# Intranasal Administration of Naloxone by Paramedics

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## Abstract

**Introduction.** Naloxone is a medication that is frequently administered in the field by paramedics for suspected opioid overdoses. Most prehospital protocols, however, require this medication to be given to patients intravenously (IV) or intramuscularly (IM). Unfortunately, intravenous line placement may be problematic and time-consuming in chronic IV drug users. There may also be a delay in patient response to opioid reversal with IM absorption of naloxone. Additionally, routine use of needles in high-risk populations poses an increased risk of occupational blood exposures to paramedics. **Objective.** To prospectively test the effectiveness of intranasal (IN) naloxone administration by paramedics. This preliminary report summarizes the first month's experience in the city of Denver. **Methods.** Naloxone was first administered to patients found unconscious in the field using a nasal mucosal atomizer device (MAD). Patients were then treated using standard prehospital protocols, which included IV line placement and medications, if they did not immediately respond to IN naloxone. Time to patient response was recorded. **Results.** A total of 30 patients received IN naloxone in the field over a one-month period. Of these, 11 patients responded to either IN or IV naloxone. Ten (91%) patients responded to IN naloxone alone, with an average response time of 3.4 minutes. Seven patients (64%) did not require an IV in the field after response to IN naloxone. **Conclusions.** Intranasal naloxone may provide a safe, rapid, effective way to manage suspected opioid overdoses in the field. Use of this route may decrease paramedic exposures to blood-borne diseases. The addition of IN naloxone administration to prehospital protocols should be considered as an initial therapy for suspected opioid abusers. **Key words:** naloxone; opioid; overdose; paramedics; intranasal; drug abuse.

PREHOSPITAL EMERGENCY CARE 2002;6:54–58

When confronted with a patient suffering from a suspected opioid overdose, the drug of choice is naloxone (Narcan) given by intravenous (IV) or intramuscular (IM) route. Unfortunately, opioid addicts who inject drugs can often have limited peripheral venous access. Valuable time may be lost in trying to gain IV access if multiple attempts are required. Although the IM and subcutaneous (SQ) routes have been shown to be effective, they have a much slower rate of absorption and typically require a much longer time period for the patient to respond.[1,2] Additionally, emergency medical services (EMS) personnel are at risk for inadvertent needlesticks when attempting to place IV lines or give IM or SQ injections in the field. These patients typically pose an increased risk of blood-borne diseases such as hepatitis B, hepatitis C, and HIV.

Other routes of naloxone administration such as sublingual, intralingual, and submental injections also require the use of needles and have shown a delayed onset of action.[3–5] Endotracheal administration of naloxone[6,7] requires placement of an endotracheal tube, and nebulized naloxone is ineffective in reversing opioid effect.[8]

Intranasal (IN) absorption of naloxone has been shown to be almost as rapid as the IV route with sim-



FIGURE 1. The mucosal atomizer device (MAD) attached to a syringe showing the spray pattern of medication.

ilar bioavailability in both animal and human models.[9–11] We are not aware, however, of any published data on the effectiveness of IN naloxone in opioid overdoses often observed in patients such as heroin addicts. Since EMS personnel encounter the majority of these patients in the field, we sought to evaluate the effectiveness of IN naloxone in a prospective prehospital study. This report summarizes our first month's experience.

## METHODS

### Design

This study was performed by the Denver Health Paramedic Division as a prospective evaluation of IN naloxone in all patients who presented with altered mental status (AMS), as "found down" (FD), or with suspected opioid overdose (OD). These patients would otherwise have an IV placed and receive IV naloxone (1–2 mg) by protocol. The preliminary study was performed from February 1 to February 28, 2001, as part of a Paramedic Division Quality Assurance Evaluation of IN naloxone. Institutional review board (IRB) approval was granted.

