CASE SERIES

PEER REVIEWED

Extended-Release Injectable Buprenorphine for Opioid Use Disorder Involving Tianeptine and Kratom: Two Case Reports

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Abstract

Tianeptine and kratom misuse are emerging concerns due to their opioid-like effects and lack of regulation. We describe 2 men with opioid use disorder (OUD) complicated by tianeptine and kratom use, both successfully managed with extended-release injectable buprenorphine. Case 1 involved a 40-year-old man with daily kratom use with intermittent tianeptine exposurewho achieved abstinence and stability following transition to extended-release injectable buprenorphine. Case 2 involved a 23-year-old man with early-onset OUD who also achieved improved control of opioid cravings and withdrawal symptoms, with no further reported kratom or tianeptine use after dose adjustment, although ongoing alcohol use and intermittent polysubstance exposure required continued monitoring. These cases describe outpatient stabilization with extended-release injectable buprenorphine in 2 patients with OUD involving self-reported tianeptine and kratom use.

Introduction. Tianeptine is a substance that has been approved as a tricyclic antidepressant in over 60 countries within Europe, Asia, and Latin America. However, it has not been approved by the US Food and Drug Administration (FDA) for medical use.[1-3] Its mechanism is thought to involve glutamate modulation and full μ-opioid receptor agonism. At higher doses, it can produce euphoria, prompting several countries to impose prescribing restrictions or update labeling to warn of addiction potential.[4,5] Reports indicate that tianeptine has been used in combination with kratom, a plant-derived product native to Southeast Asia, often obtained through sales on the internet and at brick-and-mortar retail outlets, most commonly convenience stores, gas stations, smoke shops. Kratom is sought after based on its stimulant and opioid-like effects, as it contains alkaloids that act as partial agonists at the μ-opioid receptor.[6,7]

Despite its lack of regulatory approval, tianeptine is widely available online and in certain retail outlets, including gas stations, where it is often sold in elixir or powder form.[8,9] This unregulated distribution has led to its misuse, with some individuals referring to it as the lay term, “gas station [6,10]

heroin due to its opioid-like effects when taken at high doses.[5,10] Adverse events are more likely when tianeptine is consumed at doses exceeding the general prescription doses of 25 to 50 mg daily for the treatment of major depressive disorder. However, when taken recreationally, doses exceed 3,000 mg daily.[5,9,10] Many individuals struggle to discontinue tianeptine use, often experiencing withdrawal symptoms.[9] The clinical presentation of tianeptine abuse and withdrawal closely resembles that of opioid toxicity and withdrawal. The signs of toxicity usually include gastrointestinal, neurologic, and cardiovascular symptoms. Withdrawal symptoms usually include chills, sweating, depression, anxiety, and myalgias.[5]

The increasing popularity of tianeptine, coupled with its potential for misuse and dependence, has raised concerns within addiction medicine and public health, as its use can lead to severe withdrawal symptoms and significant health risks. In the United States, reports of adverse effects associated with tianeptine use have been steadily rising. Poison control centers documented a significant increase in cases, rising from just 11 reported incidents between 2000 and 2013 to 151 in 2020 alone.[4,8]

This report discusses 2 cases of patients presenting with severe opioid use disorder (OUD) and daily kratom use with intermittent tianeptine exposure, focusing on the successful use of extended-release buprenorphine as a treatment strategy. The patients' OUD was diagnosed according to DSM-5 criteria, based on clinical assessment during intake interviews conducted by board-certified addiction medicine providers. Approval from the institutional review board was obtained for this investigation. Written informed consent for publication was obtained from both patients described in this case series.

Case Presentation 1

Introduction. A 40-year-old man presented to an outpatient addiction medicine clinic with escalating tianeptine and kratom use over the past year.

History. The patient obtained tianeptine online and took it orally at doses of up to 50 mg every 2 to 3 days over the previous year. His pattern of use was continuous but episodic, marked by several unsuccessful attempts to quit independently. He described severe withdrawal symptoms, including musculoskeletal pain, sweating, chills, anxiety, insomnia, and gastrointestinal distress. Concurrently, he reported daily use of kratom, purchased from online and retail sources, for its stimulant and opioid-like properties. Before initiating tianeptine and kratom, the patient used prescription opioids intermittently over several years. Periods of abstinence typically lasted a few months. He denied use of alcohol, benzodiazepines, synthetic cannabinoids, or nitrous oxide.

The patient's past medical history was significant for attention-deficit/hyperactivity disorder (ADHD), managed with amphetamine-dextroamphetamine 40 mg daily. He also had a history of generalized anxiety disorder, major depressive disorder, and concurrent chronic neuropathic pain, all of which were treated in the past with escitalopram 20 mg daily. He denied prior psychiatric hospitalizations, suicide attempts, or active suicidal ideation. His family history was notable for celiac disease in 1 parent and siblings, rheumatoid arthritis, and hypertension in another parent. The patient lived with

his spouse and children in a stable home environment and worked full-time. He denied household exposure to substances or any history of legal issues.

