The ToxIC NOSE (Novel Opioid and Stimulant Exposure)

Report #15 from ToxIC's Rapid Response Program for Emerging Drugs

Meghan B Spyres, MD & Jessica T Kent, MD, MCISc

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Tianeptine Exposures: "Gas Station Heroin"

Introduction

Tianeptine is an atypical tricyclic antidepressant primarily indicated for the treatment of major depressive disorder as well as anxiety and irritable bowel syndrome.[1] Unlike other typical antidepressants, tianeptine is a full mu-opioid receptor agonist, similar to heroin.[1] While tianeptine has been approved for pharmaceutical use in some regions of Europe, Latin America and Asia, it has not been approved by the Food and Drug Administration (FDA) for use in the United States.[1] Despite its lack of approval, tianeptine is readily available for purchase at gas stations, convenience stores, and online, where it is often marketed to consumers as a "supplement" to provide energy and improve mood.[1,2]

The ToxIC Novel Opioid and Stimulant Exposure (NOSE) Reports

Through the ongoing support of the Opioid Response Network (ORN) since 2020, the American College of Medical Toxicology (ACMT) Toxicology Investigators Consortium (ToxIC) has implemented an enhanced sentinel detector field within the ToxIC Core Registry to identify novel and emerging opioid and stimulant exposures. Once an emerging trend or risk is identified, ToxIC releases a quarterly report.

The goal of this project is to disseminate this novel information to the medical toxicology community as well as the ORN as part of a Rapid Response program.

For more information on the ToxIC Core Registry and data collection, please visit: www.toxicregistry.org

As the opioid crisis within the United States continues to worsen, tianeptine has become an alternative opioid substance, and is colloquially referred to as "gas station heroin."[1,2] As with all opioids, regular use of tianeptine can lead to misuse and dependence, and if stopped abruptly, can result in opioid withdrawal.[3] In addition, the tianeptine that is readily available for purchase in the United States is not regulated and often contains illicit contaminants such as synthetic cannabinoids which can cause further harm to unsuspecting people that use these products.[4]

Tianeptine has emerged as a novel substance of misuse and exposures have been increasingly identified by the ToxIC Core Registry's sentinel event detector. This report summarizes the features of tianeptine exposures reported to the ToxIC Core Registry.

ToxIC Data Review

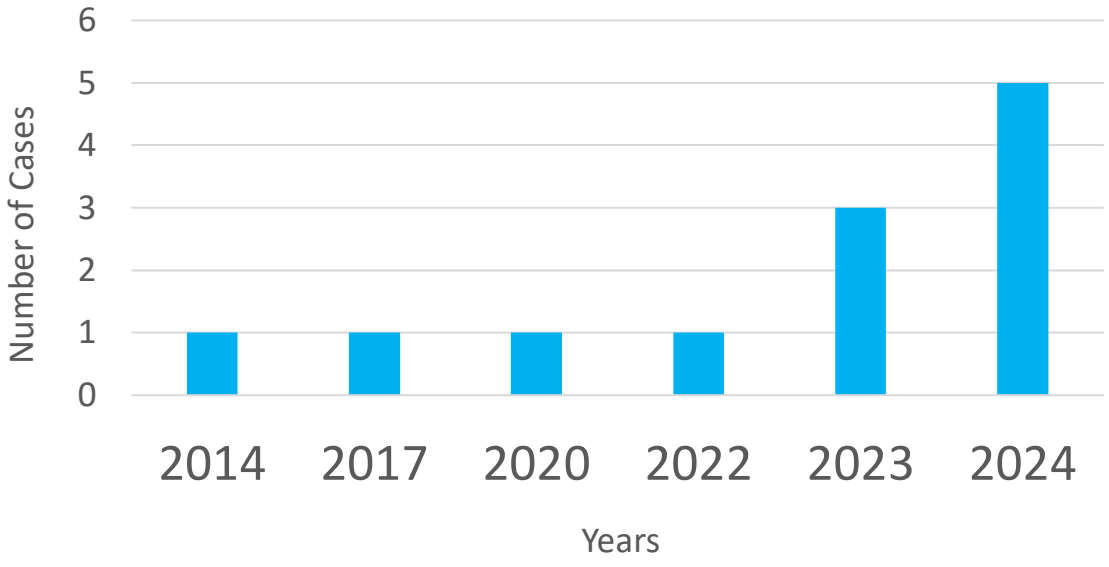
A search of the ToxIC Core Registry identified 12 patients with tianeptine exposure that were evaluated by a medical toxicology physicians within the United States between November 2014 and August 2024. The majority of patients (67%) were reported between January 2023 and August 2024 (Figure 1). Most cases were males (75%) with an average age among all patients of 42 years. Co-ingestants of other substances with tianeptine were reported in 5 patients (42%). The most common additional substance of exposure was another "supplement" with opioid properties, kratom (Mitragyna speciosa), which was taken by 3 patients (25%). The second most common co-ingestant was phenibut, a sedative hypnotic substance, reported in 2 patients (17%). One of the patients with tianeptine and kratom exposure had agitation, psychosis, hallucinations, and bradycardia (heart rate less than 50 beats per minute). Of the 3 patients with tianeptine and kratom exposure, none of them received naloxone.