### Procedure

Patients encountered by paramedics with AMS, FD, or OD were initially administered 2 mg of naloxone IN using a disposable Mucosal Atomizer Device (MAD; Wolfe-Tory Medical, Inc., Salt Lake City, UT) and syringe (Fig. 1). The IN naloxone dose was chosen because 2 mg is the initial IV dose mandated by the Denver Health Paramedic Protocol and bioavailabilities appears to be similar by the two routes.[9–11] One milliliter of the 1-mg/mL solution was administered into each nares, for a total volume of 2 mL (Fig. 2). Paramedics were then instructed to continue to treat all patients as per standard protocols, including airway management, IV line placement, and medications, unless the patient responded and no further treatment was required. If a patient did not respond to IN naloxone within an appropriate time to establish an IV and an airway if necessary, then an IV dose of 2 mg was administered. Times were recorded to the hour and minute on a study sheet (Fig. 3) by paramedic providers and included: time of initial patient encounter, IN naloxone administration, IV insertion, IV naloxone administration, and patient response. Additionally, paramedics were asked to report any obvious abnormalities noted in the patient's nasal mucosa (such as bleeding, deformity, mucus) at the time of IN drug administration.

### Outcomes

The rate of patient response to IN naloxone, defined as a significant improvement in level of consciousness as



FIGURE 2. The mucosal atomizer device (MAD) being used for intranasal administraion of naloxone on a patient (paramedic volunteer).

determined by paramedics, prior to IV insertion or to IV administration of a second dose of naloxone was measured. Additionally, the time of response to naloxone was measured.

## RESULTS

During the study period a total of 30 patients received IN naloxone using the MAD. A total of 13 patients (43%) responded to either naloxone by any route (*n* = 11) or dextrose (*n* = 2) given by paramedics in the field. There were 11 patients with AMS listed as the indication for naloxone administration, seven patients with FD listed, and 12 patients with suspected OD listed. Of these, one patient responded to naloxone in the AMS group (9%), no patients responded in the FD group (0%), and ten patients responded in the OD group (83%).

Of the 11 naloxone responders there were ten patients (91%) who responded to IN naloxone alone. The average time of response was 3.4 minutes (range 2 to 6 minutes). One patient responded to IV naloxone and not to IN naloxone alone. Appropriate response occurred at 11 minutes after IN administration and the patient was noted to have a significant amount of epistaxis. Seven of the 11 naloxone responders (64%) did not require IV placement in the field.

## DISCUSSION

The use of IN drug administration has long been considered a alternative route for a wide variety of medications. More importantly, IN administration of several medications used in the prehospital setting (atropine, dextrose, diazepam, epinephrine, glucagon, lidocaine, midazolam, morphine, naloxone, and nitroglycerine (Table 1) has been studied to assess the effectiveness of this route of therapy.[11–20] While effective in many circumstances, however, the IN route has yet to

## PREHOSPITAL INTRANASAL NARCAN
(For Quality Assurance/Performance Improvement Purposes Only)

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***PROTOCOL FOR DEVICE USE:***

1) Time of first contact noted as acurately as possible.

2) Load syringe with 2 mg of Narcan and nasal atomizer.

3) Administer intranasal Narcan via rapid intranasal mist spray of 1cc to each nostril.

4) Time of administration accurately noted and whether patient responded.

5) Continue normal attempt(s) to gain IV access and secure airway as needed.

6) Record time of IV Narcan if given and whether patient responded.

   ***NOTE:  Protocol stops after patient response.***

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***PATIENT DATA:***

DATE: _____          TRIP #: _____

INDICATION for Narcan:   Opioid overdose   Altered mental status   Found down

Other: _____

1)  TIME OF FIRST PATIENT CONTACT: _____

2)  TIME INTRANASAL NARCAN ADMINISTERED: _____

3)  TIME IV LINE STARTED: _____

4)  DID THE PATIENT AROUSE AFTER INTRANASAL NARCAN:   Yes   No
    *(If No, then continue with Intravenous Narcan)*

5)  TIME IV NARCAN GIVEN: _____ RESPONSE:   Yes   No

6)  RESPONSE TO OTHER MEDICATION:   Yes (med) _____   No

7)  TIME OF PATIENT RESPONSE: _____

NASAL abnormalities noted:   Septal abnormality   Epistaxis   Mucous
                             Trauma       Other: _____

COMPLICATIONS/COMMENTS: _____

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**\*\*\* NOTE \*\*\* PLEASE ATTACH COMPLETED FORM TO TRIP SHEET**

FIGURE 3. The paramedic recording sheet for the prehospital intranasal naloxone study.

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replace standard IV therapy in the vast majority of prehospital treatment protocols.

