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Health Alert

In Philadelphia, medetomidine, a potent non-opioid veterinary sedative, has been detected in the illicit drug supply.

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SUMMARY POINTS

- Drug-related morbidity and mortality remain high in Philadelphia and is complicated by a dangerous and changing drug supply.
- Medetomidine, a veterinary alpha-2 agonist that is more potent than xylazine, has been detected in Philadelphia's drug supply.
- All samples that contained medetomidine were 'dope' samples and contained xylazine and fentanyl.
- Introduction of medetomidine to Philadelphia's drug supply can likely be attributed to events involving symptoms of hypotension, bradycardia, and prolonged sedation that is not reversed by naloxone.
- Patients may report symptoms of withdrawal from medetomidine that may be responsive to clonidine, a similar alpha-2 agonist.
- Withdrawal management should prioritize treating opioid withdrawal with buprenorphine or methadone and add clonidine early for patients who are hemodynamically stable and have persistent symptoms.

Drug-related morbidity and mortality remains high in Philadelphia, where more than 1,400 individuals died from unintentional overdoses in 2022 and thousands more experienced non-fatal overdoses and skin and soft tissue infections. Complicating both the medical and public health response to this crisis is the widespread adulteration of the illicit drug supply. While the focus is often placed on new opioid analogues of known illicit substances, monitoring adulterants in the drug supply is equally as important.

The Philadelphia Department of Public Health (PDPH) Surveillance Drug Checking Program has detected **medetomidine** in Philadelphia's drug supply. This is the first time medetomidine has been detected in illicit drugs being used in Philadelphia. Medetomidine has previously been detected in Maryland, Ohio, Florida, and Canada.[1] In Philadelphia, medetomidine was identified by the Center for Forensic, Science, Research, and Education in drug samples submitted by PDPH during the timeframe of 4/29/2024-5/1/2024. The samples were submitted as part of PDPH's ongoing surveillance of drugs associated with overdose. Reports of patients presenting to hospitals during this timeframe included symptoms of prolonged sedation, bradycardia, and hypotension, which are consistent with the expected clinical effects of medetomidine. At this point, a link to these adverse drug events and the introduction of medetomidine to Philadelphia's drug supply has not been established. To date all samples that contained medetomidine also contained xylazine and fentanyl.

Clinical Effects of Medetomidine

Similar to xylazine, medetomidine is a synthetic alpha-2 adrenoreceptor agonist sedative used in veterinary medicine. In human medicine, medetomidine is most similar to dexmedetomidine (Precedex®) and clonidine. However, medetomidine is not approved for human use and understanding of its clinical effects is based on veterinary literature.

In the veterinary literature, the effects of medetomidine include sedation, analgesia, muscle relaxation and anxiolysis (i.e., anti-anxiety).[2] Medetomidine is more potent than xylazine and produces greater

and longer acting sedation.[3,4] Medetomidine is metabolized by the liver, and, when used alone, peak plasma levels occur within 10-30 minutes of administration and the elimination half-life is 1.6 hours.[3] The duration of sedation provided by medetomidine lasts for 2-3 hours, but sedation can be prolonged with co-administration of opioids.[4–6]

Adverse Effects of Medetomidine

Medetomidine use among humans is not well described, and adverse effects may be similar to those associated with dexmedetomidine, such as bradycardia and hypotension.[7] Based on veterinary studies, medetomidine has been shown to cause bradycardia, hyperglycemia, diuresis, and low cardiac output.[4,5] In addition, medetomidine may cause several adverse gastrointestinal effects, such as vomiting, decreased gastric motility, and bloody diarrhea.[3,4,6] Peripheral vasoconstriction caused by medetomidine has been widely described, which may impact wounds and wound healing among people who use drugs in Philadelphia.[2,4,5]

In the veterinary literature, medetomidine-mediated peripheral vasoconstriction has complicated presentations of cyanosis and interpretations of pulse oximetry.[1,2,5] It is possible that individuals who use medetomidine in Philadelphia have falsely low pulse oximetry results. Medetomidine has also been associated with muscle twitching and hypothermia.[2] Lastly, in the veterinary literature, medetomidine has been shown to associated with respiratory depression, as well as greater respiratory depression when co-administered with opioids.[1,2,4] Again, medetomidine use among humans is not well described. Dexmedetomidine, the closest proxy to medetomidine in human medicine, is not known to cause respiratory depression.[8]

Similar to xylazine, the effects of medetomidine may be reversed by atipamezole or yohimbine.[6] However, atipamezole and yohimbine are not approved for human use. Administration of atipamezole or yohimbine to someone regularly using illicit drugs in Philadelphia may lead to harmful and abrupt alpha-2 agonist withdrawal symptoms, such as hypertension, tachycardia, and agitation.[9] Thus, atipamezole nor yohimbine should not be used to reverse adverse effects of medetomidine. Individuals who experience severe symptoms of bradycardia, hypotension, and sedation attributed medetomidine use can be best managed with evidence-based critical care, such as airway management and cardiovascular support.

