (AHI) with tirzepatide, suggesting an impact on disease severity.
- The Action: Clinicians should consider the metabolic profile of their OSA patients, as therapies like tirzepatide may address both weight and sleep-related respiratory disturbances.

Obstructive sleep apnea affects millions globally, with prevalence estimates rising in parallel with the obesity epidemic. The condition is not merely a nuisance of snoring and daytime fatigue; it is a serious medical disorder associated with increased risks of hypertension, cardiovascular disease, stroke, and type 2 diabetes. Standard treatment, continuous positive airway pressure (CPAP), is highly effective when used consistently, but adherence rates are notoriously suboptimal, leaving a substantial unmet need for alternative or adjunctive therapies. Surgical options exist, but they are invasive and not suitable for all patients.

The pathophysiology of OSA is complex, involving anatomical factors, neuromuscular control of the upper airway, and systemic inflammation. A significant proportion of patients with OSA also present with obesity, insulin resistance, and other features of metabolic syndrome. This strong epidemiological link has long prompted speculation that therapies addressing metabolic dysfunction might also ameliorate OSA severity. Tirzepatide, a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, has already demonstrated substantial efficacy in weight management and glycemic control, making it a logical candidate for investigation in OSA.

The Mechanism of Action in OSA

Tirzepatide's primary mechanism of action involves activating both GIP and GLP-1 receptors, leading to enhanced glucose-dependent insulin secretion, suppression of glucagon secretion, and delayed gastric emptying. These actions

collectively contribute to significant weight loss, which is a key factor in OSA pathogenesis. Reduced visceral and subcutaneous fat can decrease pharyngeal soft tissue volume, thereby enlarging the upper airway lumen and reducing its collapsibility during sleep. This direct anatomical improvement is a primary driver of any observed benefit.

But the impact of tirzepatide may extend beyond simple weight reduction. GLP-1 receptor agonists have been shown to have anti-inflammatory effects and may improve endothelial function, both of which are often impaired in OSA. Some preclinical and early clinical data also suggest that GLP-1 agonism might influence central respiratory drive or upper airway muscle tone, although these mechanisms are less well-established in the context of OSA. The relationship between metabolic health and respiratory control is intricate, and tirzepatide's broad metabolic effects could offer multiple pathways to improvement.

Patient Populations and Study Design

Clinical investigations into tirzepatide for OSA have typically focused on adult patients with moderate to severe OSA, often defined by an apnea-hypopnea index (AHI) of 15 events per hour or higher. These studies frequently enroll individuals with a body mass index (BMI) in the overweight or obese range, reflecting the strong comorbidity between obesity and OSA. Patients are usually required to have stable cardiovascular disease, if present, and often have co-existing type 2 diabetes or prediabetes, given the drug's established indications.

The primary endpoint in these trials is consistently the change in AHI from baseline, measured by polysomnography. Secondary endpoints often include changes in body weight, glycemic parameters (HbA1c, fasting glucose), blood pressure, and patient-reported outcomes such as Epworth Sleepiness Scale scores and quality of life measures. Some studies also assess changes in oxygen desaturation index (ODI) and other polysomnographic parameters. The design typically involves a placebo-controlled, randomized approach, with participants receiving either tirzepatide at various doses or placebo for a defined treatment period, often 52 weeks or longer, to allow for sustained weight loss and its potential downstream effects on OSA severity.

What the Clinical Data Shows

Clinical trials investigating tirzepatide in OSA have demonstrated a reduction in AHI. This reduction is generally observed across various subgroups, including those with and without type 2 diabetes. The magnitude of AHI improvement appears to correlate with the degree of weight loss achieved, reinforcing the hypothesis that weight reduction is a primary mediator of the benefit. Patients receiving tirzepatide also show improvements in secondary endpoints, such as reductions in BMI, waist circumference, and HbA1c levels, consistent with the drug's known metabolic effects.

The impact on patient-reported outcomes, such as daytime sleepiness, also appears favorable. Patients often report feeling more rested and experiencing an improved quality of life, which is a critical aspect of OSA management. These subjective improvements, coupled with objective reductions in AHI, suggest a meaningful clinical benefit. The data supports the notion that addressing underlying metabolic dysfunction can have a tangible positive effect on respiratory parameters in OSA.

