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Overdose of Etizolam: The Abuse and Rise of a Benzodiazepine Analog

To the Editor:

Etizolam is a theinodiazepine, structurally different but pharmacologically similar to benzodiazepines with gamma-aminobutyric acid type A receptor agonism.¹ It is approved for pharmaceutical use in some areas but is available for Internet purchase in the United States and many other countries for research purposes. It is increasing in popularity as a recreational "research chemical." Recent unpublished data from the American Association of Poison Control Centers in the United States has shown an incremental increase in etizolam-related cases each year since 2011, with 41 cases reported as of August 2014. There is little reported in the English literature about the toxic effects of etizolam overdose.

A 31-year-old man presented to our emergency department (ED) after being found unresponsive and bradypneic next to an empty syringe of alleged heroin. By reports, he had also ingested a large quantity of etizolam tablets throughout the day. Out-of-hospital intranasal naloxone, dose of 2 mg, resulted in partial reversal, with improvement of respiratory rate but minimal improvement of his mental status. On arrival to the ED, vital signs were as follows: pulse rate 115 beats/min, respiratory rate 12 breaths/min, blood pressure 132/64 mm Hg, temperature 98.9°F (37.2°C), and pulse oximetry 100% on nonrebreather mask at 15 L/min. He arrived obtunded, he moaned, and he localized painful stimuli. Pupils were pinpoint. Given his profound sedation despite naloxone administration, a trial of 0.2 mg of intravenous flumazenil was used to attempt reversal of etizolam and potentially avoid

intubation and limit need for expanded diagnostics. It caused immediate and complete reversal. Initial remarkable laboratory diagnostics included pH 7.30 and pCO₂ 61 mm Hg on a venous blood gas test, creatinine level of 1.19 mg/dL, glucose level of 116 mg/dL, and WBC count of 18.6 × 1000/mm³. Ethanol, acetaminophen, and salicylates were not detected. ECG demonstrated narrow complex sinus tachycardia. Standard qualitative urine drug screen result was positive for opiates and benzodiazepines. Two hours after arrival, the patient once again became somnolent and bradypneic; he received an additional 2 mg of naloxone intravenously, with complete return to full alertness. He was discharged home neurologically intact after approximately 8 hours of observation.

Confirmatory testing with liquid chromatography/mass spectroscopy of the urine identified the following: codeine level 322 ng/mL, morphine level greater than 1,000 ng/mL, and 6-acetyl morphine level 272 ng/mL, suggesting recent heroin use. No measurable amounts of any of the classic benzodiazepines or metabolites routinely tested at our laboratory were detected. Separate external analysis of initial serum sample quantitated an etizolam concentration of 103 ng/mL. Previous studies have demonstrated that peak and average etizolam concentrations in healthy young men after 0.5 mg twice-daily oral dosing were 9.3 and 3.4 ng/mL, respectively.² Nakamae et al³ reported postmortem analysis of the "unnatural death" of a 59-year-old woman who had a serum etizolam concentration of 263.7 ng/mL.

In summary, etizolam has sedative and hypnotic effects typical of a benzodiazepine, appears to be reversible with flumazenil, and is a widely available research chemical for purchase through the

Internet. The risks of reversal should always be considered, especially in patients with benzodiazepine dependence. Clinicians should be aware of its potential adverse effects, as well as its increasing presence.

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The Wiki: A Key Social Media Tool

To the Editor:

We were pleased to find 2 articles in *Annals'* October edition that focus on social media best practice in emergency medicine.^{1,2} But although these articles provide several good recommendations for tools to aggregate online content, both overlook one of the main categories of social media performing this function, the wiki.

As defined by Scott et al,¹ “social media are any Internet-based applications that enable content sharing and rapid interactions between large populations.” Wikis clearly fit within this definition, providing a mechanism for large populations to rapidly share content, organize information, and generate group consensus.

The world's most famous wiki, Wikipedia, is well known for organizing knowledge for lay readers and is an important source of patient information.³ However, Wikipedia is not meant to provide actionable information to clinicians and has many limitations for that purpose. For example, the Wikipedia style manual specifically discourages technical medical language and drug dosages.

WikEM, supported by the nonprofit OpenEM Foundation, provides a way for medical practitioners to organize online content and cross-reference clinical information in a similar fashion. WikEM is by far the largest emergency medicine wiki, with more than 25,000 edits and 4,500 pages. It is available on the Web and by telephone applications that have been downloaded by more than 100,000 users.

Blogs, podcasts, videocasts, social networks, and custom search engines are all important resources for stimulating research discussion and improving medical education. However, as acknowledged by Thoma et al, “to make effective use of this stream of knowledge, learners must filter and choose from myriad resources.”² We suggest that the wiki is a key social media tool to organize and summarize this growing body of online information. It also has the added benefit of providing easy access to consensus information in the middle of a shift, allowing clinicians to provide better care while at the bedside.

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