

Naloxone

Opioids are commonly prescribed for treating chronic pain and are often misused and abused to achieve euphoria. Illicit opioids, including heroin, fentanyl/fentanyl analogs and numerous synthetic opioids, are also responsible for overdoses and deaths. Opioid overdoses can result in life-threatening effects such as respiratory depression, hypoxia, coma, bradycardia, hypotension/hypertension, and CNS depression.

Mechanism/Indications: Naloxone is used as an antidote for opioid overdose and to rule out opioid overdose due to its mechanism as a pure opioid competitive antagonist at all receptor sites (μ , κ , and δ). As a result, naloxone reverses coma and respiratory depression from all opioids, including partial agonists such as buprenorphine, without adding any agonist effects (respiratory depression, sedation, analgesia, miosis). Precautions should be taken in individuals who are opioid dependent as naloxone could induce withdrawal symptoms in tolerant individuals. Naloxone can be safely used in mixed/unknown overdoses for therapeutic or diagnostic purposes; however, removing the opioid protective effect with naloxone could reveal sympathomimetic or anticholinergic effects in mixed cocaine/opioid or anticholinergic/opioid overdoses.

Dosing: Naloxone is usually administered intravenously or intranasally. Other possible routes include intramuscular, subcutaneous and endotracheal. Nebulized naloxone can also be used but cannot be considered if severe respiratory depression. Naloxone is not orally bioavailable.

Adults and Children >6 years old without opioid-dependence:

- Initial bolus dose: 0.4 to 2 milligrams intravenously (up to 4 mg intranasally)
- Repeat dose: 2 milligrams every 2-3 minutes up to 10 milligrams if desired response or respiratory depression improvement is not seen. Larger doses may be required for opioids such as fentanyl and buprenorphine. If no response is seen after 10 mg, the presence of an opioid is questionable. Naloxone has a short duration of action (20-90 minutes); therefore, repeat doses may be needed for longer-acting opioids. Patients should be observed for recurrence of respiratory depression after naloxone administration.

Opioid-Dependent Individuals >6 years old:

- Smaller doses (starting with 0.04mg) may be used to achieve desired effect without precipitating withdrawal. Use escalating doses every 1-2 minutes to reverse respiratory depression. However, if the patient is apneic, a higher starting dose (i.e 0.4mg) can be given.
- If withdrawal symptoms are observed (nausea, vomiting, sweating, tachycardia, hypertension, anxiety, tremulousness), stop the naloxone, allow symptoms to abate and resume at a lower dose capable of maintaining ventilation without causing withdrawal.

Children \leq 6 years old:

- Initial dose is 0.4 mg. If no adequate response is seen, may repeat with 0.1 mg/kg to a maximum of 10 mg.

Naloxone (continued)

Children \leq 6 years old with opioid dependence (including neonates born to opioid-dependent mothers):

- 0.001 mg/kg with concomitant supportive care.

Intravenous Infusion—for symptom recurrence due to long-acting opioids:

- Utilize 2/3 of the initial naloxone bolus on an hourly basis by adding 10 times this dose to each liter of D5W or NS and infusing at a rate of 100 mL/hour. Readminister 1/2 of the initial bolus dose 15 minutes after initiation of the continuous infusion. Titrate the dose and rate to the patient's response.

Other Considerations:

- Naloxone is available without a prescription to be given by bystanders (e.g., family members, friends, law enforcement) who suspect someone is experiencing a life-threatening opioid overdose.
- Opioid tolerant/dependent individuals: smallest dose of naloxone should be used to evade precipitating withdrawal symptoms which includes vomiting and the potential for aspiration pneumonitis; the goal in these patients is reversal of respiratory depression not CNS depression.
- Pregnant women: smallest dose of naloxone should be used to reverse life threatening opioid effects. Naloxone detoxification in pregnant opioid addicts could result in opioid withdrawal in the fetus, fetal distress, meconium staining, or fetal death.
- Post-operative patients: cardiovascular adverse effects have occurred in post-operative patients with underlying cardiac disorders.
- Reversing opioid effects might unmask effects of other drugs and heroin adulterants, such as sympathomimetics (e.g cocaine) and anticholinergics (e.g. diphenhydramine, scopolamine).

Contraindications:

- Hypersensitivity to naloxone

Adverse Effects:

Naloxone administration to reverse opioid overdose is safe and results in few adverse effects. Adverse effects are related to opioid withdrawal and include flushing, sweating, nausea/vomiting, trembling, tachycardia, agitation and delirium. Serious effects are rare but can include chest pain and seizures. Acute lung injury has occurred with naloxone administration, but it has not been proven that this is directly related to naloxone. Most likely, the acute lung injury results from the opioid itself with naloxone acting as an unmasking agent.

For more on naloxone:

- Barton ED, Ramos J, Colwell C, Benson J, Baily J, Dunn W. Intranasal administration of naloxone by paramedics. *Prehosp Emerg Care.* 2002 Jan-Mar; 6 (1): 54-8.
- Boyer EW. Management of Opioid Analgesic Overdose. *N Engl J Med.* 2012; 367(2): 146-55.
- Caravati EM, McGuigan MA, MacGregor Whyte I, Dawson AH, Seifert SA, Schonwald S, Yip L, Keyes DC, Hurlbut KM, Erdman AR, Dart RC. *Medical Toxicology.* 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2004. Chapter 128, Opioid Medications; p.776-777.
- Kim KK, Nelson LS. Reversal of Opioid-Induced ventilator depression using low-dose naloxone (0.04mg): a case series. *J. Med. Toxicol.* 2015 Aug 20 [Epub ahead of print].
- Hoffman RS, Howland MA, Lewin NA, Nelson LS, Goldfrank, LR. *Goldfrank's Toxicologic Emergencies.* 10th ed. New York: McGraw Hill Medical; 2015. Chapter 38, Opioids; p.511-514.