



The ToxIC NOSE (Novel Opioid and Stimulant Exposure)

A Report from ToxIC's Rapid Response Program for Emerging Drugs of Abuse

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An Infant Presents with Severe Opioid Toxidrome. Could Breast Milk Be the Culprit?

Introduction

Confusion and misinformation surround the transmission of opioids into breast milk. This topic is particularly important to mothers on medications such as methadone and buprenorphine for medications for addiction treatment (MAT) for opioid use disorder (OUD). The case of an opioid toxic breast fed infant, as well as recent data from ACMT's ToxIC Registry, and a review of relevant medical literature are described here. This report helps to illuminate safety considerations regarding breast feeding and medication storage for parents on opioids.

The Case and ToxIC Data

The Case

A 3-month-old girl was found pulseless by EMS. Per the mom, she became limp, unresponsive, and blue while being fed expressed breast milk from a bottle. EMS started CPR and gave naloxone with return of pulses en route to the hospital. She sedated again in the ER and received a second dose of naloxone four hours later. Her work up showed a positive methadone screen but was otherwise unremarkable including negative head CT, chest x-ray, and basic labs. She was transferred to a tertiary care toxicology center.

On arrival, approximately 5 hours after the initial event, she was found to be minimally responsive to noxious stimuli and was given 0.4 mg IV naloxone with return of normal mental

The ToxIC Novel Opioid Stimulant Exposures (NOSE) Reports

As a project of the ORN, ACMT 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.

status. She was started on a naloxone drip. That morning, she was noted to have pinpoint pupils but did not have significant respiratory or mental status depression. Naloxone drip was discontinued 12 hours after initiation, and the patient was observed an additional 8 hours. No other naloxone doses were given.

Advanced toxicology testing, including gas chromatography mass spectrometry (GCMS) test and opioid screen, were significant only for methadone. No other opioids or other substances were found. Several weeks later, a quantitative serum methadone level resulted elevated at 330 ng/mL.

Investigation into the possible source of methadone revealed that the mother and father were both on daily methadone as part of medications for addiction treatment (MAT) for opioid use disorder (OUD). The mother had been on a stable dose and used no additional opioids. Methadone was kept in a locked box in the home. The baby was fed expressed breast milk once in the morning and once in the evening, but otherwise was formula fed. The clinical question arose as to whether the source of the methadone toxicity could be breast milk consumption.

Toxic Data

In 2020, 57 young pediatric (age <7) cases involving opioid ingestions were reported to the Toxic Registry. This represented 9% of all Registry cases in this age group during 2020. Of these, all were unintentional ingestions except for one case that involved a medication error in a therapeutic use medication, and one case that was a consult for interpretation of lab data for possible malicious intent.

Ages ranged from 1 month to 6 years of age, average age 21 months (1.8 years). 13 cases (22.8%) involved more than one substance. Of the opioid substances in these cases (n=60), the most common was buprenorphine (37%), followed by fentanyl (30%). See Table 1. Naloxone administration was required in 60% of cases. There were no deaths reported.

Substance	Incidence Reported
Buprenorphine	22
Fentanyl	18
Methadone	5
Oxycodone	5
Opioid Unspecified	4
Tramadol	2
Naloxone	2
Hydrocodone	1
Morphine	1

Discussion

There has long been confusion and misinformation clouding the risk of maternal opioid transmission into breast milk. In the medical community, this is in part fueled by a controversial case of an infant death initially attributed to rapid maternal metabolism of codeine to morphine and resultant delivery of toxic morphine concentrations to breast milk.¹ Subsequent data has suggested direct administration of codeine to the infant as the cause for toxicity.² The medical literature contains several other cases of severe opioid toxicity in breastfeeding infants; however, many are incompletely documented and lack a clear link to breast milk as the source.^{2,3} These fears, combined with known metabolic and clearance deficiencies in the neonate³ underly breastfeeding safety concerns for mothers on methadone or buprenorphine for MAT.

The American College of Obstetricians and Gynecologists (ACOG) guidelines assert that it is safe for mothers on MAT to breastfeed their babies, and in fact, they encourage it.⁴ Stipulations include that mothers should be on stable doses of their medications and not using other opioids. Despite expert recommendations supporting this practice, unease among families and clinicians persists. Two toxicologist-authored reviews offer guidance on the risks of opioid transmission into breastmilk.^{2,3} The reviews detail the physiology of xenobiotic transmission into breast milk with specific attention to potential opioid concentrations. Both reviews conclude that the percentage of opioids transmitted into breast milk is exceedingly low across the board. With regards to methadone, only 1.2-7% of the mother's weight adjusted dose is transmitted into breast milk (Relative Infant Dose, RID). For buprenorphine, the RID is 0.4%.³ The serum methadone level reported in this case (330 ng/mL) was well above levels reported in breast feeding infants of mothers on methadone (<8 ng/mL) and consistent with levels reported in infant fatalities.⁵

Conclusion

In light of the above data, it is implausible that the otherwise healthy baby described in this case developed such a high methadone level as a result of breast milk from her mother. It is safe and healthy for women who are stable on MAT to breastfeed their children should they choose to do so.

An additional learning point from this case is the high risk of recurrent and prolonged opioid toxidrome after methadone ingestion. The half-life of methadone is extremely long, and toxicity can recur after naloxone wears off. It is common for these patients to become repeatedly symptomatic after initial naloxone administration; continuous naloxone infusions may be required. Patients who have been exposed to long-acting opioids such as methadone or buprenorphine should be observed for an extended period of time to ensure that they do not become recurrently symptomatic. Children are particularly susceptible to prolonged toxicity due to their small size.

Although maternal MAT therapy is low risk to breast feeding children, opioid toxicity in young children occurs easily via other methods. Notably, exploratory ingestions of improperly secured medications and intentional administration of opioids by caregivers does occur.

This case and the published data reviewed supports the safety of breastfeeding for mothers on stable MAT therapy. Exploratory ingestions represent the vast majority of recent opioid cases in young children reported to the ToxIC Registry. Buprenorphine, presumably for MAT therapy, was common in this series. Such data highlight the need for proper storage of all medications, in particular opioids or other medications and substances that can be life-threatening to children.

References

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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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