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Morbidity and Mortality Weekly Report (MMWR)

Notes from the Field: Suspected Medetomidine Syndrome Among Fentanyl–Exposed Patients—Philadelphia, Pennsylvania, September 2024–January 2025

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Summary

What is already known about this topic?

Medetomidine, a nonopioid sedative not approved for use in humans, replaced xylazine as the preferred adjuvant in the Philadelphia, Pennsylvania, illegal opioid supply during the last 4 months of 2024.

What is added by this report?

During September 2024–January 2025, 165 patients at three Philadelphia health systems with fentanyl withdrawal complicated by profound autonomic dysfunction, including severe hypertension, were identified. This syndrome was resistant to medications that had previously been effective in managing fentanyl withdrawal but was responsive to dexmedetomidine.

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Medetomidine, a synthetic alpha-2 adrenoreceptor agonist, is a new drug adulterant that was found in opioid samples tested in Philadelphia, Pennsylvania, during the last 4 months of 2024. During this period, xylazine (previously the most common adulterant) decreased from 98% to 31% of samples (1). Multiple hospitals in Philadelphia noticed an increasing number of hospitalized patients with a severe opioid withdrawal distinct from fentanyl and xylazine withdrawal, characterized by profound autonomic dysfunction, including hypertension and tachycardia. This report aims to increase awareness of the presence of medetomidine in the supply, characterize the emerging medetomidine withdrawal syndrome, and describe measures for the care for this life-threatening syndrome.

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Investigation and Outcomes

During fall 2024, in response to emerging awareness of a newly recognized medetomidine withdrawal syndrome, medicine and medical toxicology faculty members at three Philadelphia health systems (health systems A, B, and C) began maintaining a list of patients identified with the syndrome, including those they had helped care for, as well as patients referred by other health care providers. The faculty members reviewed medical records of patients who were admitted to the three health systems during September 1, 2024–January 3, 2025. The withdrawal syndrome was characterized by severe signs and symptoms that were not resolved with standard protocols for fentanyl and xylazine withdrawal. Overall, 165 patients were identified who demonstrated signs or symptoms such as agitation, anxiety, severe hypertension, tachycardia, tremor without clonus, vomiting, resistant to increasing doses of opioids (e.g., fentanyl, hydromorphone, methadone, or morphine), benzodiazepam, droperidol, haloperidol, lorazepam, midazolam, phenobarbital, or propofol, and adjusted to withdrawal medications (clonidine, ketamine, olanzapine, ondansetron, or tizanidine) (2). Median age was 33–43 years). This evaluation was reviewed and approved by the institutional review boards of the three health systems.

Among the 165 patients, 150 (91%) required intensive care unit (ICU) care, including 39 (24%) who required intubation (Table). A total of 137 (83%) patients were treated with and responded to dexmedetomidine, which was eventually recognized as potentially effective; medetomidine is an enantiomer[†] of dexmedetomidine. Dexmedetomidine exposure can induce a withdrawal syndrome manageable with controlled ventilation. Traditional dosages of dexmedetomidine (0.2–1.5 µg/kg/hr) (3) were used and titrated to control symptoms in patients with intubation. In a majority of patients requiring dexmedetomidine, the drug was titrated to a maximum of 1.5 µg/kg/hr. Duration of infusion varied, depending on the patient. Use of oral alpha-2 agonists was limited because of vomiting. Patients were also treated with antihypertensive medications titrated to control blood pressure.

however, they were responsive to dexmedetomidine, as described in the management of dexmedetomidine toxicity (4,5). Health care providers and public health agencies need to be aware of this life-threatening complication because it can require substantial escalations in care compared with the typical opioid and xylazine overdose. Public health agencies should consider testing for medetomidine in their regional drug supplies.

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* Dexmedetomidine is an alpha-2 agonist medication that is used for sedation in an ICU and o

[†] Enantiomer molecules are mirror images of each other and are not superimposable (e.g., right

§ Posterior reversible encephalopathy syndrome is a neurologic disorder characterized by brain swelling and seizures. The syndrome is diagnosed by cross-sectional brain imaging when blood pressure is severely increased.

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TABLE. Characteristics of patients hospitalized with combined opioid and sus withdrawal syndrome — three health systems, Philadelphia, Pennsylvania, S January 2025

Characteristic	No. (%)		
	Health system A (n = 55)	Health system B (n = 48)	He sys (n
Age, yrs, median (IQR)	37 (33–45)	38 (35–41)	3
Sex			
Female	12 (22)	20 (42)	
Male	43 (78)	28 (58)	
Race and ethnicity*			
Black or African American, non-Hispanic	6 (11)	6 (13)	
White, non-Hispanic	44 (80)	34 (71)	
Hispanic or Latino	5 (9)	0 (—)	
Other	0 (—)	8 (17)	
Clinical findings and hospital course			
Maximum heart rate (beats per minute), median (IQR)	144 (125–155)	136 (118–156)	1

Characteristic	No. (%)		
	Health system A (n = 55)	Health system B (n = 48)	Health system C (n = 48)
Patient-directed discharge	14 (26)	13 (27)	14 (29)
Residential drug treatment	14 (26)	7 (15)	14 (29)
Law enforcement custody	12 (22)	0 (—)	14 (29)

* Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic or non-Hispanic.

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