NALOXONE PRESCRIPTIONS FOR OVERDOSE: OUTSIDE OF MISUSE AND ABUSE

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DISCLOSURES

• Consultant/Independent Contractor: McNeil Pharmaceuticals, Purdue Pharmaceuticals
• Speaker's Bureau: AstraZeneca, Depomed Pharmaceuticals, Iroko Pharmaceuticals
LEARNING OBJECTIVES

• Explain the opioid crisis occurring in the United States
• List the patients at risk for potential opioid overdose
• Recognize the appropriate population to prescribe naloxone to, to prevent an opioid emergency

WHAT WE KNOW...
OPIOID MISUSE/ABUSE IS A MAJOR PUBLIC HEALTH PROBLEM

Improper use of any opioid can result in serious AEs including overdose & death

This risk can be greater w/ ER/LA opioids

- ER opioid dosage units contain more opioid than IR formulations
- Methadone is a potent opioid with a long, highly variable half-life

In 2011,
- 34.2 million Americans age ≥12 had used an opioid for nonmedical use some time in their life

In 2010,
- 425,247 ED visits involved nonmedical use of opioids
  - Methadone involved in 30% of prescription opioid deaths


DEATH RATE BY ALL DRUG POISONING NOW GREATER THAN VEHICULAR COLLISIONS


U.S. PRESCRIPTION OPIOID-RELATED MORTALITY

Number of Deaths from Prescription Opioid Pain Relievers in the U.S., 2001-2014

Source: CDC Wonder


PRESERVATION OPIOID MORTALITY

• 16,235 in 2013 1
• 18,893 in 2014 1
  • 16% increase
  • ~ 52 people die from prescription opioids every day in the U.S.
• 2 deaths every hour

RATES OF RISK INCREASE CONCURRENTLY WITH DAILY DOSAGE OF OPIOIDS

Studies show a dramatic increase in risk between 50 and 100 mg and a further increase with doses above 100 mg/day. This suggests many patients receiving opioids for chronic non-cancer pain at doses >50 mg/day are at increased risk for life-threatening OIRD and overdose.


OIRD=Opioid-Induced Respiratory Depression

HOW OPIOIDS WORK...
OPIOIDS ARE EFFECTIVE ANALGESICS

- Most bind to mu-opioid receptors in the central and peripheral nervous system in an agonist manner to elicit analgesia\(^1\)
- Have been used for thousands of years to treat acute and chronic pain\(^1\)
- Are a mainstay of medical therapy used by millions of patients each year\(^2\)


BENEFITS AND RISKS OF OPIOIDS

**Benefits**
- Pain management\(^1\)
  - Acute
  - Cancer
  - Chronic
- Cough suppression\(^1\)
- Treatment of dependence and abuse\(^2\)

**Adverse Effects\(^3\)**
- Constipation
- Nausea
- Vomiting
- Sedation
- Dizziness
- Physical dependence
- Tolerance
  - **Respiratory depression**

OPIOID-INDUCED RESPIRATORY DEPRESSION

CO₂ stimulates the respiratory drive. CO₂ levels signal the brainstem to increase the respiratory rate.

Opioids block the CO₂ feedback loop. Breathing slows or stops.

Self-potentiating cycle may result in life-threatening OIRD, associated hypoxemia, and/or respiratory arrest.

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Opioids depress a patient’s respiratory drive

• Characterized by a significantly reduced respiratory rate and tidal volume
• If prolonged, may result in hypoxemia
• Brain injury from apnea eventually leads to cardiac dysrhythmias, cardiac arrest, and death

• Opioid-induced sedation (CNS depression) generally precedes significant respiratory compromise

OIRD=Opioid-Induced Respiratory Depression; CNS=Central Nervous System

HOW NALOXONE WORKS

Naloxone (N) in the Brain

- Opioid receptors activated by heroin and prescription opioids
  - Pain Relief
  - Pleasure
  - Reward
  - Respiratory Depression

- Opioids broken down and excreted
  - Reversal of Respiratory Depression
  - Opioid Withdrawal
WHO IS AT RISK – BEYOND MISUSE AND ABUSE

- Chronic Hepatitis or Cirrhosis
- On Antidepressents,
- Bipolar or Schizophrenia Disorder
- Ever treated for Chronic Pulmonary Disease
- Chronic Kidney/Renal Disease

WHAT TO TEACH FAMILY AND FRIENDS...

