Breaking the Cycle: GLP-1/GIP Agonist Treatment and Alcohol Use Disorder

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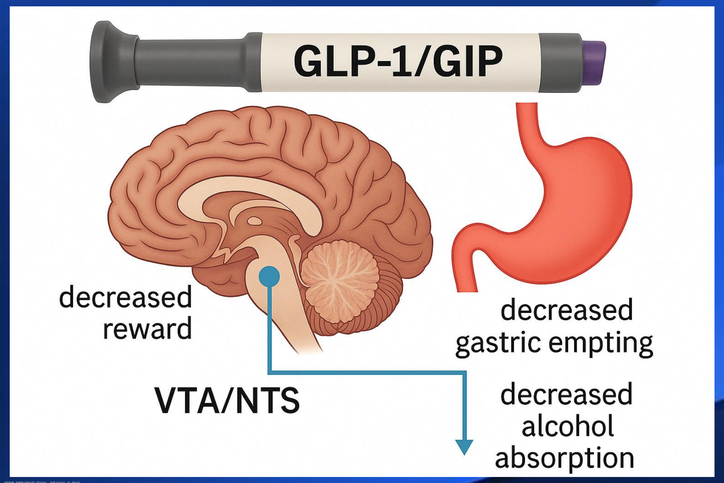
Introduction

Emerging research suggests GLP-1 agonists may be a groundbreaking treatment for alcohol use disorder (AUD)[1-2] but the role of dual GLP-1/GIP agonists remains unclear.[2]

Mechanisms of GLP-1 agonists in reducing alcohol use[1-3]:
1) Activate receptors in the nucleus tractus solitarius, reducing dopaminergic neuron excitability.
2) Target GABAergic neurons and glutamine receptors
3) Interact with the hypothalamic-pituitary-adrenal axis, reducing stress-induced relapse behaviors.
4) Slow gastric emptying, increasing gastric metabolism of alcohol and decreasing systemic alcohol absorption.

Mechanisms of GIP agonists are less frequently described in literature and thought to significantly overlap with GLP-1 mechanisms (Fig 1).[1,3] We know that dual GLP-1/GIP agonists (tirzepatide) are more effective than GLP-1 agonists (semaglutide) for glycemic control and weight loss. Whether dual GLP-1/GIP agonists are superior for AUD treatment remains unknown.



Case Presentation

Patient Background:
- Woman in her 50s with a history of severe alcohol use disorder (AUD) and class I obesity.
- Consumed 20-40 standard drinks daily before treatment.

Initial Treatment:
- Started on intramuscular (IM) naltrexone, reducing alcohol consumption to 4-8 drinks per day.
- Acamprosate was added but did not further reduce drinking.
- Despite adherence to medication, counseling, and lifestyle changes, cravings persisted for six months.

Challenges Prior to Tirzepatide:
- Required oral naltrexone 50 mg daily one week before her IM naltrexone injection to prevent relapse.
- Struggled with sustained weight loss and metabolic health concerns.

Introduction of Tirzepatide (Dual GLP-1/GIP Agonist):
- Initiated at 2.5 mg subcutaneously weekly for weight management.

Over three months, she experienced:
- Significant reduction in alcohol cravings, especially nighttime urges.
- Reduced alcohol intake to <4 drinks per day.
- No longer required oral naltrexone before IM injections.

Patient-Reported Benefits:
- Improved satiety, reduced stress, and mild nausea with alcohol consumption.
- Weight loss of 7 kg; BMI decreased from 32 to 29.
- Mild nausea was the only side effect, limiting dose escalation beyond 2.5 mg weekly (target for obesity is 15 mg).

Outcomes & Conclusion:
- Maintained adherence to IM naltrexone and continued psychosocial therapy.
- Tirzepatide appeared to synergistically enhance AUD treatment, leading to
- improved alcohol use outcomes.

Conclusion

This case highlights the potential role of tirzepatide, a dual GLP-1/GIP receptor agonist, in the treatment of alcohol use disorder (AUD) in a patient with comorbid obesity.

The patient experienced meaningful reductions in alcohol consumption, attributed to enhanced satiety, reduced reactivity to alcohol-related cues, and decreased stress. Beyond clinical outcomes, these agents may appeal to individuals motivated to address obesity, even if not yet ready to engage in alcohol-focused treatment. Given the stigma and limited access associated with FDA-approved AUD medications, GLP-1/GIP agonists—already widely accepted for metabolic conditions—may represent a less stigmatizing alternative.[4]

As their use expands, these medications could offer dual benefits for patients with overlapping metabolic and substance use disorders.[5] Further studies are needed to establish their efficacy, safety, cost-effectiveness, and optimal use in this context. In the interim, it may be reasonable to prioritize these agents for approved indications when AUD coexists.

Disclosures

No financial disclosures to report. Unlabeled use of tirzepatidie is reviewed. Our figure was created by ChatGPT 4o on April 16, 2025.

References

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