Impact of GLP-1RA treatment on alcohol consumption in adults

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CONTEXT

Alcohol use disorder (AUD) affects approximately 5% of people worldwide and is considered a key risk factor for noncommunicable disease[3]. Alcohol use is also a leading modifiable cause of morbidity and mortality, accounting for an estimated 4-5% of disease burden and 2.6 million deaths per year globally[1].

There are limited approved pharmacological treatments for AUD, most commonly naltrexone, acamprosate, and disulfiram. Though these substances display favorable effects in some studies, they do not seem to work effectively for all individuals affected by AUD[3]. Underutilization of these therapies, whether attributed to lack of awareness or stigma, accounts for one of the largest known health care treatment gaps, with less than 10% of those with AUD reporting treatment in the past year and less than 2% of those receiving pharmacotherapy[1].

GLP1-RA have been found to reduce alcohol consumption in non-human populations and the role of GLP-1RA in reward-related processes common to both use of drugs of abuse/alcohol and food intake has been demonstrated in preclinical studies, suggesting potential clinical applications for GLP1-RA in the treatment of AUD[2].

RESEARCH OBJECTIVE

Our objective was to assess the efficacy of GLP 1-RA medications in reducing alcohol consumption in adults.

DESIGN & METHODS

Evidence-based review using searches of PubMed, JAMA, Dynamed, and NEJM with key words including: “alcohol,” "alcohol use disorder," “GLP 1,” “dulaglutide,” “exenatide,” "semaglutide," "liraglutide," "tirzepatide," "lixisenatide." Three randomized controlled trials met search criteria and were reviewed.

PATIENT POPULATION AND STUDY DESIGN

- A total of 326 adults aged 18-75 years old with baseline alcohol consumption. Two out of three trials enrolled treatment seeking individuals, and two out of three studies enrolled adults specifically with AUD according to DSM5 criteria.
- Trials occurred at the University of North Carolina (UNC)- Chapel Hill School of Medicine[1], four outpatient clinics in the suburbs of Copenhagen, Denmark[2], and at University Hospital in Basel, Switzerland[3].
- Exclusion criteria included pregnancy, pre-existing treatment with GLP-1 agonists, unstable psychiatric conditions[3]; other drug use disorder, current or history of withdrawal from alcohol, diabetes (type 1 and 2), liver/renal/pancreatic dysfunction, cardiac disease, concomitant pharmacotherapy against alcohol dependency[2]; actively attempting to reduce alcohol consumption, BMI <23, and current medical or neurological illness precluding participation based on physician judgement[1].
- Participants were randomized to receive weekly injections of standard doses or lowest dose sequences of GLP1-RA medications or weekly placebo NaCl/sham injections over nine[1], twelve[3], and twenty-six[2] week periods.

VALIDITY TABLE

Study	Random -ized	Concealed Allocation	Intention to Treat	Baseline Characteristics	Equal Treatment	Blinded	Follow Up Complete	Conflict of Interest	Sample Size Med/Placebo	Comments
Sema glutide	Yes	Yes	Yes	Yes	Yes	Yes, double	Yes (87.5%)	No	n=48 24/24	Short duration, small sample
Exenatide	Yes	Yes	Yes	Yes	Yes	Yes, double	No (45.7%)	Yes	n=127 62/65	Conflict of interest, poor follow-up
Dula glutide	Yes	Yes	Yes	Yes	Yes	Yes, double	Yes (80%)	No	n=151 76/75	Confounding variable, secondary analysis

RESULTS

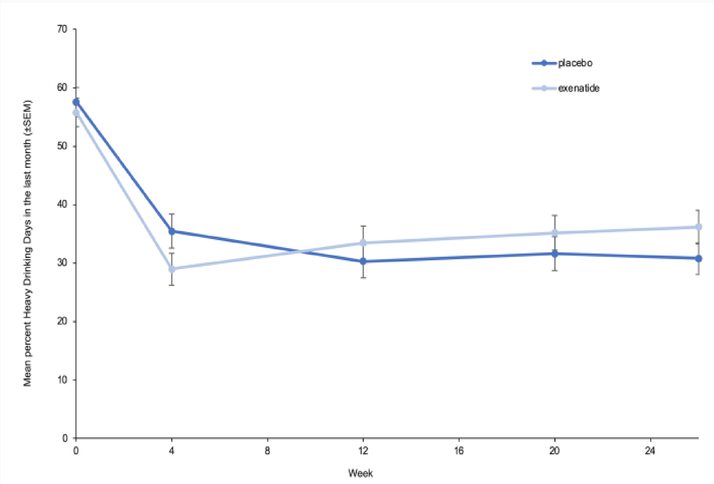


Figure 3. Reduction in heavy drinking days. Mean percentage heavy drinking days in the last 30 days, measured with the Time-Line Follow Back (TLFB) method, at all assessments (week 0, week 4, week 12, week 20, week 26). Data were analyzed with an ANOVA adjusted for baseline, and missing data were imputed with the use of multiple imputations as described in the text (n = 127). Data represent mean ± SEM.

Exenatide

Number of heavy drinking days reduced (19.6 days vs-26.8 days, P = 0.37) .

Total alcohol intake reduced (-1304 g per 30 days vs 1313 g per 30 days, P = 0.86).

No statistically significant difference between treatment and placebo groups[2].

