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ANHEDONIA AND INCREASED ALCOHOL CONSUMPTION FOLLOWING TIRZEPATIDE USE: A CASE REPORT

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OBJECTIVE: Tirzepatide is a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist. Beyond appetite regulation, GLP-1–based therapies may modulate dopaminergic signaling within the brain's reward circuitry.

While selective GLP-1 receptor agonists primarily suppress appetite, dual GIP/GLP-1 receptor activation may exert broader neurobehavioral effects. We report a case of marked anhedonia temporally associated with tirzepatide use, followed by increased alcohol consumption and psychiatric hospitalization.

CASE: A 49-year-old male was initiated on tirzepatide in an endocrinology outpatient clinic for weight loss. During treatment, he developed prominent anhedonia, decreased motivation, appetite suppression beyond the expected pharmacological effect, sleep disturbance, and anxiety symptoms. In an attempt at self-medication, he began consuming approximately 7–8 standard alcoholic drinks per day. He subsequently discontinued tirzepatide on his own and presented to the psychiatry outpatient clinic.

He denied prior alcohol withdrawal symptoms, alcohol-related functional impairment, psychiatric diagnoses, or family psychiatric history. There was no suicidal ideation. Although he did not meet DSM-5 criteria for Alcohol Use Disorder, he was hospitalized due to worsening depressive symptoms, functional decline, and rapidly escalating alcohol consumption as a maladaptive coping strategy.

Mental status examination revealed dysphoric mood, restricted affect, psychomotor retardation, and reduced spontaneous speech without psychotic features. Following detoxification and supportive interventions, sertraline was initiated and titrated to 100 mg/day. Acamprosate 999 mg/day was added to prevent relapse. At discharge, he was euthymic and abstinent from alcohol.

Written informed consent was obtained.

DISCUSSION: Although clinical trials report a low incidence of major psychiatric adverse effects with tirzepatide, this case highlights possible individual vulnerability. Dual GIP/GLP-1 modulation may enhance inhibitory effects on mesolimbic dopaminergic pathways, potentially inducing a clinically significant "reward deficit." In susceptible individuals, such pharmacologically induced anhedonia may paradoxically promote compensatory alcohol use. Further research is warranted to clarify the neuropsychiatric safety profile of dual incretin agonists

Keywords: Alcohol use, anhedonia, case report, GLP-1 receptor agonist, reward system, tirzepatide