Intranasal Naloxone Administration

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The following text summarizes information provided in the video.

OVERVIEW

Intranasal naloxone is used to treat patients with respiratory and central nervous system depression that is known or suspected to be caused by an opioid overdose. Opioid overdose should be suspected in patients with impaired arousal and respiratory depression, which can lead to hypoxemia and cyanosis if left untreated. Miosis is generally expected in patients with opioid overdose but may not be present if there has been concomitant use of other drugs that also affect pupillary size. Opioid intoxication can also be complicated by hypothermia, seizure, and aspiration pneumonia, and patients with prolonged loss of consciousness may have rhabdomyolysis. The clinical presentation may be influenced by the type and dose of the opioid used, the presence of active opioid metabolites, and the patient’s opioid tolerance.

When an opioid overdose is suspected, it is important to rule out alternative causes of loss of consciousness, such as hypoglycemia and stroke, and to obtain a blood glucose level, if possible. Some patients with opioid overdose have simultaneously used additional substances, and in such cases a reversal of the effects of the opioid may not achieve the desired clinical response.

The safety of medical personnel should be considered during the treatment of a patient with suspected opioid overdose. There may be needles in the patient’s clothing or other belongings. Personal protective equipment, including gloves, should be worn if available and the situation allows.

PHARMACOLOGY AND USES OF NALOXONE

Naloxone is a synthetic derivative of thebaine, a morphinane alkaloid, and has a chemical structure resembling that of oxymorphone. Oxymorphone and other opioids exert their effects by binding to and activating opioid receptors in the central nervous system, causing analgesia, respiratory depression, and other sequelae.

Although its precise mechanism of action is not fully understood, naloxone appears to act as a competitive antagonist at these opioid receptors and has the greatest affinity for mu opioid receptors. In binding to the opioid receptors, naloxone displaces opioid agonists and thereby reverses their effects. Because naloxone is a low-molecular-weight, lipophilic, uncharged compound, it is readily absorbed. Its reversal effect is usually rapid and complete but also short-lasting. Naloxone has a half-life of approximately 2 hours, a shorter duration of action than most opioids. Therefore, careful monitoring of respiration is warranted when naloxone is used as an antagonist to longer-acting opioids.

Naloxone is available in two formulations for clinical use: an injectable formulation intended for intravenous, intramuscular, or subcutaneous administration and
a concentrated formulation intended for intranasal administration. Intranasal administration of the injectable formulation of naloxone has been reported, but this approach has not been approved by the Food and Drug Administration, is less effective than injection of this formulation, and requires time-consuming assembly of an atomization device.\(^1\)

The intravenous route of administration is favored if intravenous access is easily obtained. When naloxone is administered intravenously, the plasma level rises immediately, and the onset of action is usually apparent within 2 minutes. When naloxone is administered intranasally, it is still effective but acts more slowly; an equipotent dose achieves more than 50% of the peak plasma level within 10 minutes and achieves the peak level within 15 to 30 minutes.\(^2\) The advantages of the intranasal delivery of naloxone include ease of administration, rapid onset of action, and the avoidance of a phenomenon known as the first-pass effect, in which the concentration of a drug administered orally is reduced before it reaches the systemic circulation. The nasal mucosa is highly vascularized and permeable, making it a suitable portal for the systemic delivery of drugs (Fig. 1). With intranasal administration, drug diffusion depends on the concentration gradient at the absorption site. Changes in nasal blood flow and local vasoconstriction or vasodilatation can alter the increase in the plasma level of the administered compound and, consequently, the onset of the drug’s effect.

**PROCEDURE FOR INTRANASAL ADMINISTRATION OF NALOXONE**

Naloxone nasal spray is available in cartons with two blister packs, each containing a 4-mg dose in a 0.1-ml aqueous solution. To start the procedure, open one of the packs by peeling back its tab. Do not prime or test the spray. Each blister pack contains a single dose of naloxone and cannot be reused. Place the patient in the supine position. With one hand, support the back of the patient’s neck, allowing the head to tilt (Fig. 2). Hold the nasal spray in your other hand. Place your thumb on the end of the plunger and your first and middle fingers on either side of the nozzle. Then, administer the nasal spray by gently inserting the tip of the nozzle into one of the patient’s nostrils until both fingers are pressed against the patient’s nostril (Fig. 3). Press the plunger firmly to make sure that the entire dose has been delivered.

If the patient remains unresponsive or has a relapse of respiratory depression, a new pack can be opened and the spray can be administered every 2 to 3 minutes until the patient becomes responsive. However, if spontaneous breathing does not occur or remains insufficient despite the use of intranasal naloxone, additional supportive and resuscitative measures should be taken and the patient’s airway secured (Fig. 4).

**COMMON PROBLEMS AND COMPLICATIONS**

The administration of naloxone can precipitate symptoms of opioid withdrawal, including diaphoresis, a runny nose, nervousness, and shivering or trembling.\(^3\) Adverse cardiovascular effects, such as tachycardia and hypertension, as well as stomach cramping, nausea, vomiting, or weakness, may also occur.

**POSTPROCEDURAL CARE**

After successful reversal of opioid toxicity, monitor the patient for complications such as opioid withdrawal and, in rare instances, noncardiogenic pulmonary edema, and maintain surveillance. Provide cardiovascular and respiratory support as needed. Once the patient is conscious, obtain a complete patient history and conduct a physical examination to identify any coexisting conditions or injuries.
Patients with complications such as pulmonary aspiration or anoxic brain injury may require airway management and admission to an intensive care unit. A complete evaluation for substance use disorder and a referral for treatment are critical, since the short-term mortality for survivors of nonfatal opioid overdose is high, particularly in the first 2 days after overdose.4

**SUMMARY**

Timely intranasal administration of naloxone can prevent irreversible anoxic brain injury or death by reversing life-threatening depression of the central nervous and respiratory systems caused by an opioid overdose.

No potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

**REFERENCES**


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