

Kratom Use Disorder with naltrexone precipitated withdrawals: acute withdrawal management and longitudinal treatment

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Case Report

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Abstract

Background

Buprenorphine/naloxone, a partial mu-opioid receptor agonist, remains a first-line pharmacotherapy for opiate use disorder (OUD) and, when appropriately timed following a period of abstinence sufficient to allow onset of withdrawal, can be safely initiated to reduce cravings and stabilize patients with opiate dependence. However, its role is less studied in the treatment of kratom dependence. Current literature review consists of a handful of case reports and series documenting successful use of buprenorphine in kratom dependence.

Case Presentation

We present a novel case of a 30-year-old male with a complex multisubstance use history encompassing alcohol use disorder (AUD), prolonged Kratom dependence, and comorbid generalized anxiety disorder (GAD) experiencing an acute withdrawal episode precipitated by concurrent naltrexone and Kratom ingestion. We further discuss the use of buprenorphine/naloxone therapy in Kratom cessation, and prolonged abstinence.

Conclusions

There appear to be no documented cases of precipitated withdrawals from Kratom after initiation of naltrexone. Alcohol use disorder carries significant morbidity and high rates of relapse even after extended periods of sobriety. Naltrexone remains a cornerstone pharmacotherapy for both alcohol use disorder and opioid use disorder; however, its receptor antagonist properties carry important clinical implications when administered to patients with concurrent opioid dependence, as it may precipitate acute withdrawal in physiologically dependent individuals.

Background

Kratom (*Mitragyna speciosa*) is a plant native to Southeast Asia that is consumed by chewing its leaves fresh, dried, or steeped into a tea. Traditionally used to reduce fatigue and pain for increased productivity or in ceremonial and social contexts, Kratom has recently gained popularity in the US as a drug that can be used to manage pain, anxiety, and substance use disorders.^{1,2} In 2021, an estimated 1.62% of people aged ≥ 12 in the US had ever used Kratom, and this percentage increased to 1.84% by 2023, suggesting an uptick in Kratom use and popularity.³ Despite this, research related to the health effects associated with Kratom use alone or concurrently with other substances is limited. The DSM V currently has no definitions for Kratom use disorders due to the novelty of this compound.

Kratom involves both opioid and non-opioid pathways in its mechanisms of action. Mitragynine and 7-hydroxymitragynine, two of the six psychoactive alkaloids present in Kratom, have shown morphine-like agonist effects in human μ -opioid receptors and antagonist activity with κ -opioid receptors and δ -opioid receptors. However, their effects differ from classical opioids. Kratom alkaloids activate the G-protein coupled pathway rather than the beta-arrestin pathway, which may be associated with the drug's lack of respiratory depression compared to classical opioids. Mitragynine also has non-opioid pain-relieving effects and anti-inflammatory pathways through α -2 adrenoceptor stimulation, inhibition of cyclooxygenase-2 mRNA, CYP inhibition, GABA-B receptor activation, NMDA receptor antagonism, and acetylcholinesterase inhibition.^{1,2}

Kratom poses a theoretical risk for drug interactions as it is processed in the liver by CYP enzymes. Kratom alkaloids inhibit CYP3A4, CYP2D6, and CYP2C9, which may impact drugs with narrow therapeutic windows by inhibiting the liver's metabolism of drugs and other substances.^{1,2}

Kratom is commonly used as a means of reducing or abstaining from non-prescription opioids, abstinence from alcohol (as in this case), easing drug withdrawal symptoms, to relieve chronic pain, or to reduce anxiety and improve well-being.⁴ Kratom has also been used to self-treat alcohol dependence.⁵ A 2017 anonymous online survey showed that pain (91%), anxiety (67%), and depression (65%) were the primary drivers of Kratom use for participants.⁶

Another 2017 survey noted that gastrointestinal symptoms including nausea, vomiting, and constipation were common adverse effects of Kratom use.⁷ In addition, neurological complications, including dizziness or drowsiness, seizures and coma, aphasia, and headaches have been associated with Kratom use.^{7,8,9} Cardiovascular effects including tachycardia, hypertension, ventricular arrhythmia and cardiopulmonary arrest have also been associated with Kratom use.¹⁰