Safety and Tolerability Profile

The safety profile of tirzepatide in OSA patients aligns with its established profile in diabetes and weight management studies. Gastrointestinal adverse events, such as nausea, diarrhea, and vomiting, are the most commonly reported side

effects. These are typically mild to moderate in severity and tend to decrease over time as patients adapt to the treatment. Dose escalation strategies are often employed to mitigate these effects.

Less common but serious adverse events include pancreatitis, gallbladder-related issues, and acute kidney injury, particularly in patients with pre-existing renal impairment or those experiencing severe gastrointestinal side effects leading to dehydration. Thyroid C-cell tumors have been observed in rodents with GLP-1 receptor agonists, leading to a contraindication in patients with a personal or family history of medullary thyroid carcinoma or in those with Multiple Endocrine Neoplasia syndrome type 2. These safety considerations necessitate careful patient selection and monitoring, as detailed in the Oxford Handbook of Endocrinology and Diabetes.

Where it Falls Short

While the data for tirzepatide in OSA is encouraging, several considerations temper enthusiasm. The long-term durability of AHI reduction after treatment cessation remains an open question. Weight regain is a common challenge once anti-obesity medications are discontinued, and it is reasonable to expect that OSA severity might also revert if weight is regained. This implies that tirzepatide, if approved for OSA, would likely be a chronic therapy, raising questions about long-term adherence and cost.

The trials also typically exclude patients with severe cardiovascular disease or other significant comorbidities, meaning the generalizability of the findings to a broader, sicker OSA population requires further investigation. The effect of tirzepatide on OSA in patients who are not obese or those with OSA driven primarily by non-weight-related anatomical factors is also not fully elucidated. While AHI reduction is a critical objective measure, the direct impact on hard cardiovascular outcomes in OSA patients treated with tirzepatide has not yet been definitively established in dedicated outcome trials. This is a crucial gap, given the strong link between OSA and cardiovascular morbidity and mortality. For a deeper understanding of the diagnostic market, our previous coverage on AI and wearables in sleep diagnostics provides additional context.

The cost-effectiveness of tirzepatide for OSA also needs careful evaluation. These medications are expensive, and their widespread use for OSA would represent a significant healthcare expenditure. Payers will undoubtedly scrutinize the magnitude of benefit relative to cost, especially when compared to established, less expensive therapies like CPAP. The question of whether tirzepatide can replace CPAP or serve as an adjunct, and for which specific patient profiles, will be central to its clinical adoption.

The current evidence, while showing a reduction in AHI, does not suggest that tirzepatide is a standalone solution for all OSA patients. It appears to be most effective in those with obesity, where weight loss is a primary therapeutic target. For patients with severe OSA, particularly those with significant oxygen desaturations, CPAP remains the gold standard for immediate and robust airway support. Tirzepatide may offer a valuable alternative or complementary therapy for those who cannot tolerate CPAP or for whom weight loss is a critical component of their OSA management strategy. The ongoing evolution of sleep quality assessment will also help refine patient selection for such therapies.

> **CLINICAL IMPLICATIONS**
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> The prospect of a pharmacological agent like tirzepatide for obstructive sleep apnea is genuinely exciting, particularly for the vast number of patients struggling with CPAP adherence. For clinicians, this means

a potential new tool in the armamentarium, especially for those obese patients who also have metabolic comorbidities. It shifts the conversation from purely mechanical solutions to addressing underlying systemic issues.

But we must temper expectations. Tirzepatide is not a magic bullet that will replace CPAP for everyone. It is likely to be most impactful for patients where obesity is a primary driver of their OSA, and where weight loss can meaningfully reduce upper airway collapsibility. Identifying these patients accurately will be key, and a thorough assessment of their metabolic profile will become even more critical in the sleep clinic.

The financial implications cannot be ignored. These drugs are expensive, and their long-term use for OSA will present a significant cost burden. Payers will demand clear evidence of sustained benefit and cost-effectiveness compared to existing therapies. This will inevitably lead to debates about patient selection criteria and access, potentially creating disparities in care.

Tirzepatide represents a step towards personalized medicine in OSA. It offers a compelling option for a specific subset of patients, but it will require careful integration into existing treatment algorithms. The goal remains to improve patient outcomes, and if tirzepatide can help those who currently fall through the cracks of conventional therapy, it will be a welcome addition.

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