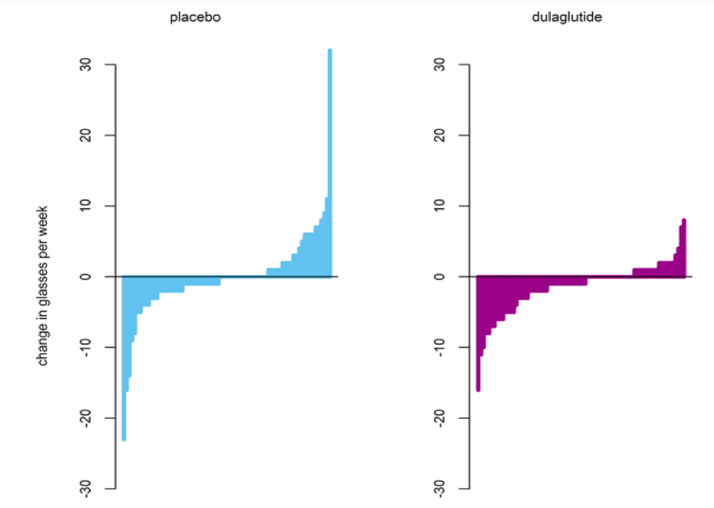


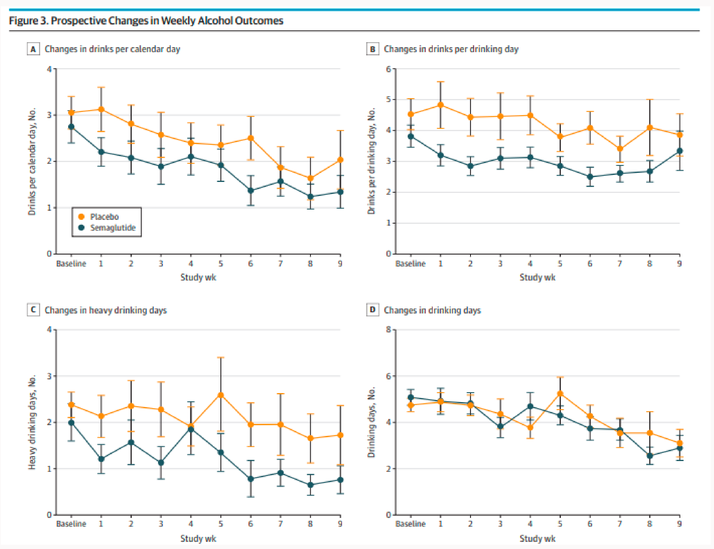
Figure 2. Changes in weekly alcohol consumption. Changes in glasses of alcohol consumed per week from baseline to week 12 for each participant according to treatment group. The bars represent individual data points.

Dulaglutide

Mean change in weekly alcohol consumption was –1.4 (SD 3.7) standard drinks in the dulaglutide group and –0.1 (SD 6.3) standard drinks in the placebo group.

At week 12, dulaglutide group drank an estimated 29% less .

(baseline alcohol intake adjusted relative effect = 0.71, 95% CI 0.52–0.97, P = 0.04)[3].



Semaglutide

Significantly decreased drinks per drinking day (β, −0.41; 95% CI, −0.73 to −0.09; P = .04) and weekly cravings.

(β, −0.39; 95% CI, −0.73 to −0.06; P = .01),

There was no significant difference in drinks per calendar day (β, −0.27; 95% CI, −0.63 to 0.09; P = .17) or number of drinking vs abstinent days.

(β, 0.90; 95% CI, 0.73 to 1.12; P = .89)[1]

CONCLUSION

Clinical Recommendation	SOR	Reference
In adults with any baseline alcohol use, GLP1-RA medication use does reduce alcohol intake	C	Hendershot 2025, Klausen 2022, Probst 2023
In adults with AUD, GLP1-RA medication use does reduce alcohol intake	C	Hendershot 2025, Klausen 2022

STEPS

Safety- GLP 1-RAs are generally considered safe, although risks of pancreatitis, thyroid cancer (rare), and gallstones do exist. There are also concerns that with significant substance use, medications may be metabolized differently than in the general population.

Tolerability- GLP 1-RAs sometimes cause nausea, vomiting, diarrhea, constipation. Some patients may not tolerate self-injections or have adverse reactions at injection sites.

Effectiveness- GLP 1-RAs may lead to decreased alcohol consumption in some patients, but this has yet to be proven consistently.

Price- GLP 1-RAs are expensive unless patients have another FDA-approved indication to allow for insurance coverage.

Simplicity- Simple once weekly dosing; possibility to reduce medication burden in setting of comorbid metabolic disease.

DISCUSSION

GLP 1-RA medication use was weakly shown to decrease alcohol consumption over the 9-26 week course of treatment for adults with current alcohol use. The available studies had significant limitations.

Two out of three studies used the lowest dosing sequences available to maintain better safety and tolerability, which is considerably lower than what is often prescribed for other indications. Duration of treatment was also limited.

Validity was impacted by conflict of interest in one study, and another was a secondary analysis of a study designed to investigate smoking cessation.

The populations of these studies had key differences. They varied significantly in baseline amount of alcohol consumption, desire for treatment, AUD diagnosis, other baseline demographics, and confounding factors (comorbid tobacco use disorder).

More studies are warranted to determine the impact on alcohol use and clinical significance.

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