Treatment of Kratom Withdrawal and Addiction With Buprenorphine

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In this article, we describe a middle-aged woman with a history of addiction to opioid medications who eventually became dependent on kratom. Her kratom-related withdrawal symptoms responded to a trial of buprenorphine-naloxone. Subsequently, she was maintained on this medication.

Key Words: buprenorphine, kratom, opioids

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Mitragyna speciosa, commonly known as kratom, is a tropical tree native to Southeast Asia (Hassan et al., 2013; Rech et al., 2015) where it has been used as a traditional folk medicine to treat a number of conditions, most notably musculoskeletal pain (Hassan et al., 2013; Cinosi et al., 2015). Kratom leaves may be chewed, smoked, or transformed into a powder that can be used to make a tea (Hassan et al., 2013). Mitragynine and 7-hydroxymitragynine are likely the main alkaloids in kratom responsible for its opioid agonist effects (Hassan et al., 2013). Kratom has been indicated to have stimulant effects in low doses and opioid agonist effects at higher doses (DEA, 2013; Rech et al., 2015). Kratom use is associated with a withdrawal syndrome that includes increased aggression, lacrimation, muscle and bone aches, and jerky limb movements (DEA, 2013). Kratom use cannot be detected by routine toxicology screening tests. Definitive tests like liquid chromatography-tandem or ion mass spectrometry are required (Cinosi et al., 2015).

There has been an increase in kratom marketing in the USA, being advertised as a dietary supplement and a treatment for opioid withdrawal symptoms (DEA, 2013; FDA, 2016). Increased use of kratom in the United States is evidenced by increased calls to poison control centers related to kratom (CDC, 2016), and reports of kratom-related deaths (DEA, 2016). Furthermore, a multistate outbreak of *Salmonella* infections in early 2018 was linked to products containing kratom and resulted in recall of some of these products in the USA (FDA, 2018). Kratom is not scheduled under the Controlled Substances Act, though some individual states have banned it (DEA, 2013; Federal Register, 2016).

CASE PRESENTATION

A 52-year-old woman with long-standing history of major depressive disorder was admitted to an inpatient acute psychiatry unit with a chief complaint of increased depression, anxiety, and fleeting suicidal thoughts. She felt current depression was triggered by exacerbation of chronic pain issues. She also reported symptoms consistent with opioid withdrawal that included dysphoria, nausea, muscle aches, sweating, goose bumps, and insomnia.

Her medical history was significant for addiction to opioid medications over the past 9 years, which developed in the context of treatment of a number of chronic painful conditions including: lymphangioleiomyomatosis, costochondritis, degenerative disk disease, and fibromyalgia. Hidden from her family and her doctors, she ultimately obtained a powdered form of kratom, that she ordered over the internet, and used it regularly over the course of the 9 months preceding this admission. She started using it because it was advertised as working like an opioid, but not addictive. Her use escalated gradually from a quarter of a teaspoon daily, to 1 tablespoon 4 to 6 times daily in an effort to achieve pain relief. She started experiencing withdrawal symptoms that included rhinorrhea, diarrhea, upset stomach, anxiety, restless legs, and increased pain. Her last use of kratom was on the day of this admission.

Upon admission, she was on sertraline 100 mg daily, trazodone 50 to 100 mg at bedtime, gabapentin 300 mg 3 times daily and clonazepam 0.5 mg twice daily. Admission labs including a complete blood count, comprehensive metabolic panel, and urinalysis were largely unremarkable. Her urine toxicology screening was positive only for benzodiazepines.

The patient was induced on sublingual buprenorphine-naloxone 4/1 mg given every 2 hours as she was closely monitored for mental status and withdrawal symptoms. The interval between doses was set at 2 hours to allow each dose of buprenorphine to achieve maximal effect. Four doses (total of 16/4 mg of buprenorphine-naloxone) were administered on the first day before the patient reported improvement of her withdrawal symptoms. The initial plan was to taper off

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buprenorphine-naloxone and her dose was decreased to 2/0.5 mg 4 times daily on the second day. On day 3, she expressed interest in maintenance treatment and her dose was, therefore, kept on buprenorphine-naloxone 2/0.5 mg 4 times a day for the rest of admission.

Upon admission, she had also reported sporadic jerks in limbs and neck—not typical of opioid withdrawal—that subsided with 2 doses of lorazepam 1 mg given oral 6 hours apart on the first day, and 1 dose of 2 mg on the second day of admission. Clonazepam was tapered off over 4 days. She was also given baclofen 20 mg 4 times daily for 2 days, and then reduced to 5 mg 4 times daily for the next 3 days to further help with attenuation of withdrawal. She received trazodone 100 mg every night as needed for difficulty sleeping. The patient also continued to receive sertraline 100 mg daily and gabapentin was increased from 300 to 600 mg 3 times daily after admission to help with anxiety.