Overdose Response

Naloxone administration is the first step in responding to a drug overdose. As with xylazine, medetomidine may cause prolonged sedation which emphasizes the role of administering rescue breaths, placing an individual in the rescue position, and monitoring the individual after administration of naloxone. Monitoring should be focused on breathing and ensuring that individuals who experience an overdose are able to protect their airway, which may be compromised in the setting of prolonged sedation. Once individuals are breathing on their own and taking a minimum of one breath every six seconds, they no longer require more naloxone. All overdose responses should include calling 911 so the individual can receive medical therapy, which may include supplemental oxygen.

Withdrawal Management

All samples that tested positive for medetomidine also contained fentanyl, so withdrawal management should prioritize treatment of opioid withdrawal with methadone and buprenorphine. Medetomidine withdrawal has not been well described but is likely similar to dexmedetomidine withdrawal that has been well described in the pediatric critical care literature and includes hypertension, tachycardia, and agitation.[9] Clonidine has been shown to be an effective therapy in the treatment of dexmedetomidine withdrawal and is an adjunctive medication for the treatment of opioid withdrawal. So, for patients who

are hemodynamically stable and have persistent withdrawal symptoms despite optimizing opioid agonist therapy, providers should add clonidine early in withdrawal management and titrate to effect.

Wound Care

It is not clear if medetomidine causes wounds similar to those associated with xylazine use. Medetomidine has been shown to cause vasoconstriction in the veterinary literature, which may have implications for wound healing and wounds associated with drug use. Providers should follow best practices for the care of people with xylazine-associated wounds, which can be found here.

Treat Substance Use Disorder (SUD)

SUD is a treatable chronic health condition. All clinicians registered with the Drug Enforcement Administration (DEA) can prescribe buprenorphine for the management of opioid use disorder and opioid withdrawal. In addition to buprenorphine, hospital-based clinicians can treat opioid use disorder and opioid withdrawal with Methadone. In the outpatient setting, clinicians can refer patients with opioid use disorder to an opioid treatment program for methadone initiation using the resources below. Patients with stimulant use disorder can benefit from behavioral therapies, such as contingency management, as well as from off-label medications following guidance from the American Society of Addiction Medicine and the American Academy of Addiction Psychiatry.

Prevent Initiation of Illicit Drug Use

Clinicians should be equipped with the skills and expertise to engage their patients in a respectful, trauma-informed, and patient-centered conversation about drug use. A guide in using non-stigmatizing language to talk about drug use can be found here. Early screening and successful treatment of psychiatric illness may prevent illicit drug use. Providers should also regularly screen for unhealthy drug use as part of routine care, and use the Prescription Drug Monitoring Program (PDMP) to inform their treatment plans. The PDMP should not be used punitively.

Prevent Harms Associated with Illicit Drug Use

For patients who have initiated illicit drug use, providers should be equipped with the skills and expertise to provide strategies to reduce the harm associated with drug use. These include:

- Always carrying Naloxone
  - Dispense naloxone directly to patients in your clinical setting.
  - See resources below for obtaining naloxone from PDPH.
- Testing drugs
  - There are test strips available to test drugs for the presence or absence of Fentanyl and Xylazine; However, there are currently no test strips available to test for Medetomidine.
  - See resources below for obtaining test strips from PDPH.
- Recommend patients to try not to use alone; if that is not possible, provide resources below.
- Recommend patients reduce the amount taken.

What is PDPH Doing:

- The Surveillance Drug Checking Program is testing illicit substances across clinical and community settings in Philadelphia to detect changes in the illicit drug supply.
- PDPH disseminates information about the drug supply to community partners who serve people who use drugs.
- The Division of Substance Use Prevention and Harm Reduction informs hospital-based clinicians of changes in the drug supply to inform and improve the care for people who use drugs in Philadelphia.

- The Medical Examiner's Office is updating the testing of overdose decedents to reflect the changing drug supply in Philadelphia.
- PDPH partners with DBHIDS, EMS, and other City agencies to share data and strategically support City-wide initiatives aimed at ending the overdose crisis and improving the lives of people who use drugs.
- PDPH distributes naloxone, fentanyl test strips, and xylazine test strips to community organizations and individuals across Philadelphia.

Resources

Substance Use Disorder Treatment

- Behavioral Health Services Initiative (uninsured): 1-215-546-1200
- Community Behavioral Health (Medicaid): 1-888-545-2600
- CareConnect Warmline: 484-278-1679
- DBHIDS Medication Assisted Treatment: https://dbhids.org/services/addiction-services/mat/
- SAMHSA National Helpline: 800-662-HELP (4357)

Recommend patients try not to use alone. If that is what they are doing, then provide resources:

- Never Use Alone: 877-696-1996
- The Brave App – free to download on app stores
- Canary App – free to download on app stores

Learn how to get and use naloxone – www.substanceusephilly.com

Get naloxone & fentanyl test strips for free and confidentially – https://nextdistro.org/philly

Learn how to use fentanyl test strips:

- https://www.cdc.gov/stopoverdose/fentanyl/fentanyl-test-strips.html
- https://www.youtube.com/watch?v=GmhE6UOZ9YY

Take a wound care training - https://www.substanceusephilly.com/healthcare-providers

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