RECOGNIZING AN OVERDOSE

• Unresponsiveness to yelling or stimulation, like rubbing your knuckles on breast bone

• Slow, shallow, or no breathing

• Turning pale, blue or gray (especially lips and fingernails)

• Choking sounds
WHAT NOT TO DO DURING AN OVERDOSE

• DO NOT put the individual in a bath
  • They could drown.
• DO NOT induce vomiting or give the individual something to eat or drink
  • They could choke.
• DO NOT give over-the-counter drugs or vitamins (eg, No-Doz or niacin)
  • They don’t help and the patient could choke.

RESPONDING TO A SUSPECTED OPIOID OVERDOSE
STEP 1 - RUB TO WAKE

• Rub your knuckles on the bony part of the chest (sternum) to try to get them to wake up and breathe.

STEP 2 - GIVE NALOXONE

Injectable:
• Give naloxone (discard any opened naloxone within 6 hours of using) Injectable naloxone: inject into the arm or upper outer top of thigh muscle 1 cc at a time always start from a new vial

Intranasal:
• Squirt half the vial into each nostril, pushing the applicator fast to make a fine mist.
STEP 3 - CALL 911

Tell them
• The address and where to find the person
• A person is not breathing
• When medics come tell them what drugs the person took if you know
• Tell them if you gave Naloxone

AVAILABLE NALOXONE FORMULATIONS

• Naloxone for Medical Settings
  • Vial and syringe for Injection
  • Prefilled Glass Cartridges for Injection
• Take-Home Naloxone
  • Naloxone Auto-injector
  • Naloxone Nasal Spray
• Other Naloxone Option
  • Intranasal (IN) Delivery Kit - Prefilled Cartridge for Injection adapted for IN Administration with Mucosal Atomizer
INJECTABLE NALOXONE PRODUCTS FOR MEDICAL SETTINGS

Approved and Intended for Healthcare Professional Use

Used for >40 years in hospital settings for the reversal of OIRD


TAKE-HOME NALOXONE

Nasal Spray (naloxone HCl) Auto-injector (naloxone HCl injection) & Trainer for Practice
OTHER NALOXONE OPTION

- Not FDA approved as a combination product
- Not widely available in retail pharmacy settings
- Utilized mainly among harm reduction/needle exchange and select law-enforcement
- Requires assembly of multiple parts and substantial training (non-standardized kits and instructions for use)

Intranasal (IN) Delivery Kit (glass cartridge, syringe and nasal atomizer)


COMPARISON OF ROUTES OF ADMINISTRATION BY PRE-HOSPITAL EMERGENCY CARE PROFESSIONALS

Naloxone response (n=52) in Barton et al.¹
- 43 patients responded to IN kits
  - No nasal abnormalities
- 9 did not respond to IN kits, but responded to IV rescue naloxone
  - Nasal abnormalities present (n=5)⁷

¹Epistaxis, nasal mucus, nasal trauma, septal abnormality, intranasal damage (cocaine)

<table>
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<th></th>
<th>No. Patients</th>
<th>IM or IN</th>
<th>&gt;10 Respirations per minute</th>
<th>% Requiring Additional Naloxone</th>
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<td>Kelly et al.²</td>
<td>155</td>
<td>IM</td>
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<td></td>
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<td>Kerr et al.³</td>
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<td>IM</td>
<td>78%</td>
<td>4.5%*</td>
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<tr>
<td></td>
<td></td>
<td>IN</td>
<td>72%</td>
<td>18%*</td>
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*Statistically significant OR 4.8 [95% CI 1.4, 16.3] after controlling for age, gender and suspected concomitant alcohol and/or drugs.
IN=Intranasal; IM=Intramuscular

IMPORTANCE OF AN OPIOID EMERGENCY PLAN

• Patients should be educated
  • OIRD is a risk of opioid therapy
  • Mistakes can happen during treatment
  • Patients may witness an opioid emergency and could be in best position to help save their lives

• Family, friends or other caregivers should be prepared to respond
  • Their role in adherence to opioid therapy
  • How to recognize an opioid emergency
  • How to respond and manage an opioid emergency, including the importance of seeking definitive emergency care and follow-up treatment

• Need for ongoing response preparation and practice
  • Equip patients and caregivers with take-home naloxone
  • Evzio Trainer allows for ongoing practice and preparation with ability to expand network of those trained to respond to opioid emergencies

OIRD=Opioid-Induced Respiratory Depression

Questions?

Thank You!