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.

- ER opioid dosage units contain more opioid than IR formulations.
- Methadone is a potent opioid with a long, highly variable half-life.
- Methadone involved in 30% of prescription opioid deaths.

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

- 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**


2. Deaths per 100,000 People.

Deaths per 100,000 People:
- Motor vehicle collisions
- All poisoning
- Drug poisoning
- Unintentional drug poisoning

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

Source: CDC Wondrak

- 16,235 in 2013
- 18,893 in 2014
- 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

Dose and Risk of Overdose for Patients With Chronic Pain, by Study

- Bihari, et al
- Dunn, et al


$^{4}$OIRD=Opioid-Induced Respiratory Depression

$^{5}$Hazard Ratio

$^{6}$8

$^{7}$7

$^{8}$6

$^{9}$5

$^{10}$4

$^{11}$3

$^{12}$2

$^{13}$1
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.  
- Have been used for thousands of years to treat acute and chronic pain.  
- Are a mainstay of medical therapy used by millions of patients each year.  

BENEFITS AND RISKS OF OPIOIDS

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Adverse Effects</th>
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<tbody>
<tr>
<td>Pain management[^1]</td>
<td>Constipation</td>
</tr>
<tr>
<td>Acute</td>
<td>Nausea</td>
</tr>
<tr>
<td>Cancer</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Chronic</td>
<td>Sedation</td>
</tr>
<tr>
<td>Cough suppression[^1]</td>
<td>Dizziness</td>
</tr>
<tr>
<td>Treatment of dependence and abuse[^2]</td>
<td>Physical dependence</td>
</tr>
<tr>
<td></td>
<td>Tolerance</td>
</tr>
<tr>
<td></td>
<td>Respiratory depression</td>
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</table>

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.


Opioids binding to μ receptors in brainstem suppress chemoreceptor responses to hypercapnia. Self-perpetuating cycle may result in life-threatening OIRD, associated hypoxemia, and/or respiratory arrest.

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

OIRD=Opioid-Induced Respiratory Depression

OPIOID-INDUCED RESPIRATORY DEPRESSION (OIRD)

Opioids depress a patient's respiratory drive1
• 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 compromise3

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


HOW NALOXONE WORKS
WHO IS AT RISK – BEYOND MISUSE AND ABUSE

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

TAKING MEDICATIONS APPROPRIATELY... BUT STILL AT INCREASE RISK

- Opioid Dependence
- 1 or more ER visits in past 6 mos
- Hospitalized 1 or more days in past 6 mos
- Use of ER/LA Opioid
- On Methadone
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 (e.g., 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 1cc 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 OIRD1

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)

<table>
<thead>
<tr>
<th></th>
<th>Kelly et al2</th>
<th>Kerr et al3</th>
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<tbody>
<tr>
<td>No. Patients</td>
<td>155</td>
<td>172</td>
</tr>
<tr>
<td>IM or IN</td>
<td>IM 82%</td>
<td>IM 76%</td>
</tr>
<tr>
<td>&gt;10 Respirations per minute</td>
<td>IN 26%</td>
<td>IN 4.5%*</td>
</tr>
<tr>
<td>% Requiring Additional Naloxone</td>
<td>13%</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 drug use.

FTP: intranasal (IN), nasal mucosa, nasal trauma, septal abnormality, intranasal damage (cocaine)
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

Questions?

Thank You!