Naloxone Does Not Treat Medetomidine Withdrawal

Clinical Scenario

A 34-year-old man is brought to the ED following naloxone administration in the field. He is initially sedated and bradycardic. Naloxone is repeated twice; he briefly becomes responsive, then progressively develops tachycardia, hypertension, and agitation refractory to standard sedation. The emergency physician asks: why is this patient getting worse?

The Pearl

Medetomidine is an alpha-2 adrenergic agonist used in veterinary anesthesia. It is increasingly detected as an adulterant in the illicit opioid supply alongside xylazine, and it acts through a fundamentally different mechanism than fentanyl or heroin. **Naloxone reverses opioid receptor-mediated sedation. It does not reverse alpha-2 adrenergic agonism.** When the medetomidine effect wears off or when relative opioid reversal unmasks the sympathetic rebound, the withdrawal phenotype is a hyperadrenergic crisis: tachycardia, hypertension, diaphoresis, agitation, and delirium.

Supply data from Philadelphia, Delaware, and Maryland (1,153 samples, 2024 to 2025) show medetomidine present in 64.8% of illicit opioid samples, exceeding xylazine at 42.2%. The first Rhode Island case of medetomidine withdrawal was reported in 2026. That geographic progression places the Mid-Atlantic corridor, including Virginia, directly in the exposure path.

Why It Matters

A standard opioid immunoassay panel does not detect medetomidine. Neither does a standard urine drug screen. The Porto et al. case was identified only because a **comprehensive toxicology panel** was ordered. Without that, the clinical picture is a patient who received adequate naloxone and is still deteriorating: the differential that comes to mind is inadequate reversal, another coingestant, or a medical complication. Medetomidine withdrawal does not come to mind unless someone has seen it or read about it.

The clinical management difference is significant. Opioid withdrawal is managed with supportive care and opioid agonist therapy. Hyperadrenergic crises from alpha-2 agonist withdrawal are managed with alpha-2 agonists (clonidine, dexmedetomidine) or other sympatholytic approaches. Giving additional naloxone to a patient in medetomidine-mediated sympathetic crisis is not only ineffective; it removes any remaining opioid-mediated anxiolysis.

Bottom Line: When a patient's condition worsens despite adequate naloxone, or when a sedated, bradycardic patient develops refractory tachycardia and hypertension, include alpha-2 agonist withdrawal in the differential. Order a comprehensive toxicology panel, not a standard drug screen. In the Mid-Atlantic and New England corridor, medetomidine is now more prevalent in the illicit supply than xylazine.

References

1. Porto GD, Galeano K, Binder W. The storm after the calm: a case of medetomidine withdrawal. *R I Med J.* 2026;109(9):53-55. PMID 42647839.

2. Hochstatter KR, Nadel T, Gryczynski J, et al. Same name, different drugs: variability of fentanyl products sold under the same label. *Int J Drug Policy.* 2026;157(Pt A):105476. doi:10.1016/j.drugpo.2026.105476. PMID 42659903.

3. Hochstatter KR et al., and related Mid-Atlantic medetomidine prevalence surveillance. See also: Cotter DL et al. (PMID 42258631); Friedman J et al. (PMID 42547711).

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