

limits drug absorption and central nervous system (CNS) accumulation. Loperamide is also extensively metabolized via CYP3A4, decreasing its oral bioavailability. Bioactive flavanoids found in grapefruit juice are inhibitors of both p-gp and CYP3A4, and cimetidine is a reversible inhibitor of CYP3A4. When ingested together with these substances, loperamide can accumulate in the serum and CNS, producing desirable central opiate effects like analgesia and euphoria. Cessation of loperamide abuse can lead to withdrawal symptoms similar to those seen with other centrally-acting opiates.

Conclusion: While usually considered safe, clinicians should be aware of the abuse-potential of loperamide when used in conjunction with CYP3A4 and p-glycoprotein modulators like grapefruit juice and cimetidine.

Keywords: Loperamide, Abuse, Withdrawal
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45. Abuse and Withdrawal from the Veterinary Agent Zolazepam-Tiletamine

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Background: Zolazepam-tiletamine is a combination veterinary anesthetic which combines the N-Methyl-D-aspartate (NMDA) antagonist tiletamine with the pyrazolodiazepinone derivative zolazepam which is structurally related to benzodiazepines. Abuse of this agent is a rarely reported phenomenon. We report a case of chronic abuse and withdrawal from this combined anesthetic agent.

Case Report: A 43 year old veterinary technician presented to the emergency department with tremors that progressed to chorea-like movements. The patient reported using intravenous zolazepam-tiletamine for 2 years and had recently increased her use to more than 5 times per week. She became more depressed and developed auditory hallucinations. Due to these symptoms, she abruptly ceased her use and 1 day later developed tremors, first in her hand and then in her legs.

Initial vital signs were within normal limits. Her exam was significant for both tremors and overwhelming chorea-like movements of bilateral upper and lower extremities. The movements increased with intention, all in the setting of a normal mental status without a defined toxidrome. The patient also had ataxia with finger to nose testing, and a narrow based, ataxic gait.

Initial treatments with diphenhydramine and haloperidol were not effective. She was then given diazepam with gradual improvement in her symptoms. An MRI showed mild cerebral and cerebellar cortical volume loss. At 6 month follow-up the patient had persistent mild tremor of her upper extremities but the coarse movements had ceased.

Case Discussion: Zolazepam-tiletamine is a 1:1 mix of zolazepam, a benzodiazepine agonist, and the NMDA antagonist tiletamine. The combination is commonly used as a small animal general anesthetic. Reports of human use are rare with no prior reports of withdrawal from these agents.

Recent research has found that glutaminergic neurons act in conjunction with dopaminergic neurons in the striatum to help coordinate voluntary movements. Excess excitatory input caused by abrupt withdrawal of the NMDA antagonist tiletamine could result in an imbalance between excitatory and inhibitory input resulting in abnormal movements. We theorize that this mechanism could explain our patient's symptoms along with the improvement with benzodiazepines.

Conclusion: We report a case of abuse and withdrawal from the veterinary anesthetic zolazepam-tiletamine. Toxicologist need to be aware of additional health care sites like veterinary offices as sources of emerging drugs of abuse.

Keywords: Abuse, Withdrawal, Dissociative
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46. Prevalence of Serious Adverse Events by Injection or Inhalation of Prescription Stimulants

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Background: According to the National Survey on Drug Use and Health, there were 1.4 million individuals who abused prescription stimulants in the US in 2013. As with prescription opioids, some of these individuals tamper with these products to obtain a greater high. This study assesses whether abuse cases that reported either injecting or inhaling a prescription stimulant were more likely to experience a serious adverse event (SAE) than those that did not.

Methods: Data from the RADARS[®] (Researched Abuse, Diversion, and Addiction-Related Surveillance) System Poison Center Program were used. Route of administration of prescription amphetamine and methylphenidate pills were analyzed from abuse cases reported to the participating poison centers between 1Q2010-4Q2014. An SAE was defined as a medical outcome of major or death or where the case resulted in admission to a health care facility. Only cases with known medical outcomes and routes of administration were included. Multiple logistic regression was used to determine whether use via injection or inhalation was significantly associated with a greater odds of an SAE. Potential confounders were controlled for such as the age in years of the case, gender, and number of substances.

Results: There were 3546 prescription stimulant abuse cases that met inclusion criteria, of which 1320 (37%) experienced an SAE. There were 137 (4%) injection cases and 442 (12%) inhalation cases. Six cases (<1%) reported both injection and inhalation of a stimulant. Cases that reported injecting a stimulant had greater odds of experiencing an SAE than those that did not inject [adjusted odds ratio (AOR) = 1.75, 95% confidence interval (CI): 1.23 to 2.49, p = 0.002]. Inhalation was not significantly associated with an SAE (AOR = 0.90, 95% CI: 0.73 to 1.12, p = 0.346). Both age (AOR = 1.03, 95% CI: 1.02 to 1.04, p < 0.001) and the number of substances reported with the cases (AOR = 1.30, 95% CI: 1.22 to 1.39, p < 0.001) were positively associated with an SAE.

Conclusion: Injecting a prescription stimulant is associated with SAEs among abuse cases. As with prescription opioids, tamper resistant formulations of prescription stimulants could potentially reduce the number of SAEs.

