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Clinical Review

REVIEW OF INTRANASALLY ADMINISTERED MEDICATIONS FOR USE IN THE EMERGENCY DEPARTMENT

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☐ **Abstract—Background: Intranasal (IN) medication delivery is a viable alternative to other routes of administration, including intravenous (IV) and intramuscular (IM) administration. The IN route bypasses the risk of needle-stick injuries and alleviates the emotional trauma that may arise from the insertion of an IV catheter. Objective: This review aims to evaluate published literature on medications administered via the IN route that are applicable to practice in emergency medicine. Discussion: The nasal mucosa is highly vascularized, and the olfactory tissues provide a direct conduit to the central nervous system, bypass first-pass metabolism, and lead to an onset of action similar to IV drug administration. This route of administration has also been shown to decrease delays in drug administration, which can have a profound impact in a variety of emergent scenarios, such as seizures, acutely agitated or combative patients, and trauma management. IN administration of midazolam, lorazepam, flumazenil, dexmedetomidine, ketamine, fentanyl, hydromorphone, butorphanol, naloxone, insulin, and haloperidol has been shown to be a safe, effective alternative to IM or IV administration. As the use of IN medications becomes a more common route of administration in the emergency department setting, and in prehospital and outpatient settings, it is increasingly important for providers to become more familiar with the nuances of this novel route of medication delivery. Conclusions: IN administration of the reviewed medications has been shown to be a safe and effective alternative to IM or IV administration. Use of IN is becoming more commonplace in the emergency department setting and in prehospital settings.** © **2017 Elsevier Inc. All rights reserved.**

☐ **Keywords—emergency department; intranasal; medication; nasal; prehospital**

INTRODUCTION

The oral route of drug administration is the most widely available and often the preferred route for systemic drug delivery. However, in the emergency department (ED) setting, it is likely that the oral route may not be available because of different clinical factors (e.g., level of consciousness, intolerance, obstructions, and trauma), and an alternative route is needed. Intranasal (IN) medication delivery has been shown to be a viable alternative to other invasive routes of administration, including intravenous (IV) and intramuscular (IM) administration (1,2). IN drug administration requires less technical skill compared to the IV route. The IN route bypasses the risk of needle-stick injuries and attempts to alleviate the potential emotional trauma that may arise from pain caused by insertion of an IV catheter if an IV is not necessary otherwise. In addition to safety concerns, the

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delivery of IM medications depends on accurate drug delivery into the IM space rather than the subcutaneous tissues. In addition, IN drug delivery can be used in a variety of patient populations, regardless of age, body habitus, clinical condition, or level of patient cooperation. IN administration has also been shown to decrease time to drug administration compared to IV administration, which can have a profound impact in certain emergent scenarios, such as seizures, acutely agitated or combative patients, and trauma management (3). In addition, IN medication administration may be useful in patients where obtaining IV access is challenging, such as those who abuse IV drugs.

DISCUSSION

Physiology of Intranasal Drug Administration

The nose is divided into two halves, and each half consists of four areas: the vestibule, atrium, respiratory region, and the olfactory region. The respiratory mucosa is primarily responsible for systemic drug delivery. The nasal mucosa receives an extensive amount of blood flow per unit of tissue compared to other major organs, such as the liver or brain. The nasal cavity can hold approximately 15–20 mL and has a surface area of ≤150 cm (2). This extensive network of highly vascularized territories, combined with the olfactory tissues, provides some pharmacokinetic advantages for drug administration. Specifically, there is a direct conduit for the drug to enter the central nervous system and systemic circulation (4,5). This, in addition to bypassing first-pass metabolism by the liver, leads to an onset of action similar to IV drug administration. However, because of the slower rate of absorption, larger IN doses may be necessary wherein safety features should be put into place to limit medication errors related to dosing differences between IV and IN administration. In addition, not all medications are suitable for IN administration. Drug product characteristics that are considered advantageous include poor gastrointestinal solubility or those that undergo extensive first-pass metabolism (2).

Preparation and Administration

Unlike IV drug administration, IN medication administration does not require a sterile access site or medications prepared in a sterile manner. This enhances the rapidity of drug preparation and drug delivery. Using both nostrils when administering medications also helps optimize medication delivery because a limited volume can be administered in a single nostril at one time. Products that are more concentrated are preferred, because volumes >1 mL per nostril have a higher propensity to saturate the mucosal surface and result in drug runoff into the proximal pharynx. In addition, if less concentrated products are used it would necessitate dividing the dose into several attempts at administration, therefore delaying care and potentially increasing anxiety for the patient. Some common IN administration considerations are outlined in Table 1 (6,7).

For systemic drug absorption to occur, a drug has to pass the mucus layer and the epithelial membrane. In addition, the extent of drug absorption is reliant upon several factors, most importantly placement of the drug and the rate of mucociliary clearance of drug out of the nasal cavity. A variety of delivery methods have been used for IN administration, including manual application of drug (usually topical preparations), sniffing, insertion of drops, or use of atomization/spray devices. Atomizers are often the most efficient method for systemic drug delivery because they reduce drug runoff and enhance drug delivery over a larger surface area to improve nasal bioavailability. The administration of drugs using atomizers generally results in higher success rates because of patient comfort and successful drug delivery being independent of head position; however, they are not required for IN drug administration (8). Manual application or sniffing typically results in reduced drug delivery because larger proportions land on the external nostrils or anterior aspects of the nasal cavity.

Patients should first be evaluated to determine if they are a candidate for IN medication administration. Potential contraindications would include any condition in which the nasal passages, mucosa, or airway are compromised (Table 2). The majority of patients appear to tolerate IN medication administration well; few adverse events have been reported. Local irritation is the most common adverse event, but others include poor taste, increased lacrimation, and a burning sensation. Some medications may have other known drug-specific adverse effects that may not be limited to the route of administration (Table 3).

Table 1. Intranasal Medication Administration Considerations

Strategy	Impact on Drug Delivery
Concentrated products are preferred, ideally volumes <1 mL per nostril should be used	Reduces likelihood of mucosal saturation and drug runoff into the posterior pharynx
Divide doses between both nostrils	Optimizes absorptive capacity and reduces the likelihood of mucosal saturation
Products administered by this route should not be inhaled	Minimizes drug delivery into the lungs
Avoid blowing nose or sniffing postadministration	Maximizes drug absorption at target sites