The risk of occupational blood exposure to prehospital providers has been demonstrated to increase with more years of service. In fact, a risk as high as 25 blood contacts per 1,000 EMS calls has been reported in the literature.[21] While only about 2–5% of these are needlestick exposures, there is also significant risk with exposures to nonintact skin, mucous membranes, and eyes (from splashes).[22] Routine use of IV lines and medications, especially in nontrauma patients, may account for the majority of these exposures. Similar risks have been observed in the hospital setting, and the response over the past several years has been to develop safer needle disposal systems as well as needle-less drug delivery IV lines. Unfortunately, these systems are unavailable or cumbersome to use in the prehospital setting. Consequently, the risk of paramedic needle exposures to blood-borne infectious diseases continues to pose a significant threat.

Naloxone has been found to have almost 100% bioavailability through the nasal mucosa in animal models and in human opioid addicts.[9–11] Subsequently, IN naloxone has an onset of action and plasma level that make it indistinguishable from IV naloxone.[9] Though accepted as an alternative route of

administration, no studies have been previously reported using IN naloxone as an initial mode of treatment in overdose patients. We chose a staged protocol using the IN route first, followed by an IV dose if necessary. This was done to determine both the rate of response within a limited time period and the number of IV attempts that could be avoided in the field if the patient responded appropriately. Issues such as informed consent and blinded treatment protocols would be more difficult to perform in the prehospital setting for an appropriate comparison study.

This study attempts to address the efficacy of IN naloxone by rapidly administering the IN drug upon initial patient evaluation. Standard prehospital treatment protocols were subsequently followed. The purpose of such a protocol was to assess the rate of response of patients given IN naloxone relative to subsequent IV line placement and need for repeat doses of IV medication. The results demonstrate a 91% response rate to the IN naloxone for all patients who responded to naloxone. This result strongly suggests that the IN route could be used successfully in a majority of patients to speed reversal of opioid intoxication. With rapid administration and easy access to the nasal mucosa, the IN route may, in fact, reduce the duration of respiratory depression and decrease the number of prehospital intubations often seen in this patient population. Additionally, a significant number of patients in this study (64%) did not require IV placement in the field, which may be a safer practice when treating opioid abusers outside of the emergency department.

The one patient in our series who did not respond to IN naloxone and subsequently responded to IV naloxone was noted to have epistaxis. Physical factors such as nasal septum abnormalities, trauma, epistaxis, excessive mucus, and mucosal destruction from other intranasal drug use (i.e., cocaine) may have a significant effect on the rate and amount of absorption of IN medications. Drug abusers might be a population at higher risk for these nasal abnormalities for a variety of reasons. Additionally, paramedics should continue to use blood exposure precautions for external sources of bleeding, such as epistaxis, in these patients. Prospective evaluation of the nares to assess for any abnormalities may be required prior to the administration of IN naloxone. Further study will most likely elucidate what percentage of these patients will continue to require IV naloxone.

## CONCLUSION

Intranasal naloxone has been demonstrated to be a very easy route for drug administration in the field with a high patient response rate in this preliminary study. This method utilizes an inexpensive device that provides rapid administration of the medication with

TABLE 1. Intranasal Medications Previously Studied* for Systemic Indications

| Indication | Medications |
| --- | --- |
| Analgesia | Fentanyl[23] |
| | Sufentanil[24] |
| | Buprenorphine[25] |
| Antiemetics | Meclizine[26] |
| | Metoclopramide[27] |
| Antihypertensives | Angiotensin II[28] |
| | Hydralazine[29] |
| | Nifedipine[30] |
| | Nitroglycerine[31] |
| | Propranolol[32] |
| | Verapamil[33] |
| Cardiac arrest/ACLS | Atropine[34] |
| | Epinephrine[35] |
| | Lidocaine[36] |
| Drug overdose | Naloxone[10] |
| Headache therapy | Butorphanol[37] |
| | Dihydroergotamine[38] |
| | Lidocaine[39] |
| | Sumatriptan[40] |
| Hypoglycemia | Dextrose[41] |
| | Glucagon[42] |
| Sedation | Diazepam[43] |
| | Ketamine[44] |
| | Midazolam[45] |
| Seizures | Diazepam[46] |
| | Midazolam[47] |
| Miscellaneous | Gentamycin[48] |
| | Neostigmine[49] |

*For complete reference citations, see the reference list. ACLS = Advanced Cardiac Life Support.

minimal risk of blood-borne exposure. Use of an IN naloxone protocol may promote a safer practice for paramedics while maintaining effective treatment for patients with opioid overdoses.

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