Diagnostic testing. Although the patient's tianeptine use was lower than or within typical therapeutic daily dosing, dependence and withdrawal symptoms have been described with chronic use, even at lower doses.[10] In this case, kratom use, which was reported as daily, likely represented the primary opioid agonist exposure, with tianeptine potentially contributing to the overall pattern of dependence. Standard urine drug screening was positive for opioids; however, the assay did not specifically test for tianeptine, kratom, or their metabolites. Therefore, the diagnosis was based on clinical assessment and DSM-5 criteria

Differential diagnoses. The differential diagnoses included primary depressive disorder, stimulant dependence (due to prescribed amphetamine-dextroamphetamine), and generalized anxiety disorder–related insomnia. However, the temporal relationship between cessation of tianeptine and emergence of withdrawal symptoms, along with prior opioid exposure, supported opioid use disorder as the primary diagnosis.

Treatment and management. At intake in November 2024, the patient reported symptoms consistent with opioid withdrawal: diaphoresis, nausea, cold and heat intolerance, myalgias, dizziness, weakness, and anxiety. His primary care provider had started clonidine 0.2 mg every 12 hours, ondansetron 8 mg every 8 hours, and ibuprofen 400 mg every 6 hours, and the patient was referred to the addiction medicine department. After comprehensive education on treatment options, including the risks and benefits of buprenorphine, methadone, and naltrexone, the patient opted to begin treatment with buprenorphine-naloxone films.

An induction protocol was initiated, with a starting dose of 4 mg/1 mg, titrated as needed. By day 3, due to persistent withdrawal symptoms, the dose was increased to 16 mg/day. In November, the dose was titrated to 24 mg/day. Following stabilization, the patient expressed a strong interest in long-term treatment with extended-release injectable buprenorphine. In late November, he was initiated on 300 mg every 28 days. Supplemental buprenorphine-naloxone films were briefly prescribed for reported breakthrough symptoms, including in mid-December and early January 2025. He continued to report mild cravings but no relapse. In late January, he received his third 300 mg injection.

Outcome and follow-up. By February 2025, he was stable, and the dose of extended-release injectable buprenorphine was decreased to 100 mg monthly, which continued through March, April, and May 2025, with no reported use of tianeptine, kratom, or opioids. He discontinued supplemental films after the second injection. He described cravings as manageable, resumed counseling, and was started on duloxetine, titrated to 60 mg daily, for better control of his anxiety, depression, and neuropathic pain.

The patient reported stable functioning, continued employment (up to 60 hours/week), and high engagement with treatment. Follow-up visits in June and July 2025 confirmed continued stability with no dose adjustments or return of symptoms.

Case Presentation 2

Introduction. A 23-year-old man presented to an outpatient addiction medicine clinic with a history of OUD and ongoing kratom and tianeptine misuse.

History. The patient reported a history of opioid use beginning at age 16, progressing from intermittent use to daily consumption during late adolescence. Approximately 3 years ago, he experienced an accidental overdose involving a counterfeit pill containing synthetic fentanyl. Since then, he reported abstinence from opioids but persistent cravings for tianeptine.

He described regular use of kratom over the past year, initially consumed as powdered kratom for energy and relaxation. Despite multiple attempts, he was unable to discontinue kratom. Additionally, he used tianeptine, which resulted in hospitalization after an overdose characterized by loss of consciousness.

The patient's medical history was significant for hypertension, alcohol use disorder, stimulant use disorder, and nicotine dependence. His psychiatric history included depression, which was treated with bupropion and escitalopram; he recently discontinued taking both. He denied suicidal ideation, prior psychiatric hospitalizations, or suicide attempts. His family history was notable for OUD and cardiovascular disease. The patient lived independently, worked full-time on alternating 24-hour shifts, and reported spending quality time with his family.

Diagnostic testing. Our clinical assessment and patient history were consistent with recent kratom and tianeptine use, and urine toxicology was positive for opioids. However, we did not specifically test for tianeptine or kratom. Therefore, the diagnosis was based on clinical assessment and DSM-5 criteria.

Differential diagnoses. Our diagnosis considerations included stimulant use disorder relapse, alcohol use disorder–related withdrawal, and generalized anxiety disorder. However, his symptom pattern and response to buprenorphine treatment confirmed that tianeptine and kratom dependence were the principal contributors.

Treatment and management. At presentation in February 2024, after discussion of FDA-approved treatment options for OUD, including buprenorphine, methadone, and naltrexone, the patient expressed a preference for extended-release injectable buprenorphine. He was initiated on buprenorphine-naloxone sublingual films at 1 mg every 2 hours, as needed, up to 8 mg daily, with plans for weekly follow-up and eventual transition to extended-release injectablebuprenorphine.

