



The Toxic NOSE (Novel Opioid and Stimulant Exposure)

Report #4 from Toxic’s Rapid Response Program for Emerging Drugs of Abuse

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Buprenorphine: Toxicity in the Pediatric Population

Introduction

Buprenorphine (trade named Subutex or Suboxone when combined with naloxone) is a lifesaving medication that has revolutionized the management of opioid use disorder (OUD). However, the rise in buprenorphine prescriptions has led to an increased incidence of pediatric exposure.¹⁻³

The mu opioid receptor is the primary receptor associated with opioid dependence. Full mu agonists, such as heroin or fentanyl, lead to the desired feeling of euphoria, but also generate the deadly undesired effect of decreased respirations and oxygenation. Buprenorphine is an opioid that binds the predominant opioid receptor, the mu receptor.

However, in therapeutic doses buprenorphine acts as a partial agonist at this receptor, partially activating the pathway to decrease cravings and ultimately decrease relapse without overt euphoria or respiratory depression.⁴

The Toxic Novel Opioid and Stimulant Exposures (NOSE) Reports

As a project of the Opioid Response Network (ORN), the American College of Medical Toxicology (ACMT) Toxicology Investigators Consortium (Toxic) is using the enhanced sentinel detector field to identify and report on novel and emerging opioid and stimulant exposures reported in Toxic every quarter over a 2-year period.

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.

An accidental overdose of buprenorphine in adults is not a major risk when compared to full agonists like methadone or fentanyl. In children however, buprenorphine is considered a “one pill can kill” agent, indicating a risk of significant opioid toxicity and/or death after accidental ingestions of even small doses of buprenorphine.⁵

This report highlights a pediatric buprenorphine exposure detected in the Toxicology Investigators Consortium (ToxIC) Core Registry Novel Opioid and Stimulant Exposure (NOSE) indicator. This case prompted a deeper look at other pediatric buprenorphine exposures in the ToxIC Core Registry.

The Case

A 2-year-old boy opened a child proof medication bottle and ingested ½ a sublingual tablet of his father’s buprenorphine/naloxone (8/2mg). After placing the tablet in his mouth, the boy informed his father, and the father was able to recover some of the tablet out of the child’s mouth. The child was brought to the emergency department where he had multiple episodes of emesis and became lethargic. He received three doses of naloxone (1 mg each; 2 intramuscular and 1 intravenous) and was transferred to a hospital with a medical toxicologist on staff. Upon arrival, the child was more awake with a normal mental status and was able to eat and drink. No additional naloxone was given, and he was admitted to the ICU for monitoring overnight. The following morning, more than 12 hours after ingestion, the patient was noted to be lethargic again with pinpoint pupils and was not easily arousable. His vital signs were below normal range for his age, with a blood pressure of 80/45 mmHg, heart rate of 90 beats per minute (bpm), and respiratory rate of 14 breaths per minute with an O₂ saturation of 97% on room air. He was initially given 0.01 mg/kg (0.2 mg total) naloxone intravenously without effect. A subsequent dose of 0.8 mg naloxone was then administered with reversal of sedation and restoration of normal mental status along with an increase in blood pressure and heart rate (96/54 mmHg and 116 bpm, respectively). The patient was observed in the ICU for the remainder of the day but did not develop recurrent symptoms.

Toxic Data

A review of the ToxIC Core Registry revealed 223 pediatric (age ≤12 years) buprenorphine exposures between 2010-2021. This represented 35% of the total cases of pediatric opioid exposures reported to the registry during that period. When single agent buprenorphine

exposures (N=172) were reviewed, the majority of the cases were in children under 7 years of age (N= 168, 98%), more than half of which were under age 2. Most cases (97%) were “unintentional exploratory ingestions” similar to the case presented above. Mental status depression was common (68%) and respiratory depression was reported in 28% of the cases. Naloxone was administered in 52% of cases.³

Discussion

The instinct of a small child to explore their environment by putting objects in the mouth puts them at unique risk for what the medical toxicology community terms “pediatric exploratory ingestions.” Though a single pill ingestion of most medications does not often cause life-threatening toxicity, there are a few medications that can be lethal to a child even in small amounts.⁵ Buprenorphine is one such medication; the risk is compounded by increased use of buprenorphine in OUD, and fast absorbing dissolvable formulations such as sublingual disintegrating tablets. Once exposed, prolonged or recurrent toxicity in children is a known risk due to buprenorphine’s prolonged half-life of 24-48 hours.

Conclusion

Buprenorphine, an effective and safe medication for OUD in adults, can cause significant and prolonged opioid toxicity in young children. Practitioners prescribing this medication should educate their patients on the danger of overdose in children, safe medication storage, and the need for medical evaluation for all cases in which a child is exposed to buprenorphine.

References

1. Boyer EW, McCance-Katz EF, Marcus S. Methadone and buprenorphine toxicity in children. *Am J Addict.* 2010;19(1):89-95.
2. Geib AJ, Babu K, Burns Ewald M, Boyer EW. Adverse Effects in Children After Unintentional Buprenorphine Exposure. *Pediatrics.* 2006;118(4):1746-51.
3. Rege SV, Ngo DA, Ait-Daoud N, Rizer J, Sharma S. Epidemiology of pediatric buprenorphine and methadone exposures reported to the poison centers. *Ann Epidemiol.* 2020;42:50-57.
4. Contet C, Kieffer BL, Befort K. Mu opioid receptor: a gateway to drug addiction. *Current Opinion in Neurobiology.* 2004;14:370–378.
5. Koren G, Nachmani A. Drugs that can kill a toddler with one tablet or teaspoonful: A 2018 updated list. *Clin Drug Investig.* 2019;39(2):217-220.

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About the *Opioid Response Network (ORN)*:

ORN provides free, localized training and education for states, communities, organizations and individuals in the prevention, treatment and recovery of opioid use disorders and stimulant use. Learn more and submit a request at www.OpioidResponseNetwork.org.

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