Medetomidine Withdrawal Is Not Opioid Withdrawal

Clinical Scenario

A patient with fentanyl use disorder presents six hours after last use with agitation, severe diaphoresis, and uncontrollable vomiting. The clinical team scores COWS at 14 (moderate severity) and initiates standard opioid withdrawal management with clonidine and loperamide. Over the next two hours, blood pressure rises to 195/110 mmHg, heart rate reaches 145 bpm, and the patient develops altered mental status. The COWS score does not reflect the hemodynamic deterioration.

The Pearl

The Clinical Opiate Withdrawal Scale (COWS) was designed to quantify opioid receptor dysregulation: lacrimation, rhinorrhea, piloerection, yawning, GI hyperactivity, and subjective anxiety. It does not measure blood pressure, heart rate, or the degree of sympathetic activation. In a patient with concurrent medetomidine dependence, a COWS score of 14 is fully compatible with a life-threatening catecholamine surge occurring simultaneously.

Medetomidine produces profound physiologic α2-adrenergic receptor dependence. When abruptly withdrawn, the net effect is **unopposed sympathetic discharge, not opioid receptor rebound.**[1] The resulting syndrome (hypertension, tachycardia, encephalopathy, refractory vomiting) requires α2-agonist replacement, not opioid dose escalation. Alpha-2 agonist bridging with clonidine is first-line; when enteral therapy fails due to refractory vomiting or severity, IV dexmedetomidine at infusion rates that may exceed standard ICU sedation protocols is the specific treatment.[1,2]

Why It Matters

A multicenter Philadelphia series (n=209) characterizing this syndrome found that **77.5% of patients required ICU admission** and 73.7% received IV dexmedetomidine infusion.[1] An additional 20.1% required intubation. Severe complications included encephalopathy (35.4%) and myocardial injury (28.7%).

Protocols built around COWS-driven escalation are calibrated to opioid withdrawal severity. In a patient co-exposed to medetomidine, that calibration is wrong. OTPs, emergency departments, and addiction treatment programs in communities where medetomidine is present in the supply need explicit protocols for α2-agonist escalation that are not triggered by COWS score alone.[2]

Bottom Line: In patients with fentanyl use disorder presenting in withdrawal, do not rely on COWS to gauge severity if medetomidine co-exposure is possible. Hemodynamic deterioration (BP >180/110, HR >120, encephalopathy) can occur with a moderate COWS score. Initiate alpha-2 agonist bridging early; escalate to IV dexmedetomidine when enteral therapy fails or when severity is high. Treat concurrent opioid withdrawal separately.

References

1. London KS, Huo S, Murphy L, et al. Severe fentanyl withdrawal associated with medetomidine adulteration: a multicenter study from Philadelphia, PA. *J Addict Med.* 2026;20(2):231-237. doi:10.1097/ADM.0000000000001560 [Primary Data]

2. Zimmerman DE, Goodstein D, Durney PA, Patel-Francis SH, London KS. Presentation and management of acute medetomidine withdrawal. *Am J Health Syst Pharm.* 2026. doi:10.1093/ajhp/zxag141 [Clinical Review]

William L. Bundy Jr., PharmD | ToxiPharm LLC | toxipharm@toxipharm.org

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