Naloxone administration in emergency department presentations with suspected opioid toxicity: What proportion have analytically confirmed opioid exposure?

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Introduction: Naloxone is used to reverse suspected opioid-related respiratory depression. In practice, naloxone is often administered empirically before the toxicological cause is known, relying on the presenting opioid toxidrome of miosis, sedation and respiratory depression. We describe the proportion of emergency department (ED) presentations administered naloxone with and without analytically confirmed opioid detection.

Methods: De-identified ED presentations were extracted from the Emerging Drugs Network of Australia (EDNA) registry for patients aged ≥16 years who received naloxone (prehospital or in-hospital) between October 2023 and December 2025. Presentations were classified as 'opioid-positive' or 'opioid-negative' according to opioid detection in blood.

Results: Naloxone was administered in 1,000 presentations (median age 38 years [range 16–70]; 68.3% male): 483 (48.3%) were opioid-positive and 517 (51.7%) opioid-negative. Heroin (54.2%), methadone (9.5%), and tramadol (8.9%) were the most common opioids detected. Frequently detected sedatives in opioid-negative presentations included gamma-hydroxybutyrate (62.3%), diazepam (28.0%) and pregabalin (19.0%), while 7.9% had no sedatives detected. The median Glasgow Coma Scale score was 6 in both groups. Miosis was recorded in 61.1% and 42.1% of opioid-positive and opioid-negative presentations respectively, while respiratory depression (respiratory rate of ≤10 breaths/minute) was recorded in 57.2% and 27.1%, respectively. A positive response to naloxone was documented in 46.8% (72.0% opioid-positive, 23.2% opioid-negative).

Discussions and Conclusions: Almost half the patients receiving naloxone in this cohort did not have an opioid detected. This reflects a clinically appropriate empirical use of naloxone. Gamma-hydroxybutyrate was the most common detection in opioid-negative presentations, occurring in almost two-thirds of this subgroup.

Implications for Practice or Policy: Gamma-hydroxybutyrate appears to be a common opioid poisoning mimic and should be considered in cases of a suspected opioid toxidrome that does not respond to naloxone.

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