



## Kratom Tramadol Toxicity With Seizure, Hypokalemia, Marked Q-T Prolongation, and Cognitive Impairment: A Case Report

Thomas P. Beresford, M.D.,<sup>1,2</sup> Carrie Keffler, MD, <sup>2</sup> Pari Nouri, MD, <sup>2</sup>  
Mitzi Wasserstein, MD, <sup>1,2</sup> Patrick Ronan, Ph.D., <sup>3,4</sup>

<sup>1</sup> Laboratory for Clinical and Translational Research in Psychiatry, Rocky Mountain Regional VA Medical Center, Aurora, CO 80045;

<sup>2</sup> Department of Psychiatry, University of Colorado School of Medicine, Aurora, CO;

<sup>3</sup> Research and Development Service, Sioux Falls VA; <sup>4</sup> Department of Psychiatry and Basic Biomedical Sciences, Sanford USD School of Medicine, Sioux Falls, SD 57105



UNIVERSITY OF  
SOUTH DAKOTA  
SANFORD SCHOOL OF MEDICINE



### ABSTRACT

**Background:** Kratom is an opiate-like agent that is advertised and sold over-the-counter and is not FDA regulated. As such no clinical trials have been done that assess the safety of this agent nor is it subject to most of the restrictions that would normally attach to agents with central nervous system effects.

**Method:** We report experience with a case of Kratom toxicity and disguise identifying details to project privacy. The case is that of a late 20's male suffering chronic pain who had been ingesting Kratom daily at substantial doses for one year and had added tramadol a few days prior to hospitalization. The patient was admitted for toxic effects and discharged 5 days later with normal mental and physiological state.

**Results:** Immediately prior to admission, this patient was rendered unconscious during a witnessed, tonic-clonic seizure and fell to the floor without striking his head. There is no warning seizure when the patient emitted a high-pitched shout experience contractions of the neck and paraspinal muscles along with tonic-clonic motions. This episode lasted a matter of 10-15 seconds and was self-limiting. Following that postictal slowing of consciousness presented along with cognitive impairment, specifically patient's inability to remember the names of his young children. He was immediately taken to hospital where he was found to have hypokalemia at 2.7 (hospital norm xx) and corrected QT prolongation at 676. Serum magnesium was also low at 1.9. Mental status included marked mood lability and difficulty with concentration. Formal bedside cognitive assessment the next day noted profound impairment in working memory, calculation ability, judgment, and frontal executive functions—all of the setting of continued mood lability that had lessened somewhat. Hypokalemia had been corrected at that point and QTc correction followed the next day. By the fourth day of admission electrolytes and QTc were normal and the cognitive impairments had returned to baseline along with normal control of mood.

**Discussion:** Kratom is marketed as a nutritional supplement, rather than a controlled substance, and acts centrally as an analgesic. There is considerable controversy as to whether kratom, including its 40-plus metabolites, results in opiate abuse. There is a small case literature on seizure occurrence. Whether it lengthens Q-Tc intervals and results in lowered serum potassium concentration remain matters of debate. Contrary to a recent review, our case was clearly associated with these phenomena as well as clear cognitive impairment consistent with a moderate to severe delirium. Metabolic competition with tramadol may have raised kratom concentrations resulting in this constellation of pathologies. This case suggests that it is not an innocuous agent and can result in severe clinical risk to physical health and to cognitive health

**Introduction:** Kratom (*Mitragyna speciosa*) is an opiate-like agent that is advertised and sold over-the-counter and is not FDA regulated. As such no clinical trials have been done that assess the safety of this agent nor is it subject to most of the restrictions that would normally attach to agents with central nervous system effects.

**Method:** We report experience in a heavily disguised case of Kratom toxicity with altered identifying details intended to project privacy. The case is that of a late 20's male suffering chronic pain who had been ingesting Kratom daily at substantial doses for one year and had added tramadol a few days prior to hospitalization. The patient was admitted for toxic effects and discharged 5 days later with normal mental and physiological state.

### Results:

#### Drug exposure:

-- For about one year prior to admission this patient self treated a pain condition with daily doses of Kratom purchased over the counter from a retail vendor near home.

-- Three days prior to the admission crisis, the patient began taking prescription tramadol, again for pain, from an urgent care facility. The dose was 50mg po four times daily for a total dose of 200mg daily.

#### History At Admission

-- **Seizure:** On the day of admission, this patient was rendered unconscious during a witnessed, tonic-clonic seizure and fell to the floor but without striking his head. There was no aura or other warning of seizure onset. Witnesses noted that the patient emitted a high-pitched shout and began to experience contractions of the neck and paraspinal muscles along with tonic-clonic motions. This episode lasted a matter of 10-15 seconds and was self-limiting.

-- **Post-ictal experience:** Following the seizure, postictal slowing of consciousness presented along with cognitive impairment. Specifically, the patient was unable to remember the names of his young children.

-- **Admission:** He was immediately taken to hospital where he was found to have hypokalemia at 2.7 mmoles/L (hospital lower limit was 3.6 mmoles/L), slightly above the potentially lethal limit of 2.7 mmoles/L. Concurrently there was marked with corrected QT prolongation at 676 well above the "borderline" QTc prolongation reported a 430-450. Serum magnesium was also slightly low than the hospital norm at 1.9 mg/dL. Mental status included marked mood lability and difficulty with concentration..

**Disclaimer:** The views expressed in this report are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs or the United States government.

-- **Course:** Formal bedside cognitive assessment the next day noted profound impairment in working memory, calculation ability, judgment, and frontal executive functions—all in the setting of sustained mood lability.  
-- First hospital day: the hypokalemia had been corrected.

-- Second hospital day: QTc corrected to the normal range.

-- Fourth hospital day: cognitive impairments had returned to baseline along with normal control of mood

**Discussion:** Kratom is marketed as a nutritional supplement, and acts centrally as an analgesic. There is considerable controversy as to whether Kratom, and its 40-plus metabolites, results in opiate abuse. There is a small case literature on seizure occurrence. Whether it lengthens Q-Tc intervals and results in lowered serum potassium concentration remain matters of debate. Contrary to a recent review, our case was clearly associated with these phenomena as well as clear cognitive impairment consistent with a moderate to severe delirium. Metabolic competition with tramadol may have raised Kratom concentrations resulting in this constellation of pathologies. This case suggests that it is not innocuous and can result in severe clinical risk to physical health.

**Conclusions:** Kratom-tramadol interaction should be considered a causative condition in cases demonstrating a) cognitive and affective failure in the setting of QTc prolongation and hypokalemia.

Improvement appears to result with cessation of use and supportive treatment targeting the hypokalemia.

### References:

Todd, D.A., Kellogg, J.J., Wallace, E.D. et al. Chemical composition and biological effects of kratom (*Mitragyna speciosa*): In vitro studies with implications for efficacy and drug interactions. *Sci Rep* 10, 19158 (2020). <https://doi.org/10.1038/s41598-020-76119-w>

Darshan Singh Ph.D., Suresh Narayanan Ph.D., Christian P. Müller Ph.D., Balasingam Vicknasingam Ph.D., Murat Yücel Ph.D., Eric Tatt Wei Ho Ph.D., Zurina Hassan Ph.D. & Sharif Mahsufi Mansor Ph.D. (2019) Long-Term Cognitive Effects of Kratom (*Mitragyna speciosa* Korth.) Use, *Journal of Psychoactive Drugs*, 51:1, 19-27, DOI: 10.1080/02791072.2018.1555345