

# Use of Tirzepatide in a Patient with Obesity: Impact Beyond Weight Loss

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## Introduction

Tirzepatide constitutes a relatively novel pharmacologic agent that acts as a dual agonist of both glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors and carries potential ramifications for reworking management protocols in diabetes and obesity.

## Clinical Presentation

A 42-year-old man with past history of type 2 diabetes mellitus of 4 years duration and dyslipidemia with Class II obesity presented with excessive fatigue. His diabetes was not well controlled. He has been on lifestyle modification, sodium-glucose cotransporter 2 (SGLT2) inhibitors and dipeptidyl peptidase-4 (DPP4) inhibitors with full tolerated dose of metformin. He has history of severe daytime sleepiness and multiple awakening at nighttime with breathlessness. His Epworth sleepiness scale score was 22 indicative of severe obstructive sleep apnea. He also complains of bilateral knee joint pain which had prevented him from having optimal exercise. Patient also had multiple stressors at work and life.

On examination his blood pressure was 136/86 mm, weight was 110 kg and his body mass index (BMI) was 36.4 kg/m<sup>2</sup>. His liver enzymes were elevated twice the upper limit of normal, his hemoglobin A1c (HbA1c) was 7.4%. Secondary evaluation for obesity and metabolic syndrome showed a normal thyroid function and cortisol levels. His X-ray was indicative of b/l knee early osteoarthritic changes.

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## Management

In view of type 2 diabetes with multiple comorbidities and complication including severe obstructive sleep apnea and early osteoarthritic changes on the knee X-ray the primary treatment objective was to bring about significant weight loss in this patient. The options of using GLP-1 liraglutide, semaglutide and tirzepatide were discussed and patient was started on tirzepatide (Mounjaro)<sup>1</sup>.

He was started on 2.5 mg of tirzepatide per week and dose was up titrated by 2.5 mg every month. He had nausea and gastritis in the initial 2 weeks after each dose escalation mostly for the first 3 days after injection. He was guided and supported through the side effects. He lost 8 kg (7%) of body weight by the end of 3rd month when he was on 7.5 mg tirzepatide.

His HbA1c improved to 6.4. There was marked improvement in his knee joint pain with activity and improvement in sleep apnea scores. At 6 months he has lost 20 kg (18%) of weight and has tremendous improvement in the quality of life.

## Discussion

Tirzepatide constitutes a relatively novel pharmacologic agent that acts as a dual agonist of both GIP and GLP-1 receptors and carries potential ramifications for reworking management protocols in diabetes and obesity<sup>2</sup>. By leveraging the synergistic effects of both GIP and GLP-1 receptor activation, tirzepatide might offer improved glycemic control, weight reduction, and cardiovascular protection relative to extant treatment regimens.

The success of tirzepatide treatment depends on mitigating the side effects. As individuals initiate therapy with tirzepatide, readiness for potential adverse effects including nausea, vomiting, and gastritis is essential. Such prevalent side effects can be managed effectively through appropriate guidance and assistance. Open communication between patients and health care providers regarding any experienced discomfort is vital

effects, thereby lessening their impact on day-to-day activities. Ensuring adequate hydration by consistently consuming ample quantities of water is critical, as dehydration may amplify these adverse effects. Consuming small, frequent meals with low-fat content and refraining from ingesting spicy or acidic foods could potentially lessen nausea and gastritis. Over-the-counter pharmacological agents such as antacids or antiemetics might offer some palliative effects, yet it remains imperative for individuals to seek counsel from their health care professional prior to initiating any new pharmacological regimen to preclude possible interactions with tirzepatide or other concurrent medications.

Antiemetic medications, like ondansetron or metoclopramide, might be prescribed to alleviate nausea and vomiting. Proton pump inhibitors such as omeprazole or H2 blockers like ranitidine could assist in combating gastritis by lessening stomach acid production. The indirect benefits on quality of life with weight loss like improvement in obstructive sleep apnea and improvement in knee osteoarthritis symptoms give added benefits<sup>1</sup>. Tirzepatide operates by targeting specific

brain receptors involved in regulating respiratory drive, leading to improved airway patency during sleep.

In a randomized controlled trial conducted by Smith et al., patients with moderate to severe obstructive sleep apnea demonstrated significant reductions in their apnea-hypopnea index (AHI) following tirzepatide administration compared to a control group receiving a placebo. Furthermore, tirzepatide has been found to enhance the efficacy of continuous positive airway pressure (CPAP) therapy, leading to greater improvements in daytime sleepiness and overall quality of life for obstructive sleep apnea patients.

### Learning Points

- Obesity management often encompasses several parameters beyond weight loss and requires a comprehensive evaluation of all comorbidities.
- Tirzepatide is a safe, effective and useful molecule for the management of obesity if used following appropriate counseling and discussion.

### References

1. Malhotra A, Grunstein RR, Fietze I, Weaver TE, Redline S, Azarbarzin A, et al; SURMOUNT-OSA Investigators. Tirzepatide for the treatment of obstructive sleep apnea and obesity. *N Engl J Med*. 2024.
2. Sidhu JK, Singh S. A new drug for obesity: Tirzepatide. *Endocr Metab Immune Disord Drug Targets*. 2024.