The patient's vital signs were stable throughout admission only significant for tachycardia more than 100 beats per minute over the first 24 hours. The patient's depressive symptoms decreased during the course of her hospital stay. On the sixth day, the patient was discharged home on buprenorphine-naloxone 2/0.5 mg 4 times daily, gabapentin 600 mg 3 times daily, sertraline 100 mg daily, trazodone 100 mg at bedtime as needed for insomnia.

After discharge, she followed up in the hospital's outpatient addiction treatment center. She stayed on buprenorphine-naloxone, which was later increased to 8/2 mg twice daily. She remained sober as per her self report and corroborated by weekly urine drug testing, with no symptoms of opioid withdrawal or craving. Compliance with buprenorphine was documented by urine testing for this substance and its metabolite, norbuprenorpine. Urine testing for kratom was not done during admission, but a urine test 6 weeks after hospital discharge, or 48 days after alleged last self-reported use of kratom, showed 4.8 ng/mL of mitragynine and was positive for 7-hydroxymitragynine, using Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS) with threshold of 1 ng/mL, despite the patient vehemently denying any use of kratom during follow-up. The second urine test for kratom 2 months later was negative for mirtagynine and 7-hydroxymitragynine. She has remained compliant with buprenorphine-naltroxone maintenance treatment 18 months after discharge from hospital.

Written informed consent for publication of her clinical details was obtained from the patient.

DISCUSSION

Only few case reports in the literature have addressed treatment of kratom addiction with buprenorphine. Boyer et al. reported a 43-year-old male who used kratom to self-manage opioid withdrawal and chronic pain. Buprenorphine/naloxone was prescribed for abstinence syndrome after stopping kratom, reaching a maintenance dose of 16/4 mg per day (Boyer et al., 2008). Another case report presented a 44-year-old male with coincidence of addiction to kratom and primary hypothyroidism. The patient was induced on buprenorphine in an inpatient setting and his opiate-type withdrawal was resolved within 3 days (Sheleg and Collins, 2011). No details of dosing during induction were mentioned in these 2 reports. Diep et al. described a 25-year-old man who was brought to emergency room and needed ICU care because of unconsciousness, seizure, and later delirium. The patient received a whole host of medications including anesthetics, antipsychotics, opioids (fentanyl and hydromorphone), and benzodiazepines. It was only on day 13, after being transferred to a psychiatric floor, when he received low-dose buprenorphine (2 mg daily) for kratom craving—the authors did not report any withdrawal signs and symptoms at this point—and around 2 weeks later, the patient required an increased dose of buprenorpine (4 mg twice daily) on account of persistent opioid withdrawal signs and symptoms. After discharge, buprenorphine was initially stopped but later started and eventually tapered off after 45 days (Diep et al., 2018). What makes our case report unique is that, unlike Boyer et al. and Sheleg & Collins, we reported the details of the induction phase, and unlike Diep et al., we started buprenorphine-naloxone shortly after admission.

Several buprenorphine induction methods have been reported in the literature for the treatment of opioid withdrawal, mainly differing on the dosing frequency and maximum dose on the first day of induction (Gunderson, 2015). The total dose of buprenorphine on the first day of induction is reported in the literature as ranging between 2 and 16 mg (Casadonte and Sullivan, 2013). The maintenance dose range of buprenorphine is typically between 4 and 24 mg daily (FDA, 2002). Although, once-daily dosing of buprenorphine is enough to cover opioid withdrawal symptoms, divided dosing may help better in opioid-dependent patients with comorbid pain issues to maximize analgesia (Alford, 2015).

In our case, urine testing for kratom, 48 days after inpatient admission day, showed mitragynine and 7-hydroxymitragynine. Studies on kratom pharmacokinetics in humans are very limited. We were not able to find any study showing how long mitragynine or 7-hydroxymitragynine would be detectable in urine. Despite short half-life of the both alkaloids in blood, their high lipophilic properties might result in storage in lipid tissue and longer detection times, especially in people who use drugs on chronic basis. More studies are necessary to investigate this possibility.

Our patient's favorable response to conventional doses of buprenorphine-nalxone offers promise to others who may be addicted to kratom. In the midst of the current opioid epidemic plaguing the United States, it seems that kratom use is gaining popularity. Therefore, greater awareness among health professionals about its potential risks and management of its associated withdrawal syndrome is necessary.

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