

TOXICOLOGY

Nebulized Naloxone for Acute Opioid Overdose

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Paramedics present to an urban emergency department with a middle aged man found unresponsive in a nearby alley. The paramedics were unable to obtain IV access due to years of drug abuse and overall poor

venous access.

Physical Exam

- General: Middle aged male, unresponsive to painful stimuli
- Vital signs: P=57/min (sinus bradycardia) RR=5 breaths/min T=97.9 F
- BP: 165/90 mmHg Pulse O₂=98% on a non re-breather
- Head: normocephalic, atraumatic
- ENT: pupils pinpoint, minimally reactive, + gag reflex
- Lungs: clear to auscultation bilaterally, decreased respiratory rate
- Cardiac: regular rate and rhythm, no murmur
- Ext: cool to touch, good pulses, no cyanosis

Clinical Course

A bedside accu-check of "97" was obtained. There were no obvious signs of trauma. Given the patient's physical exam findings of pinpoint pupils, depressed respiratory rate, and known history of drug abuse, an opioid toxidrome was recognized and the decision was made to administer naloxone. However, with the patient's poor venous access, an alternative route of administration was required.

Naloxone

The growing opioid abuse epidemic has resulted in a skyrocketing number of deaths and ED visits for opioid intoxicated patients. According to the CDC, in 2010 opioid analgesics such as oxycodone, hydrocodone, and methadone, were involved in about 3 of every 4 pharmaceutical overdose deaths (16,651)². Add in the thousands of heroin overdoses and the need for an effective and rapid reversal agent is clear.

Administration of intravenous naloxone has been the initial preferred treatment in emergency departments, but may not always be available due to poor venous access. The use of intravenous naloxone is not without risk, and has been associated with unwanted side effects including acute opioid withdrawal, emesis, diarrhea, and agitation. There is also a theoretical catecholamine surge induced by acute opioid withdrawal resulting in pulmonary edema.^{3,4,7}

The safety and difficulty of placing an IV in this specific patient population makes a nebulized route of administration a more efficacious choice. Also, as the patient becomes more alert, they are able to remove the non-rebreather mask themselves, making it a self-titratable medication and limiting the number of undesirable side effects associated with this antidote. Other possible routes when access is lacking include subcutaneous, intramuscular, and intralingual⁹; although these routes result in sporadic onset of actions.

Nebulized naloxone was first described in a case report in 2003 by Mycyk et al in Chicago⁵. The patient received the medication via this route due to an inability to gain intravenous access. The nebulized naloxone "gently and effectively reversed the intoxication" without evidence of side effects in that particular patient.

Two recent published studies have further evaluated the use of this intervention. Weber et al⁸ retrospectively studied 105 consecutive cases of nebulized naloxone administrations over a 5 month period. The primary outcome studied was patient response (a subjective measure). Twenty three (22%) had complete response, 62 (59%) had partial response, and 20 (19%) had no response. No case required assisted

ventilation, and no adverse events were documented by paramedics in the prehospital setting. They concluded that nebulized naloxone was a safe and effective alternative although these result in sporadic onset of actions.

In 2013, Baumann et al published a prospective study¹ enrolling 26 patients who had a self-reported or suspected opioid intoxication and a spontaneous respiratory rate ≥ 6 breaths/minute. The primary outcome was level of consciousness, which was recorded pre and 15 minutes post naloxone administration using the Glasgow Coma Scale (GCS) and the Richmond Agitation Sedation Scale (RASS). After nebulized naloxone administration, median GCS improved from 11 to 13. Median RASS improved from -3.0 to -2.0. With “few adverse effects” documented, the authors concluded that nebulized naloxone was “well-tolerated and led to a reduction in the need for supplemental oxygen and results in improvements in GCS and RASS scores”.

Dosing

All of these studies have utilized the dosing of 2 mg of naloxone mixed with 3 ml of normal saline for a total of 5 ml. This solution is then placed in the standard canister and nebulized. Repeated or continuous nebulizers may be required depending on the amount and type of opioid ingested. For example, methadone dosing may require repeated doses of naloxone due to a longer half-life and duration of effect.

Disposition

If the patient is intoxicated to the point that they are failing to ventilate appropriately, intravenous or intramuscular dosing of naloxone still remains the initial treatment. However, since the majority of opioid overdoses present to emergency departments with mild to moderate toxicity, nebulization of naloxone may be the quickest and safest route of administration.

Case Outcome

The patient’s GCS improved from an 8 to 14 within minutes of being placed on 2 mg of naloxone mixed with 3ml of saline in a nebulizer mask. He soon removed the mask himself and had minimal clinical side effects. The patient was discharged 4 hours later after tolerating oral fluids and a turkey/cheese sandwich. No intravenous access was obtained or necessary.

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Editor’s Note

The recent Baumann study is the best to date on this new and potentially useful intervention. But they weren’t allowed to randomize their trial; their workup and treatment had to be based on physician preference. Less than 40% of twenty-six patients who got the drug had confirmatory urine testing, and yet just over 40% needed repeated administration.

As the original Mycyk paper and prehospital papers suggest, however, in a patient with difficult access, nebulized naloxone’s rapid onset, potentially self-limited dosing, and comparatively milder adverse reactions make it a reasonable intervention to try while attempting to pursue IV naloxone.

It’s been ten years since this benign therapy was described, and in this era of opioid abuse, we could probably try nebulized naloxone more often than we do.