Kratom exposure is associated with greater odds of admission to a health care facility and more serious medical outcomes when combined with other substances.¹¹ Although fatalities related to Kratom use are attributed to the presence of Mitragynine, Kratom has not been shown to be the direct cause of death; instead, these fatalities are associated with polysubstance use, obscuring the risk of death from Kratom use alone.^{1,12}

Throughout 2015-2025, kratom exposure reports to the National Poison Data System increased by approximately 1,200%. A sharp increase in reports seen in 2025 coincided with the emergence of semisynthetic formulations of kratom, including 7-hydroxymitragynine.¹³ According to a survey dispersed by kratom vendors in 2025, whole-leaf powders were the most popular method of consumption and were reported to provide more significant pain relief, energy, and sleep improvements.¹⁴

Case Presentation

Patient Background

A 30-year-old male with a longstanding and multifaceted substance use and psychiatric history presented to discuss treatment for his Alcohol Use Disorder. He reported drinking alcohol for approximately 15 years, with peak use being a six-pack of beer supplemented by hard liquor daily. Patient initiated Kratom for self-treatment of his alcohol dependence and associated anxiety symptoms which worsened on abstaining from alcohol. He subsequently developed a 3-year history of Kratom use, primarily kratom leaf extracts in capsule form, with increasing dosage over time from 3-6 grams per day to more than 20 grams per day at time of seeking treatment (10 g divided into 2 doses, morning and evening). He noted rebounding severe anxiety and GI upset when he missed his Kratom dose. He denied any history of illicit opioid use or injection drug use. He was enrolled in school with one semester remaining at the time of initial presentation and found it difficult to maintain his academic pursuits while trying to self-taper his Kratom use.

Clinical Course

The patient initially presented to discuss the management of his alcohol use disorder. He reported nine months of continuous sobriety but disclosed significant cravings for alcohol, prompting him to seek support through the medication-assisted treatment (MAT) program. Laboratory workup demonstrated liver enzymes within normal limits, supporting safe naltrexone initiation.

Given his active cravings, and normal hepatic function, naltrexone 50mg orally once daily was initiated. His concurrent Kratom use disorder and tobacco use disorder were acknowledged but deferred by mutual agreement to subsequent visits.

The patient presented the next day with myalgias, nausea, and vomiting developing after taking naltrexone within 30 minutes of ingestion of his regular kratom dose. His presentation was consistent with naltrexone-precipitated opiate withdrawal, likely a direct pharmacodynamic consequence of high-affinity mu-opioid receptor blockade displacing Kratom's active alkaloids, from receptor binding sites.

Naltrexone was discontinued, and symptomatic withdrawal management was initiated with ondansetron as needed for nausea, ibuprofen and acetaminophen for myalgias, and diazepam for anxiety and autonomic symptom management.

At the following visit, Acamprosate 333mg, two tablets three times daily, was initiated as an alternative AUD maintenance pharmacotherapy after a thorough discussion as patient wished to continue using Kratom and Acamprosate carries no opioid receptor activity and therefore no interaction risk with Kratom. Treatment for his generalized anxiety disorder was initiated with Fluoxetine (GAD-7 score of 20 at presentation), with up-titration as tolerated and the patient was enrolled in behavioral therapy.

Over subsequent visits the patient endorsed improvement in his mental health (as noted by improving GAD-7 scores) and attempted to self-titrate his Kratom use down with the intention to quit; however, he ended up relapsing in his Kratom use. At subsequent follow up, the patient expressed openness to

initiating buprenorphine therapy for Kratom use disorder. Home induction for Buprenorphine was initiated with 2mg films every 4 hours as needed to be initiated once the patient started experiencing mild withdrawal symptoms (SOWS score of 5-12). Upon 3 day follow up, Patient was noted to be abstinent from Kratom with minimal cravings and well controlled withdrawal symptoms on 8 mg of Buprenorphine daily dose. The patient was eventually stabilized on buprenorphine/Naltrexone 4mg films twice daily at 1 week follow up. The patient continued the same dose long term along with Acamprosate, which he took for 6 more months before discontinuing, however, remains in sustained remission for both AUD and Kratom use disorder (3 years at time of his last visit). Patient was monitored with serial urine drug screens every 3 months to ensure compliance with buprenorphine/naltrexone. Patient continued CBT and Fluoxetine therapy for GAD with his last GAD 7 score of 0.

