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CASE REPORT

A CASE OF PERSISTENT HYPOGLYCEMIA AFTER RECREATIONAL KRATOM INGESTION

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ABSTRACT

Kratom (Mitragyna speciosa) is an indigenous tree of Southeast Asia, the Philippines, and New Guinea often used by local populations for its psychoactive effects. The leaves are dried and either chewed, brewed into a tea, or smoked. Kratom is used as a stimulant,[1] for religious ceremonies, and as an opiate substitute in Malaysia.[2] There have been 660 Kratom ingestions reported to poison control centers from 2010 to 2015.[3] In this case, we describe a presentation of symptomatic, persistent hypoglycemia after kratom ingestion. Kratom leaves contain a range of chemically active alkaloids and itsingestion has been linked to multiple organ system effects. The authors have not found any specific case reports linking kratom use to hypoglycemia.

INTRODUCTION

The case subject is a 65-year-old non-diabetic male who was initially evaluated by EMS after reports of a seizure. On arrival to the patient's home, his blood sugar was found to be 46. He was given 25g of 50% dextrose and had a repeat blood sugar of 227 pre-hospital.

On evaluation in the Emergency Department, the patient was confused and appeared diaphoretic. Vital signs were unremarkable. Initial laboratory evaluation included an electrolyte panel, complete blood count, acetaminophen level, salicylate level, ETOH level, liver function tests and a urine drug screen; all of which were unremarkable. A CT head was performed and was without acute abnormality. Two hours after his initial blood work, a repeat blood glucose level was 66. He was again given 25g of 50% dextrose, started on a 5% dextrose and normal saline infusion and admitted to the hospital. The infusion was discontinued upon arrival to the floor, which resulted in additional episode of hypoglycemia with glucose of 64. He was given an additional 25g of 50% dextrose and a 10% dextrose infusion was started. Despite the infusion, he had recurrent episodes of hypoglycemia with a blood sugars of 49, 69, and 57; the later value recorded 12 hours after arrival to the ED. The patient's blood sugars eventually stabilized and he was ultimately weaned from the dextrose infusion approximately 43 hours after arrival to the hospital. Laboratory work upon admission showed a C-peptide level was notably elevated (6.1 ng/mL, reference range 0.8-3.5 ng/mL). Insulin and proinsulin levelswere normal. No sulfonylureas were detected in his serum. He had a mildly elevated cortisol and normal thyroid studies. He remained in the hospital for several days, without return of symptoms.

On later questioning, the patient admitted to taking 6-7 tablets of Kratom powder throughout the day prior to arrival. The patient obtained the tablets at a local tobacco shop. He stated that he used them to make a tea, by opening them and mixing them in hot water. He denied any other ingestions and reported taking only Esomeprazole as a regular home medication.

DISCUSSION

The pharmacology of the kratom tree is complex. The phytochemical profile found in the leaves of Mitragyna speciosa displays a dose dependent response in humans: at lower doses a psychostimulatory effect is produced, while at higher doses sedative-narcotic effect results.[4] Over 25 alkaloids have been isolated from the leaves of kratom, of them the most abundant is mitragynine. Mitragynine has been

found to act as an agonist at mu and delta-opioid receptors. Additionally, animal studies suggest that it has agonist effects at postsynaptic alpha2 adrenergic receptors, and antagonist action at 5-HT2A receptors.[5,6] 7-hydroxymitragynine, a second phytochemical is less concentrated, but has a high affinity for mu and kappa opioid receptors.[6,25] Other compounds that have been isolated as contributing to the therapeutic pattern include speciociliatine, speciogynine, and paynantheine.[6]

Kratom products are increasingly advertised for their psychoactive properties and as a legal alternative to opioid medication.[20] While the legal status of kratom is being considered,[27] the use of kratom in the US appears to be increasing.[21]The characterization of the plant's side-effects and toxicity is ongoing. At a lower doses mitragynine may be relatively safe, but it does exhibit toxicity at higher doses.[6,9] Side effects that have been reported include impaired cognition and behavior, anxiety, hypertension, renal injury, hepatoxicity, respiratory distress syndrome, propagation of Torsade de Pointes, seizures, hypothyroidism, appetite suppression, and possible trans-placental effects.[7-16,26] Abstinence after regular use is associated with opioid-like withdrawal features including myalgias, insomnia, rhinorrhea, diarrhea, and anxiety.[17]

While there is a paucity of scientific literature discussing kratom ingestion and glycemic influence, there are some anecdotal reports of hypoglycemic effects associated with its use.[18,24] One possible mechanism for the effect observed in the above patient is postulated by J Purintrapiban *et al*. Their study noted that glucose transport in rat muscle cells increased after incubation with kratom extract. This was associated with an increase in GLUT1 protein content which facilitates glucose transport into cells.[19]

CONCLUSION

This case illustrates an association of Kratom use with persistent hypoglycemia, which in this case persisted 12 hours after arrival to the hospital. The patient described had no apparent co-ingestants and laboratory evaluation was suggestive of endogenous insulin release. The patient's lab work showed elevated C-peptide, but normal insulin levels. Given that the half-life of insulin is significantly shorter than C-peptide (4-6min vs 34min respectively),[22,23] it is possible that the patient may have been experiencing episodes of endogenous insulin release. Of note the patient did experience another episode of hypoglycemia 5.5 hours after the C-peptide and insulin assays were resulted and while on the dextrose infusion. Repeat insulin and c-peptide assays were not obtained at that time. It is also possible that the effects on GLUT transporters may have been playing a role. Other considerations would be the effects of other plant alkaloids, adulterants in tablet preparations, or undisclosed co-ingestants. The increase in kratom use will likely lead to more hospital encounters in the future. Further study of chemical properties and effects is warranted.

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