Naloxone Intranasal Administration in the Pre-hospital Setting – Basic Life Support (BLS) Pilot Program

A Joint Project of the Wisconsin EMS Advisory Board and the Wisconsin EMS Office
Naloxone Pilot Project

Why is this project needed?

- Increased number of narcotic overdoses.
- Accessibility to Advanced Life Support (ALS) is not the same in all areas of Wisconsin.
- Safety of EMS providers.
Decrease in Needles = Decreases in Risk

- The Centers for Disease Control and Prevention (CDC) estimates 600,000 percutaneous injuries occur each year involving contaminated sharps in the United States.
- Technological developments can increase protection.
- Education and training are the keys to a positive resolution.
Communicable Disease Population

- Not all infected people know they are infected.
- EMS scenes can be high risk events due to patient and bystander behavior, as well as environmental aspects.
Intranasal Medication Administration

- Intranasal medication administration offers a “Needleless” solution to drug delivery.
Intranasal Administration: Basic Concepts

• The intranasal delivery route has several advantages:
  • It’s easy and convenient.
  • The nose is a very easy access point for medication delivery (even easier than the arm, especially in winter).
  • No shots are needed.
  • It is painless.
  • It eliminates any risk of a needle stick to you, the medical provider.
Naloxone (Narcan)

- Pure opiate antagonist – reverses respiratory & central nervous system (CNS) depression
- High lipid solubility so rapidly enters CNS
- Roughly $10-$30 per 2 mg
- Long shelf life: 18-24 months
Naloxone Complications

- Patient withdrawal:
  - Agitation
  - Vomiting
- Patient Combativeness
- Rare: Less than 1% of the time
  - Seizures
  - Pulmonary edema
    - <1% complicated by non-cardiogenic pulmonary edema – 95% of cases occur at onset of OD
  - Arrhythmias
Patient Does Not Need to be Breathing for IN Administration
IN Administration
IN Administration

2014 Intranasal Pilot
IN Administration
The Pilot IN Protocol

Suspected Opioid Overdose Protocol for BLS Providers

• Inclusion Criteria:
  • Suspected narcotic or opiate overdose, with at least one of the following:
    • History of overdose provided by bystanders
    • Paraphernalia consistent with opiate/narcotic use
    • Medical history consistent with opiate/narcotic use
    • Respiratory depression with pinpoint pupils
  • Blood glucose level >60 mg/dl. If blood glucose < 60 mg/dl, treat low glucose first.
  • Patients age >8
  • Alteration of consciousness (defined as P or U on the AVPU scale)
  • Respiratory rate <8
The Pilot IN Protocol

Suspected Opioid Overdose Protocol for BLS Providers

• Exclusion Criteria:
  • Documented allergy to naloxone
  • Alteration of consciousness or respiratory depression of presumed traumatic etiology
  • Epistaxis, nasal trauma or nasal mucosal abnormality for IN administration. Deviate to IM administration.
The Pilot IN Protocol

Suspected Opioid Overdose Protocol for BLS Providers

• Procedure (based upon local packaging)
  • Ensure all BLS assessments and procedures are being adequately delivered.
  • Check blood glucose to assure a reading of greater than 60mg/dl.
  • Verify that inclusion and exclusion criteria support administration.
The Pilot IN Protocol

Suspected Opioid Overdose Protocol for BLS Providers

• Procedure (cont.)
  • Pre-filled syringe
    • Un-package and remove prefilled syringe
    • Remove the pop-off caps and screw together
    • Withdraw 0.4 mg - 0.5 mg of the naloxone using the 1 cc luer lock syringe and needle
  • Remove needle from 1 cc luer lock syringe
  • Vial
    • Confirm the medication
    • Remove top from the naloxone and clean the rubber top with an alcohol pad
    • Draw equal amount of air into syringe as you want to administer
    • Inject air into vial and withdraw medication to appropriate amount
    • Remove needle from 1 cc syringe
The Pilot IN Protocol

Suspected Opioid Overdose Protocol for BLS Providers

• Procedure (cont.)
  • Once medication is drawn into 1 cc syringe:
    • Attach mucosal atomizer device to the 1 cc luer lock syringe
    • Insert atomizer until flush with external nare
    • Depress plunger rapidly to ensure delivery of 0.4 mg - 0.5 mg of syringe contents
    • Remove syringe and atomizer from the patient’s nare
    • Dispose of syringe and atomizer in approved receptacle
    • Monitor patient respirations and mental status for signs of improvement and/or deterioration
    • If no improvement after five minutes and/or deterioration in the patient’s respiratory status is noted, repeat procedure using the other nare. This procedure can be continued until a max dose of 2 mg has been administered.
Understanding IN delivery: Definitions

- First pass metabolism
- Nose brain pathway
- Lipophilicity
- Bioavailability
First pass metabolism

- Molecules absorbed through the stomach, including all oral medications, enter the “portal circulation” and are transported to the liver.
- Liver enzymes then break down most of these drug molecules and only a small fraction enter the body’s circulation as active drug.
- This process is called “First Pass Metabolism.”
- Nasally delivered medications avoid the digestive system so do not suffer first pass metabolism.
Nose brain pathway

- The olfactory mucosa (smelling area in nose) is in direct contact with the brain and cerebrospinal fluid (CSF).
- Medications absorbed across the olfactory mucosa directly enter the CSF.
- This area is termed the nose brain pathway and offers a rapid, direct route for drug delivery to the brain.
“Lipid Loving”

- Cellular membranes are composed of layers of lipid material.
- Drugs that are lipophilic are easily and rapidly absorbed across the mucous membranes.
Bioavailability