Figure 1: Protocol for Suboxone (Buprenorphine/Naltrexone) Home Induction. BUP is a mobile application-based home induction tool that guides patients through buprenorphine initiation using a series of questions.¹⁵ SOWS (Subjective Opiate Withdrawal Scale) is a patient-reported assessment of the presence and intensity of opiate withdrawal symptoms and severity used to guide patients on when to proceed with at-home induction.¹⁶

Discussion

Kratom is a relatively new psychoactive product available to the general public with various uses including self-treatment of alcohol and opiate use disorder by patients. This case describes the longitudinal outpatient management of a 30-year-old male with a complex, interrelated constellation of alcohol use disorder, Kratom-induced opioid use disorder, and generalized anxiety disorder. His clinical course marked by naltrexone-precipitated withdrawal due to Kratom dependence, transition to acamprosate, psychiatric pharmacotherapy optimization, and ultimately successful patient-initiated Suboxone induction with early stabilization, illustrates the nonlinear, iterative, and deeply individualized nature of addiction treatment.

Clinicians should routinely screen for the use of kratom prior to initiating naltrexone for AUD or OUD. Patients should be routinely counseled on avoiding concomitant use of naltrexone and Kratom to avoid precipitated withdrawals, as in this case. The patient's course of treatment demonstrates a mutually reinforcing relationship between the patient's GAD and prolonged Kratom dependence. Physicians treating Kratom use addiction should consider a holistic approach to care that incorporates treatment of psychiatric comorbidities in addition to addiction pharmacotherapy.

Conclusion

This case serves as a practical illustration of the risks of naltrexone use in the setting of Kratom dependence, the clinical nuances of buprenorphine induction in Kratom-dependent patients, and the cumulative value of sustained therapeutic engagement across a longitudinal treatment course. Although Buprenorphine remains the therapeutic of choice for treatment for Kratom use disorder, the evidence for

its effectiveness is limited to a few case series and sporadic case reports. More research is needed to further study the role of buprenorphine in Kratom use disorder. We also want to note the limitation of no current DSM diagnosis of Kratom use disorder which poses further hurdles in research.

Currently, Kratom is not federally scheduled in the US, leaving regulation to the state level. In July 2026, the U.S. Drug Enforcement Administration (DEA) issued a Notices of Intent to temporarily place high-potency 7-hydroxymitragynine (7-OH) products and synthetic derivatives into Schedule I of the Controlled Substances Act.¹⁷ Kratom is banned in eight states, while in other states Kratom Consumer Protection Acts (KCPA) have been enacted to reduce harm through age-based sales restrictions, marketing restrictions, or quality control requirements. Local restrictions have also been enacted in some states, in which one or more counties have restricted Kratom.^{18,19} Further research is required to determine the risks of various kratom products and establish effective regulatory measures.

Declarations

Ethics approval and consent to participate: This research was performed in accordance with the Declaration of Helsinki and approved by IRB Valleywise (reference number: CR2026-009). Further information and documentation is available upon request.

Consent for publication: Written informed consent was obtained from the patient for the publication of this report and is available upon request.

Availability of data and materials: Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: SS and LS analyzed and interpreted the patient data regarding the precipitated withdrawal and subsequent treatment and outpatient management. All authors wrote the main manuscript text and SS and LS prepared figure 1 and finalized the manuscript text. All authors reviewed the manuscript.

