Opioid Toxicity and Naloxone: Implications for the K-12 Population

Elizabeth J. Scharman, Pharm.D., DABAT, FAACT, BCPS
Director, West Virginia Poison Center
Professor, WVU School of Pharmacy

Outline

• Definitions
• Patterns of opioid exposure grades K-12
• Opioid Toxicology
  I. Opioid toxidrome
  II. Pharmacologic differences: effect on toxicity
  III. Designer opioids: what this means for WV
• Naloxone
  I. Mechanism details
  II. Potential adverse effects
  III. Meaning of “response” to naloxone

Definitions

• Opioid
  – A drug that works by binding to the opioid receptors
  • Opioid receptors are where the body’s “natural” painkillers (endorphins for example) attach to decrease the perception of pain
  • Examples: morphine, hydrocodone, heroin, oxycodone

• Naloxone
  – Opioid antidote
  • Competitively takes the place of the opioid on the opioid receptor
Young Opioid Abusers

- Survey of 50 injection drug users 16-25 years
  - Hydrocodone/acetaminophen, oxycodone, oxycodone/acetaminophen most common initial opioid drugs misused
    - Average age first use = 14.5 years
    - Obtained from family member, their own Rx, friend/contact
    - Oral = 41, Sniffing/snorting = 8, Injecting = 1
  - Followed initial use of alcohol (avg 12.8 years of age), marijuana (avg 12.5 years of age), Rx stimulants (avg 14.1 years of age)
- Opioid misuse prior to heroin (n = 43)
  - Average age of first use = 16.1 years

WV Poison Center Data

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2 opioid calls from a school in past 10 years (2008 and 2009); no marked symptoms.

Classic Opioid Toxidrome

- Textbook description:
  - Central Nervous System (CNS) depression
  - Respiratory depression (decreased breathing)
  - Miosis (constricted pupils)
- Caveats
  - Miosis may not be recognized or present
  - Hypoxia may result in mydriasis (dilated pupils)
  - CNS and respiratory depression combination not unique to opioids
  - Hypotension (low blood pressure) is of importance but not listed
Not All Opioids are Equal

• Share the risk for CNS and respiratory depression, however:
  – Some are more potent than others (takes less to cause harm)
  – Some have drug interactions, some do not
  – Some work faster than others
  – Some work longer than others
  – Some are combined with other drugs, some are not

Some Opioids Do Other Things

• Those combined with acetaminophen can cause fatal liver injury
• Tramadol can cause seizures
• Methadone can cause fatal arrhythmias (heart rhythm abnormality)
• Injecting ground pills can cause strokes, blindness, lung injury, necrosis
• Injections of impure drugs can cause infections

Heroin Overdose

• White, bitter, powder: injected, snorted, inhaled
  – Impurities may inhibit absorption
    • Injecting the drug gets around this
• May be mixed with diluents and/or adulterants
  – Diluents used to add bulk (buyer believes he/she getting more for their money)
  – Adulteration can be inadvertent or, most commonly, purposeful in order to shortchange the buyer or enhance mood altering effects by:
    • Increasing vaporized dose of heroin
    • Additive drug action

Naloxone does not reverse these effects
OR: It may not be heroin

Increasing Fentanyl Overdoses

- Recent increase involves non-pharmaceutical fentanyl (NPF) and fentanyl analogs (e.g., acetyl fentanyl)
- Similar to heroin:
  - Same toxidrome
  - Both extremely potent
  - Same routes of administration
- Used alone or in combination with heroin
- Fentanyl not detected by many drug screens

Additional Novel Opioids of Concern

- Additional fentanyl analogues
  - Not just designer fentanyl and acetylfentanyl
- U47700
- W series (W-1 through W-32)
- Extremely potent
- Not detected with drug screening
Naloxone Closest to Ideal Antidote

- Specific for the opioid receptor
- Readily available
- Inexpensive (generic injectable formulation)
- Effective via multiple routes
- When opioid action blocked, breathing resumes
- Not perfect because:
  - Some opioids cause effects not opioid-related
  - Cannot reverse hypoxic organ damage that has already occurred
  - Potential for adverse effects exists if dependence present

When To Give Naloxone

- Opioid overdose/toxicity is possible and:
  - Person does not respond to verbal and physical stimulus
  - Person does not appear to be breathing well or at all
    - May or may not be blue

Risk vs. Benefit

- If the victim is not breathing there is more to gain by trying naloxone than there is to lose
- If the dose is kept at 0.4 mg injection, or 2 mg nasally, the risk of withdrawal is minimized
Naloxone Safety

• No documented case of anaphylaxis or allergic reaction
• No documented teratogenicity (birth defects)
• If not opioid dependent, withdrawal not a concern
  – Unfortunately, often uncertain if person is dependent or not
• If no opioid on board, cannot overdose someone with naloxone

Naloxone Treatment Goal

• Reversal of respiratory depression: NOT return to wakefulness
  
• If victim has taken an opioid overdose, but is arousable and talking, naloxone (or a repeat dose of naloxone) is not indicated at that time
  – The victim still needs close observation and follow-up

Without need, no risk is acceptable

Naloxone Risk #1

• Induction of withdrawal
  – Not usually life-threatening but person may feel like they are going to die
    • “First do no harm”: Can be considered assault if not indicated
    • Response may result in violent behavior placing themselves and the rescuer at risk for physical harm
    • Vomiting may result in aspiration pneumonia if other CNS depressants are present and depressing gag reflex
    • Massive catecholamine surge has resulted in death in medically unstable individuals
    • May cause acute pain syndrome if chronic pain patient

Prevent by giving the right dose
Naloxone Risk #2

- Reversal of sedative effects of naloxone can unmask stimulant toxicity from co-ingestant(s)
  - Victim becomes unmanageable in the outpatient setting

Naloxone Risk #3

- Pulmonary edema not common but a well documented effect
  - Can be life-threatening

=> Risk is low, so not a reason not to use naloxone. However, as risk exists, naloxone should not be given when not indicated and dose should not be excessive.

Naloxone Response

- As goal is reversal of respiratory depression
  - Response = effective respirations

- Return to wakefulness is NOT required
  - Aiming for this goal can increase risk of harm (naloxone dose too high leading to withdrawal symptoms)
  - The victim may not wake up but they may have adequate respirations now and their blood pressure may have increased
Naloxone Response

- If (+) response, opioid likely involved
  - Does not mean other substances not involved!

- If no response, the following are possible:
  - Opiate exposure does not exist
  - Other CNS depressants are on board and their effects are masking any response
    - E.g.: ethanol, antidepressants, benzodiazepines, others
  - Co-existing traumatic brain injury exists (e.g., from fall or fight)
  - Hypoxic brain injury has already occurred
  - Partial agonist involved and dose is inadequate

Why Call 911

- Response does not mean a pure opioid overdose
  - Acetaminophen toxicity can be fatal
    - Acetaminophen is a common co-ingestant
  - Adulterants, other drugs may be of concern
  - May be other injuries
  - Respiratory depression may recur
  - Oxygen saturation evaluation not available
  - Reason for overdose needs to be evaluated
    - "Near death" experience can be trigger for starting therapy
    - If from drug interaction or disease/drug interaction, a change in therapy is needed

Questions?
Call WV Poison Center
1-800-222-1222