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Case Report

Concomitant Tianeptine and Alcohol Use Disorders: Diagnosis and Treatment with Buprenorphine-Naloxone

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INTRODUCTION

Tianeptine was developed in the 20th century as an antidepressant.[1] It has been scrutinized for its uncertain mechanisms of action, with proposed pathways including the glutamate/N-methyl-D-aspartic acid system.[2,3] Classified as an atypical, non-monoaminergic antidepressant in the N06AZ group of the Anatomical Therapeutic Chemical classification system,[1] tianeptine was once believed to function as a "serotonin reuptake enhancer."[1] Current evidence, however, indicates that it acts as a full μ-opioid receptor agonist, producing opioid-like dependence and withdrawal.[4-6]

Although data remain limited,[7] tianeptine use has been associated with overdose, including fatal cases.[5,8,9] Case reports suggest that concomitant opioid use (e.g., fentanyl) may heighten overdose risk.[5,10] Its short half-life also may increase risk in older adults and patients with kidney disease.[6] Early clinical trials suggested efficacy in treating depression among Parkinson's patients, the elderly, those with post-traumatic stress disorder, and individuals with chronic alcohol use disorder.[1,11] Tianeptine is approved for use in more than 60 countries, including parts of Europe, South America, and Asia,[2,12] but it is not approved in the United States due to safety concerns.[13,14] Despite this, it remains available online and in retail outlets such as convenience stores, gas stations, and vape shops under names including *Tianaa, Zaza, Neptune's Fix, Pegasus,* and *TD Red*.[14] Several U.S. states have restricted or banned its sale,[12] and the Food and Drug Administration (FDA) has recently issued consumer and provider warnings.[13,14]

Case reports describe the use of buprenorphine-naloxone to treat tianeptine withdrawal, particularly after failed attempts with mirtazapine (likely due to its shorter half-life relative to tianeptine) and clonidine.[7,11,15] Our case is unique in that the patient also had mild alcohol use disorder per DSM-5 criteria. Notably, the patient reported increased cravings for and heavier use of tianeptine when combined with alcohol.

CASE REPORT

Our patient was a 35-year-old previously healthy male who presented to clinic seeking treatment for tianeptine dependence and mild alcohol use disorder. Two years earlier, he began using kratom (mitragynine; a μ-opioid agonist legally sold in the U.S.) for aches and pains related to his physically demanding job. Kratom initially relieved his symptoms and boosted energy, but over time the effects waned, and he developed cravings and withdrawal symptoms (e.g., flu-like illness when stopping). His use escalated to six kratom capsules, three to four times daily.

After nine months, he switched to tianeptine, which he discovered online. The initial dose relieved his pain, but tolerance developed, likely accelerated by prior kratom use, and he increased to 111 mg/day, exceeding the maximum recommended daily dose by 61 mg. He contin-ued this for 15 months. He then developed severe withdrawal symptoms (nausea, vomiting, palpitations, tremors, myalgias, abdominal pain) and sought emergency care. He reported last drinking alcohol around midnight and last using tianeptine a few hours before presentation. He also reported intermittent cannabis use and episodic heavy alcohol consumption (binge drinking, defined in men as more than five standard drinks per occasion). His vital signs and labs were unremarkable. The emergency department physician determined his symptoms were most consistent with opioid withdrawal and administered two 2-mg buprenorphine-naloxone tablets. His withdrawal resolved within six hours, and he was discharged with a seven-day prescription for 2 mg twice daily, with referral to addiction psychiatry.

At clinic follow-up, he met DSM-5 criteria for moderate opioid use disorder (cravings, withdrawal, failed attempts to cut back, tolerance, escalating dosage, continued use despite harm) and mild alcohol use disorder (desire to cut down, functional impairment, job/family strain). His alcohol consumption typically involved 750 mL of liquor (~17 standard drinks) over a weekend, triggered by work-related stress. He reported an urge to increase tianeptine use during these episodes but denied tremors, seizures, or alcohol-related hallucinations. He noted alcohol use caused more psychosocial distress than tianeptine, particularly at work and in relationships. Cannabis was used only intermittently in small amounts (<1 g).

Buprenorphine-naloxone was initiated for both tianeptine and alcohol cravings, using a micro-induction protocol to avoid withdrawal: Day 1, 1 mg film twice daily; Day 2, 1 mg four times daily; Day 3, 2 mg four times daily; then maintenance with 4 mg four times daily while tapering tianeptine and alcohol. Supportive medications (ondansetron, trazodone, hydroxyzine, loperamide) were prescribed for withdrawal symptoms, and the patient engaged in psychotherapy through an addiction treatment program.

At follow-up, his tianeptine use had decreased, but pain-related cravings persisted. His buprenorphine-naloxone dose was increased to 8 mg twice daily, which alleviated both pain and cravings. He remains stable on this regimen, with both alcohol and opioid use disorders now in early remission and continues monthly follow-up.

DISCUSSION

Our patient had no prior history of opioid misuse before turning to over the counter "gas station" products for pain relief, which ultimately led to addiction. This case highlights growing concerns about the accessibility of tianeptine, marketed and sold with minimal regulation.[5,7,12-14] Although approved as an atypical antidepressant in some countries, tianeptine is widely misused for its opioid-like effects,[13,14] especially outside prescribed dosing (25-50 mg/day), with recreational use

reaching up to 3,000 mg/day.[6]

Its unregulated availability fosters the false perception of safety,[15] increasing risks of addiction and overdose, particularly among individuals with psychiatric or substance use disorder histories.[8,15] Misleading advertising compounds this risk. The website where our patient obtained tianeptine carried a "NOT FOR HUMAN CONSUMPTION" disclaimer yet simultaneously promoted sales through discounts, reward programs, and cryptocurrency payments.[19] Customer testimonials praising its effects further obscure potential harms. Such practices underscore the urgent need for stronger oversight.[20]

Risks are heightened by limited research on drug interactions. A Centers for Disease Control and Prevention analysis of poison control calls (2000-2017) showed 47.7% of tianeptine exposures involved co-exposures, most often with phenibut,[21] alcohol, benzodiazepines, or opioids.[10] Although poorly studied, alcohol appears to alter tianeptine absorption and may interact through overlapping effects on glutamatergic and GABAergic pathways.[1,3,22] In our case, alcohol use intensified cravings for tianeptine. Further study is needed to clarify these interactions and assess risks of concurrent use. Tianeptine should not be considered for treating depression in individuals with alcohol use disorder, given the danger of dual substance misuse.

Treatment of tianeptine addiction is another major gap. No standardized protocols exist, though buprenorphine-naloxone micro-induction has been reported in a few case studies.[15,23] Additional clinical research is needed to establish effective strategies.

In conclusion, the increasing misuse of tianeptine demands urgent medical and regulatory attention. Its widespread availability, deceptive marketing, and lack of treatment guidelines pose significant public health risks. Stronger regulation and more robust clinical research are essential to protect vulnerable populations.

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