

### **193. A secondary analysis of adverse events and naloxone administration in intentional kratom exposures from 2013 – 2020 using the Toxicology Investigators Consortium (Toxic) registry**

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**Background:** Kratom, a plant indigenous to Southeast Asia that has dose-dependent opioid and stimulant effects, has gained popularity in the U.S. as a method of self-treating pain, anxiety, and opioid dependence or withdrawal. Kratom-associated toxicity, including seizures, cardiotoxicity, hepatotoxicity, respiratory toxicity, and death, are documented, yet likely remain under-identified and -reported. Likewise, naloxone administration has been recommended for reversing suspected kratom toxicity, yet few clinical data regarding prevalence and efficacy of this practice exist. Using the Toxic registry, this study characterized kratom-associated toxicity in patients to whom naloxone was administered, versus not administered, in the presence and absence of coingestants.

**Methods:** This is a secondary analysis of data from the Toxic registry, which prospectively collects prespecified data on all patients seen by the medical toxicologists. Inclusion criteria were all cases of intentional kratom exposures with and without coingestants from 2013-2020. Intentional exposures were defined as purposeful use, misuse, and reported therapeutic use. We examined prevalence of adverse effects (e.g., seizures, hepatotoxicity, cardiotoxicity, signs and symptoms of the opioid toxidrome), kratom dose, and administration of naloxone. The primary outcome was the frequency of specific adverse events, including seizures, hepatotoxicity and cardiotoxicity. Secondary outcomes were the occurrence of the opioid toxidrome and the frequency of naloxone administration in cases of kratom-associated toxicity.

**Results:** Forty-one cases of intentional kratom exposure were identified, with kratom dosing not reported for most cases. Twenty-three patients presented with a coingestant. Coingestants included sedative-hypnotics (26.1%), sympathomimetics (17.4%), anticholinergic/antihistamines (17.4%), opioids (17.4%), herbs/supplements (17.4%), cannabinoids (17.4%), anticonvulsants (4.3%), antipsychotics (4.3%), and antidepressants (4.3%). Five coingestion cases (21.7%) were administered naloxone, with two of these showing coingestion of loperamide and U-47700. Respiratory depression, bradypnea, coma, and central nervous system (CNS) depression were documented in six (26%), three (13%), and seven (43%) cases, respectively. The opioid toxidrome was noted in two patients (8.7%). Three of 18 patients with a kratom-only ingestion (16.7%) were administered naloxone. Of the kratom-only ingestions, respiratory depression, bradypnea, coma and CNS depression were documented in three (16.7%), two (11.1%), and

three (16.7%) cases, respectively. However, the opioid toxidrome was not diagnosed in any kratom-only ingestions. Seizures occurred in four of 41 total cases (8%). Hepatotoxicity was identified in a single patient (2.4%). One additional patient had hepatic injury with elevated bilirubin, and AST >100 but < 1000U/L. Ventricular dysrhythmias was noted in two patients (4.9%), QTc prolongation in three patients (7.3%), and QRS prolongation in two patients (4.9%). Four patients were diagnosed with myocardial injury or ischemia (9.8%).

**Conclusions:** Adverse effects attributable to kratom-only exposure were few but reflect concerning symptoms requiring further study. Adverse events were reported more frequently in the presence of coingestants. Although some literature recommends using naloxone to reverse respiratory depression associated with kratom toxicity, few cases have been reported. This study showed that naloxone utilization is more common in kratom toxicity patients presenting with coingestants than in patients with kratom-only exposures. It is unclear if naloxone administration is effective in reversing kratom toxicity; further work to answer this question is ongoing.