Keywords: prescription stimulants, serious adverse event, route of administration

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47. Acute Cholecystitis Associated With Kratom Abuse

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Background: Derived from *Mitragyna speciosa*, Kratom is a unique drug of abuse with opioid effects. The primary alkaloid mitragynine is thought to contribute to the mu-agonist activity of the drug. Case reports describing Kratom associated toxicity include seizures, fatalities and one report of cholestatic hepatitis. Here we describe a case of transaminitis and cholecystitis subsequent to Kratom ingestion documented with blood levels.

Case Report: A 26-year-old male with no past medical history presented to the Emergency Department (ED) describing 2 weeks of right upper quadrant (RUQ) pain, subjective fevers, and dark urine. Two weeks prior to arrival, the patient attended a party, consumed a large quantity of alcohol (15 to 20 drinks in 24 hours) and ingested a total of 15 g of Kratom. Two days later, he experienced subjective fevers, and a dull, constant RUQ pain radiating to the shoulders and left flank.

On arrival to the ED, the patient's vital signs were: BP 103/47, HR 92, RR 16, SpO₂ 98% RA, T 37°C. His physical exam was unremarkable except for RUQ tenderness to palpation with a positive Murphy's sign. While in the ED, the patient developed a fever to 38.6°C and tachycardia. The patient's initial labs included total bilirubin of 2.3 mg/dL, alkaline phosphatase 171 U/L, alanine aminotransferase (ALT) of 448 U/L, aminotransferase (AST) of 483 U/L, and an undetectable acetaminophen level.

An abdominal ultrasound showed diffuse gallbladder wall thickening with pericholecystic fluid without cholelithiasis or sludge. During admission, the patient was treated symptomatically and was noted to have negative acute viral hepatitis titers, a normal 24-hour urine copper level, and normal ceruloplasmin level. The patient's transaminases peaked at AST of 483 U/L, and ALT of 703 U/L. Transaminases, and the patient's symptoms steadily improved. The patient was discharged on hospital day 3.

Liquid chromatography-quadrupole time-of-flight mass spectrometry was used to analyze samples collected during hospitalization to quantify serum and urine mitragynine levels (see table).

Case Discussion: We present a case of a patient with evidence of acute cholecystitis following Kratom ingestion. While Kratom use has been previously associated with cholestatic hepatitis, this is

Table 1. Serum and urine mitragynine concentrations.

Sample	Time	Mitragynine Concentration (ng/mL)
HD#1 Serum	1736H	13.0
HD#2 Serum	2038H	7.4
HD#3 Serum	1535H	< LOQ (3.5 ng/mL)
HD#1 Urine	1830H	356.3

the first case report of hepatotoxicity with evidence of gallbladder pathology.

Conclusion: Kratom abuse may be associated with hepatotoxicity, including cholecystitis.

Keywords: Drug of abuse, Abuse, Hepatotoxicity

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48. Suicide Online: Google Searches and National Poison Data System (NPDS) Exposures

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Background: NPDS tracks exposures and Google Trends (GTs) provides relative search frequency data by week. We examined the relationship between GTs for medications commonly involved in suicide attempts and suicidal exposures as reported by NPDS.

Methods: We examined NPDS exposures with Reason = Suspected suicide (NRS), from Jan-2004 (the year Google was started) through Dec-2014, by week, and related NRS to GTs for suicide and substances commonly involved. Changes over time in the NRS and GTs were examined via graphical plots, linear regression and correlation analyses. Stepwise regression analysis determined the best of the 20 predictors (19 GTs + Time) for each of 7 NRS groups over 11 y (573 wk). All analyses were via SAS JMP 9.0.0.

Results: There were 2,379,285 NRSs, 551,947 in the 13–19 y group. Ratio of female to male cases was 1.8:1 for All ages and 2.8:1 in the 13–19 y group. The table shows the NRS (mean/wk and mean increase/wk), and the number of GT measures contributing to the best model for each NRS group. Strongest GT contributors for 13–19 y were GTs for 'cold medicine + suicide', 'antidepressants', and 'benadryl or diphenhydramine'; for All ages were GTs for 'commit suicide', 'aspirin', and 'teen + suicide'. NRS for antihistamines increased over time and correlated ($r > 0.733$) with several GTs including 'antihistamine', 'benadryl', and 'diphenhydramine' ($p < 0.0001$).

Conclusions: NPDS suicidal exposures were related to Google searches over this 11 year period. Suicidal exposures for All ages were best predicted by the GT predictors. These results suggest that patients at risk for suicidal overdoses may use Google to search for information prior to overdosing in self-harm attempts.

Keywords: NPDS, Public health, Suicide

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Table 1. Best GT Predictors of NPDS Suicidal Exposures 2004–2014 * $p < 0.0001$.

NPDS Exposures Reason = Suicide	Mean Exposures/Week	Increase in Exposures/Week [95% CI]	Best model (stepwise) # of GT Predictors	R ²
13–19 Y	962	0.448 [0.378, 0.517]	10	0.583*
All ages	4146	1.63 [1.54, 1.73]	7	0.750*
Acetaminophen	345	0.0105 [–0.006, 0.027]	10	0.268*
Antidepressant	747	0.230 [0.205, 0.256]	8	0.529*
Antihistamine	384	0.278 [0.025, 0.295]	7	0.739*
Aspirin	145	–0.010 [–0.017, –0.002]	6	0.154*
Cough and cold	37.6	0.0541 [0.050, 0.058]	8	0.659*