The ToxIC NOSE (Novel Opioid and Stimulant Exposure)

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Cychlorphine: An Emerging Opioid

Introduction

Cychlorphine (or N-propionitrile chlorphine) is a non-fentanyl synthetic opioid that emerged in late 2025 in the United States. It belongs to the orphines, a class of opioids that includes brorphine, which continue to have new analogs reported.[1,2] As with other opioids, there is a significant risk of fatal respiratory depression in overdose.

Increasing amounts of cychlorphine have been identified in patient samples since late 2025 by the Center for Forensic Science Research and Education (CFSRE).[2] Since then, it has been detected in the illicit drug supply in at least 10 states, with the greatest prevalence in Ohio, Texas, and Tennessee.[4] Cychlorphine often co-occurs with other

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

opioids, traditional stimulants, or novel benzodiazepines.[2] Because of its recent emergence and illicit nature, reliable data are limited, however it is thought to be as potent or more potent than fentanyl.[2,4] Due to cychlorphine's novel structure, hospital urine drug screens for opiates and fentanyl will have a negative result. In addition, fentanyl or nitazene test strips will not flag cychlorphine, putting patients at additional risk.[5]

The following report presents a case of non-fatal opioid overdose with cychlorphine identified through the Toxicology Investigators Consortium (ToxIC) Fentalog Study, an ongoing multicenter prospective observational project that includes adult patients presenting to the emergency department (ED) with suspected opioid overdose.[6] For all patients in the Fentalog Study, clinical data are collected, and residual blood specimens remaining after routine ED clinical testing are sent to the Center for Forensic Science Research and Education (CFSRE) for comprehensive toxicological analysis.

Case Presentation:

A young adult with a past medical history of chronic respiratory and kidney disease, chronic pain, depression, and polysubstance use was found unresponsive with respiratory depression. Emergency medical services administered 6 mg of naloxone intranasally with reported improved level of consciousness.

The patient was transported to an ED where the following initial vitals were recorded: blood pressure of 107/90 mmHg, heart rate of 110 beats per minute, respiratory rate of 28 breaths per minute, oxygenation of 91% on a nasal cannula, and initial temperature of 36.8° Celsius. Within the first 24 hours, the patient's range of vital signs were blood pressure 98/59 to 158/116 mmHg, heart rate 66 to 117 beats per minute, respirations 13 to 37 breaths per minute, temperature 36.4° to 37.3° Celsius and the lowest oxygenation recorded was 86% on a nasal cannula.

A hospital urine drug screen was positive for benzodiazepines and cannabinoids, and negative for amphetamine, barbiturates, cocaine, fentanyl, methadone, opiates, oxycodone, and phencyclidine.

The patient later reported that she utilized alprazolam prior to the overdose and denied any known use of an opioid. She was admitted to the floor and did not require any further naloxone in the hospital. Her discharge diagnoses included benzodiazepine overdose and moderate benzodiazepine use disorder.

CFSRE performed comprehensive toxicological testing of the patient's serum which identified acetaminophen, bromazolam, carboxy-THC, caffeine, citalopram, cychlorphine, naloxone, naproxen, and nicotine and trazodone with their respective metabolites.

Discussion

This case describes a patient exhibiting clinical signs of non-fatal opioid overdose with confirmed cychlorphine detected in the patients serum. Notably, the screening performed by the hospital included testing for both opiates and fentanyl, but it failed to detect this compound. EMS administered naloxone to the patient based on their presentation prior to any testing, highlighting the importance of clinical findings and exam guiding treatment. Knowledge of the presence of novel opioids in the illicit drug supply reinforces this approach.

It is also notable that the patient had no awareness that she had taken an opioid, instead believing that she was using a prescription benzodiazepine. This highlights the contamination of the current drug supply with emerging opioids, including its appearance in counterfeit pills. In this case, cychlorphine was found alongside the illicit benzodiazepine, bromazolam, consistent with prior reports in fatalities.[2]

While the novelty of cychlorphine limits our knowledge, other members of the orphine class have been studied. Brorphine resulted in an outbreak starting in 2019 following the scheduling

of members of the nitazene class of opioids. It was found to be 9 times more potent than morphine, but less potent than fentanyl. Clinical reports of brorphine detail a toxidrome and withdrawal state similar to other opioids.[1]

Another orphine analogue, chlorphine, shares a similar structure as cychlorphine. In previous studies, chlorphine was found to have the strongest affinity for the mu opioid receptor as compared to other orphine analogues. Additionally, the respiratory depression with chlorphine were attenuated by naloxone, though only partially in some circumstances tested.[3] The behavior of similar orphines is suggestive that cychlorphine may be expected to have increased affinity for the mu opioid receptor, and possibly longer duration of action versus brorphine.

The case presented above further demonstrates that ingestion of cychlorphine resulting in an opioid toxidrome was responsive to naloxone. Ultimately, however, more clinical and lab data is needed to definitively characterize this compound.

Conclusion

Cychlorphine is an emerging opioid that highlights the rapidly evolving illicit drug supply and the need for continued surveillance of novel synthetic opioids. Clinicians should maintain high index of suspicion for opioid toxicity in patients presenting with exam findings consistent with an opioid overdose, even when routine hospital drug testing is negative. Patients with suspected opioid overdose should be treated based on clinical findings, including naloxone administration when indicated, and offered naloxone on discharge and medications for opioid use disorder when appropriate.

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About the *Opioid Response Network (ORN)*:

Working with communities

- The SAMHSA-funded Opioid Response Network (ORN) assists states, tribes, organizations and individuals by providing the resources and technical assistance they need locally to address the opioid crisis and stimulant use.
- Technical assistance is available to support the evidence-based prevention, treatment, recovery and harm reduction of opioid use disorders and stimulant use disorders.
- The Opioid Response Network (ORN) provides local, experienced consultants in prevention, treatment, recovery and harm reduction to communities and organizations to help address this opioid crisis and stimulant use.
- ORN accepts requests for education and training.
- Each state/territory has a designated team, led by a regional Technology Transfer Specialist (TTS), who is an expert in implementing evidence-based practices.

Contact the Opioid Response Network

To ask questions or submit a technical assistance request:
Visit www.OpioidResponseNetwork.org or Email orn@aaap.org

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