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Are Incretin-Based Therapies Associated With Decreased Risk of Alcohol Use Disorder After Bariatric Surgery?

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Alcohol use disorder (AUD) is a leading preventable cause of death in the United States, with estimates suggesting it results in over 178 000 deaths per year.[1] Risk factors include genetic vulnerability, childhood trauma, and psychiatric disorders, such as mood and anxiety disorders. More recently, bariatric surgery has gained attention as an additional risk factor, with evidence linking certain procedures to heavy alcohol use. In a systematic review of 23 studies, bariatric surgery, particularly the Roux-en-Y procedure, was identified as a notable risk factor for new-onset AUD, with long-term follow-up studies showing nearly a 2-fold increase in odds (odds ratio, 1.8; 95% CI, 1.5-2.2).[2] Although current guidelines recommend screening for AUD before and after bariatric surgery,[3] conventional screening measures may underestimate risk, as even small amounts of alcohol can cause clinically significant impairment in postsurgical patients.[4] Current pharmacotherapy for AUD is effective though underused. Incretin-based therapies (IBTs), such as glucagon-like peptilde-1 (GLP-1) receptor agonists and newer dual or triple agents acting on glucose-dependent insulinotropic polypeptide and glucagon receptors, have demonstrated excellent efficacy for obesity and are supported by a growing body of literature suggesting potential benefit in the treatment of AUD.[5] Although the association between bariatric surgery and increased AUD risk is well documented,[2] few studies have examined pharmacologic treatments that might mitigate this risk.

In this issue of *JAMA Network Open*, Fakhoury and colleagues[6] explore this intriguing concept—the idea that incretin-based antiobesity medications may play a role in reducing the risk of AUD after bariatric surgery. The authors conducted a retrospective cohort study using TriNetX Collaborative Network data following 15 382 adult patients after bariatric surgery and then used propensity score matching to compare 3990 patients who received IBTs with 3990 patients who received non-IBTs for obesity. The mean follow-up period was approximately 3 years, and the cohort was limited to adults who had undergone Roux-en-Y gastric bypass and sleeve gastrectomy. The primary outcome was new-onset AUD, and the secondary outcome was a new prescription for medication for AUD (MAUD).

The results were compelling—16 patients developed AUD in the IBT group, and 35 patients developed AUD in the non-IBT group. This translated to a significantly lower hazard ratio (HR) of 0.45 (95% CI, 0.25-0.81; $P = .006$). Furthermore, nearly twice as many patients in the non-IBT group received a prescription for a MAUD.

Several limitations should be considered when interpreting these findings. The study population was restricted to patients requiring ongoing pharmacologic obesity treatment due to suboptimal weight loss after bariatric surgery, limiting the generalizability of the findings to all postsurgical patients. Another important limitation is the poor capture of AUD-specific psychotherapy in the dataset. AUD-targeted psychosocial treatments (eg, cognitive behavioral therapy, motivational interviewing, and relapse-prevention strategies) are a core component of comprehensive care and can substantially affect both weight-loss maintenance and alcohol-related outcomes after surgery. Failure to measure these interventions may bias estimates of treatment effect and underestimate the benefit of integrated postsurgical behavioral care. As in all retrospective studies using code-based analyses, underrecognition of AUD and confounding by indication are possible. Patients who continued to take IBTs after surgery may differ in motivation, access to care, or metabolic phenotype, potentially influencing outcomes.

These findings are similar to a recent study by Adeniran and colleagues[7] in *Obesity*, who also used a TriNetX dataset but focused exclusively on patients who had Roux-en-Y procedures and compared those treated with IBTs with those who were not. They found that those who had IBTs were less likely to develop AUD (HR, 0.77; 95% CI, 0.55-0.84) and had an overall lower mortality (HR, 0.497; 95% CI, 0.346-0.715). Taken together, both studies suggest that obesity and AUD may share overlapping psychological or biological pathways that could be targeted by IBTs.

This study opens an important conversation, yet several uncertainties remain. For instance, is the absence of a prescribed MAUD a true marker of lower risk, or does it simply reflect underrecognition and undertreatment? And could the relatively low number of cases be a sign that bariatric clinicians are more attentive to early behavioral changes, rather than a pharmacologic protective effect? Do GLP-1 receptor agonists and related IBTs exert benefits across all obesity phenotypes, surpassing other weight-loss medications by promoting greater weight reduction and potentially mitigating AUD? These are questions worth asking before drawing conclusions about causality.

GLP-1 receptor agonists and related incretin therapies are already transforming obesity care and have shown promising effects in reducing alcohol consumption in both preclinical and clinical studies. Beyond weight loss, their potential benefits now extend to conditions such as liver disease, cardiovascular disease, and cognitive impairment. We are only just beginning to understand how these medications influence the neurobiological circuits that govern both appetite and reward. Future prospective and mechanistic studies will help clarify whether these medications truly modify risk of AUD or simply identify patients who are more engaged with their care. Either way, this work challenges us to think more broadly about how metabolic and addiction medicine intersect.

Finally, a fundamental question remains: Can IBTs help prevent AUD—not only for patients after bariatric surgery but for others at risk as well? We may only be scratching the surface of their potential to reshape how we think about both appetite and addiction.

ARTICLE INFORMATION

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