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Figures

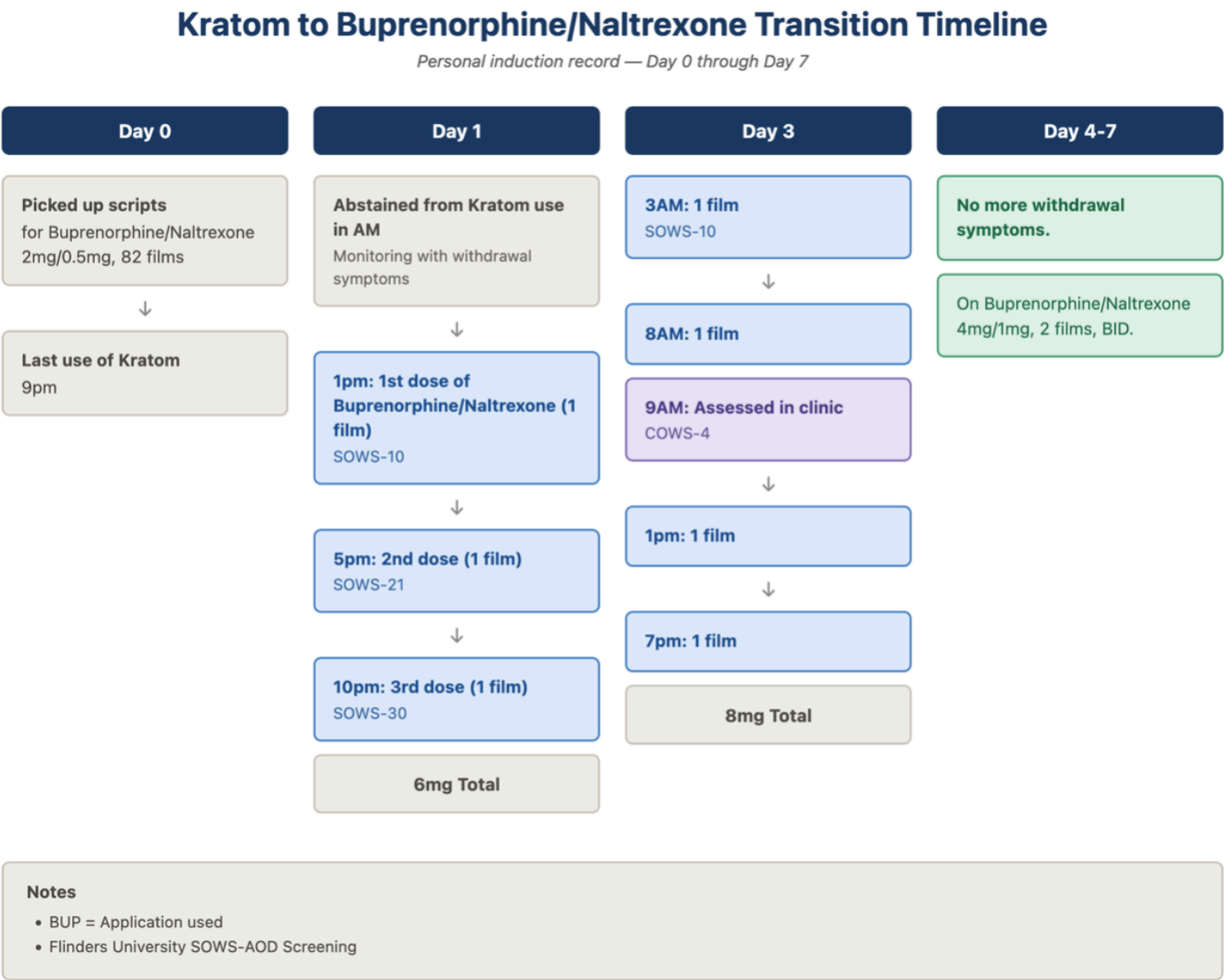


Figure 1

Protocol for Suboxone (Buprenorphine/Naltrexone) Home Induction. BUP is a mobile application-based home induction tool that guides patients through buprenorphine initiation using a series of questions.¹⁵ SOWS (Subjective Opiate Withdrawal Scale) is a patient-reported assessment of the presence and intensity of opiate withdrawal symptoms and severity used to guide patients on when to proceed with at-home induction.¹⁶