At the first follow-up in March 2024, the patient reported daily buprenorphine-naloxone use at doses

up to 12 mg, which he found stabilizing. He denied opioid or kratom use. This dose was maintained through March and early April 2024 with stable clinical status. In April 2024, the patient self-decreased his dose to 8 mg/day without experiencing withdrawal symptoms. Subsequent visits revealed intermittent alcohol use, with counseling on the risks of combining alcohol with buprenorphine. Mental cravings for tianeptine persisted, though physical withdrawal symptoms were absent. He reported one brief lapse to tianeptine use following a 2-day lapse in buprenorphine intake. Given these challenges and the inconsistency in taking the prescribed dose of buprenorphine, the decision was to transition to extended-release injectable buprenorphine injections of 300 mg every 28 days.

By mid-May, he received his first 300 mg extended-release injectable buprenorphine injection and discontinued sublingual films. He returned for follow-up in June, where he denied cravings and withdrawal symptoms, but he admitted to continued alcohol use and a single tianeptine episode. He received his second 300 mg injection. In July 2024, his dose was reduced to 100 mg, which was maintained at subsequent monthly through November 2024. The patient remained clinically stable with no further reported opioid cravings, withdrawal symptoms, or tianeptine or kratom use.

During a visit in May, the patient described some breakthrough withdrawal symptoms, and the plan was made to increase the dose if symptoms persisted. In June 2025, we increased his extended-release injectable buprenorphine back to 300 mg, and a good clinical response was reported at the next follow-up.

Outcome and follow-up. Throughout the remaining follow-up visits, the patient reported stable functioning, working regularly, and enjoying time with his family. He continued to report no opioid cravings or withdrawal symptoms and denied tianeptine or kratom use. His alcohol use persisted despite education about the risks of using alcohol and buprenorphine. At 1 follow-up visit, the patient disclosed 1-time cocaine use, which he believed was contaminated with benzodiazepines. His urine drug screening confirmed the presence of buprenorphine, ethanol, cocaine, and benzodiazepines. He remained engaged in outpatient counseling, peer support, and case management, continuing monthly extended-release injectable buprenorphine injections with close monitoring.

Discussion. Tianeptine and kratom are non-FDA-approved substances with opioid receptor activity that have emerged as substances of misuse, particularly among individuals with prior or concurrent OUD. The accessibility of these compounds via retail outlets and digital marketplaces has contributed to increasing misuse and associated health consequences. While both are marketed as legal or natural alternatives, their pharmacological properties, particularly tianeptine's full μ-opioid receptor agonism and short half-life, create a high risk for dependence, tolerance, and opioid-like withdrawal symptoms. Recent poison control data and CDC health alerts reflect a concerning rise in adverse outcomes, including multi-substance overdose and death.[2,5,11] Notably, a review of 15 tianeptine-related overdose cases found that more than half involved co-ingestion of other substances, and 9 of the 15 cases were fatal, underscoring the severe risks associated with its misuse.[11]

Despite these trends, clinical protocols for managing tianeptine or kratom-related OUD remain largely undefined. Standardized assessment tools do not routinely screen for these agents, and most guidelines focus on traditional opioids.[12] The patients described in this case series illustrate how tianeptine and kratom may become substitutes or complements in the opioid use trajectory, sometimes delaying access to evidence-based care.

By providing consistent plasma concentrations and high-affinity partial μ-opioid receptor agonism that attenuates the effects of full agonists,[13] this treatment mitigates withdrawal symptoms, reduces cravings, and lowers relapse risk. Its once-monthly dosing also enhanced adherence and reduced the potential for misuse, making it a valuable option for patients with complex opioid dependence.

Previous reports have explored the use of buprenorphine in treating tianeptine or kratom dependence individually[14,15] and focused more on inpatient rather than outpatient settings.[16] One inpatient study indicated success using a similar combination of buprenorphine/naloxone with a later transition to methadone but faced difficulties once the patient was discharged to an outpatient setting.[17]

This case series is, to our knowledge, the first to document the outpatient treatment of OUD involving both tianeptine and kratom using extended-release injectable buprenorphine. These cases highlight the potential efficacy of ERI buprenorphine in managing complex polysubstance use disorders involving emerging opioids.

More broadly, these cases highlight a gap in clinical surveillance and regulation. Tianeptine is not scheduled at the federal level in the United States, and neither it nor kratom is routinely included in standard urine drug screening panels. As such, patients may underreport or minimize use, and clinicians may lack the tools to recognize these patterns early. Public health and addiction care systems must rapidly adapt to this evolving substance landscape by incorporating education, research, and screening infrastructure that reflects the growing complexity of opioid-related syndromes.

Conclusion. This case series highlights the complexity of managing OUD complicated by self-reported use of tianeptine and kratom. Extended-release injectable buprenorphine provided a feasible outpatient treatment strategy associated with clinical stabilization, offering sustained stabilization and reducing the risk of relapse. As tianeptine and kratom misuse becomes more prevalent, clinicians must be equipped to recognize its unique challenges and employ tailored interventions to address this evolving public health issue. Further studies are warranted to establish standardized treatment and screening protocols to treat emerging opioids.

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