• How much of the administered medication actually ends up in the blood stream?
  • IV medications are 100% bioavailable.
  • Most oral medications are about 5 to 10 percent bioavailable due to destruction in the GI tract and liver.
  • Nasal medications vary, but nasal Naloxone approaches 100 percent, the same as when given intravenously.
Bioavailability

- Table demonstrating naloxone serum concentrations when given via IV and IN routes.
- Note that IV and IN serum levels are identical after about two to three minutes.
Intranasal Medication Administration: Bioavailability

- Not all drugs can be delivered via the nasal mucosa.
- Factors affecting bioavailability:
  - Medication characteristics
  - Medication volume and concentration
  - Nasal mucosal characteristics
  - Delivery system characteristics
    - Mucosal surface area coverage
    - Medication particle size
Intranasal Medication Administration: Factors Affecting Bioavailability

- Medication Characteristics:
  - Drug characteristics that affect bioavailability via the nasal mucosa include
    - Molecular size
    - Lipophilicity
    - pH
    - Drug concentration
    - Properties of the solution the drug is solubilized within
Intranasal Medication Administration: Factors Affecting Bioavailability

• Volume and concentration
  • Too large a volume or too weak a concentration may lead to failure because the drug cannot be absorbed in high enough quantity to be effective.
  • Volumes over 1 ml per nostril are too large and may result in runoff out of the nostril.
    • 1/3 to 1/2 ml per nare is ideal in an adult.
Intranasal Medication Administration: Factors Affecting Bioavailability

• Nasal mucosal characteristics
  • If there is something wrong with the nasal mucosa, it may not absorb medications effectively.
  • Examples:
    • Vasoconstrictors, such as cocaine, prevent absorption.
    • Bloody nose, nasal congestion, mucous discharge all prevent mucosal contact of drug.
    • Destruction of nasal mucosa from surgery or past cocaine abuse – no mucosa to absorb the drug.
Intranasal Medication Administration: Factors Affecting Bioavailability

- Delivery system characteristics:
  - Nasal mucosal surface area coverage:
    - Larger surface area delivery = higher bioavailability.
  - Particle size:
    - Particle size 10-50 microns adheres best to the nasal mucosa.
    - Smaller particles (nebulized) pass on to the lungs.
    - Larger particles form droplets and run-out of the nose.
Bioavailability and Particle size

- Compared to drops, atomized medication results in:
  - Larger surface area of coverage.
  - Smaller liquid particle size, allowing thin layer to cover mucosa.
  - Less run-off out the nasal cavity.
Intranasal Medication Administration: Factors Affecting Bioavailability

• Nasal drug delivery is convenient and easy, but it may not always be effective.
• Nasal drug delivery cannot completely replace the need for injections.
• Being aware of the limitations and using the correct equipment and drug concentrations will assist you in predicting times when nasal drug delivery may not be effective.
Intranasal (IN) Naloxone

• Background
  • Absorption of IN naloxone is almost as fast as IV in both animal and human models:
Intranasal (IN) Naloxone

- Atomized spray of medications show much better absorption via the IN route:
  
  
“Intranasal Administration of Naloxone by Paramedics”

- Prospective clinical trial
- Preliminary study February, 2001
  - Barton et al, *Prehosp Emer Care* 2002
- Final study completed

- Study design:
  - Required all patients to get an IV and IV naloxone (standard care) – however nasal naloxone was administered first and if the patient awoke prior to IV therapy they could stop.
Pre-hospital IN Naloxone

Results

• 43/52 (83%) = Responded to IN Naloxone
  • Median time to awaken from drug delivery = 3 min
  • Median time from first contact = 8 min

• 9/52 (17%) = Did not respond to IN Naloxone
  • Four patients noted to have “epistaxis,” “trauma,” or “septal abnormality”
  • Note: no one waited for them to respond. Once an IV was started they got IV naloxone, so some cases were given IV naloxone before the nasal drug could absorb.
Pre-hospital IN Naloxone

• Conclusions
  • IN naloxone is effective:
    • 83% response in the field
    • Potentially higher if one waits a few minutes for its effect prior to giving IV naloxone
  • Inexpensive device
    • Syringe driven atomizer
  • May decrease pre-hospital blood exposures
    • 29% of patients did not need an IV in the field (woke up before one could be started)
Pre-hospital IN Naloxone

- Take away lessons for nasal naloxone:
  - Dose and volume – higher concentration preferred so use 1 mg/ml IV solution.
  - Delivery – immediately on decision to treat, inject naloxone into nose with atomizer. Then begin standard care.
  - Successful awakening eliminates the need for any IV or further ALS care.
  - Awakening is gradual-patient doesn’t jump off the bed, but adequate respiratory efforts occur as fast or faster than IV naloxone due to no delays with IV start.
  - Not 100 percent effective- failures with IN naloxone need to be followed with IM naloxone.
What if initial intranasal Naloxone does not work?

1) Continue ABCs to support breathing and circulation.
2) Administer additional Naloxone per protocol.
3) Consider other causes for respiratory depression/coma AEIOU-TIPS.

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Give the Initial IN Dose
Time to Work

- 0.5 mg can usually correct respiratory concerns in a large person.
- Give the drug three to five minutes to work before additional doses are given.
Use of IM Administration

Use only when IN route is contraindicated.
Conclusions

• Drugs can be given IN:
  • Rapid
  • Safe to patient and provider
  • Immediate access
  • Can be given to almost anyone
    • Exception = Nasal mucosal abnormalities
Conclusions

The purpose of this medication is **NOT** to wake someone up. The purpose of this medication is to increase their spontaneous respiratory effort.

- Intranasal drug delivery is a “needleless” system.
- Reduce bloodborne exposure risks:
  - HIV
  - Hepatitis B, C
Questions?

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Resources and References

- www.intranasal.net