The majority of tianeptine exposures were intentional exposures where the patient either used the substance to elicit a euphoric or therapeutic effect and it resulted in an overdose (6 patients, 50%). An attempt to avoid opioid withdrawal was the primary reason for exposure in 5 patients (42%). One patient (8%) had an intentional exposure with subsequent withdrawal. No cases of exposure related to self-harm were reported. The most frequently reported neurological clinical signs and symptoms in both overdose and withdrawal cases were agitation (5 patients, 42%), coma (5 patients, 42%), and muscular contractions/tremor/increased reflexes (5 patients, 42%). Among the 7 patients presenting with a tianeptine overdose, 5 patients (71%) had coma and respiratory depression (breathing less than 10 times per minute) but only 3 of those patients (43%) received naloxone for these symptoms. No patients received CPR, but one patient (8%) was intubated for respiratory failure after tianeptine overdose. Of the 5 patients

with a history of recent single agent exposure to tianeptine that experienced withdrawal, 4 of them had agitation (80%) and all 4 were treated with buprenorphine.

Several cases of reported tianeptine use were accompanied by narratives providing additional insight into patterns of use. Interestingly, the first case with reported tianeptine use was in a patient with mental health issues who reported buying tianeptine online for therapeutic purposes to treat his resistant depression. He presented with CNS and respiratory depression treated with naloxone and then was discharged from the hospital with referral information on chemical dependency treatment. A second case with tianeptine use was in a patient who reported using it for health purposes along with 14 other herbal/dietary "supplements", including the psychoactive "supplement" picamilon which is currently only used in Russia for neurological conditions such as motor or speech disorders.[5] A third case with tianeptine withdrawal was in a patient who reported using 5 bottles of a product called "ZaZa Red" daily for 4 months, but was recently unable to afford the product due to the increased cost of purchasing. He developed withdrawal symptoms within 6 hours of last use, including agitation, restlessness, headache, sweating, muscle aches, yawning, nausea, and diarrhea.

Figure 1. Tianeptine cases reported to the ToxIC Core Registry by year between 2014-2024



*Note: Cases from 2024 were accrued between 1/1/2024 and 8/15/2024

Discussion

The shifting landscape in opioid use amidst the opioid crisis has created an environment where drugs with opioid effects, such as tianeptine, are now being repurposed by those with opioid use disorder (OUD) both to achieve euphoria and to avoid withdrawal from opioids. While a few patients in this cohort reported using tianeptine for its antidepressant properties or as a "supplement", for the past 4 years tianeptine use has been reported predominantly in the context of opioid misuse, including to avoid opioid withdrawal.[1,3,6-7]

This report highlights the changing nature in the reasons for tianeptine use, and it also supports an emerging trend of increased use.[1] The fact that tianeptine is unregulated and sought after as a cognitive enhancement tool has created an environment where some may inadvertently become dependent on opioids, as seen in the literature.[6] Furthermore, tianeptine may divert patients with OUD away from treatments with demonstrated safety and efficacy like buprenorphine, a partial mu opioid agonist. Patients in this report who presented with a tianeptine withdrawal were most likely to present with agitation and be initiated on buprenorphine. Buprenorphine has been shown to keep patients with OUD enrolled in treatment and reduce risk of death by up to 50%.[8] While there have been several cases of successful initiation of buprenorphine in patients with tianeptine use disorder, it is unclear whether it is as effective long term, and this represents a future area of study.[9-10]

In the cohort of patients that were exposed to tianeptine, exposures to additional substances occurred in 5 patients (42%). The most common additional substance of exposure was kratom (Mitragyna speciosa) reported in 3 of the above patients. In addition, the second most common co-ingestant was phenibut, a sedative hypnotic substance, reported in 2 patients. Both kratom and phenibut are sold as dietary substances, however the FDA has warned that neither has approval to be marketed as a dietary "supplement" within the United States.[11,12] It is unclear if the co-use of tianeptine with kratom, both with the potential for opioid toxicity, lead to a more profound opioid overdose. Of the 3 patients with tianeptine and kratom exposure, naloxone was not administered, but evaluation of co-exposure in a larger population is warranted.

Conclusion

While tianeptine was initially brought to market for its antidepressant effects, it is increasingly being purchased for its opioid effects for either euphoric purposes or to avoid withdrawal. Buprenorphine was used for many patients in this cohort and preliminary research suggest it could be a possible treatment option for patients with tianeptine use once stabilized.

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Author Information

Meghan B Spyres, MD, FACMT
Department of Medical Toxicology
Banner – University Medical Center Phoenix

Jessica T Kent, MD, MClSc
Division of Clinical Pharmacology & Toxicology
Department of Medicine, University of Toronto

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ORN has consultants in every state and territory to deploy across prevention, treatment, recovery and harm reduction.

Share your needs via the "Submit a Request" form at www.OpioidResponseNetwork.org. Within one business day, your regional point person will be in touch to learn more.

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orn@aaap.org 401-270-5900
www.OpioidResponseNetwork.org