Morphine Myths: Important Tools for End of Life

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Objectives

• Understanding the cultural context of opiates
• Demystifying the use of opiates in end-of-life care
• Understanding opiate use for ancillary effects
• Treatment of undesired effects of opiates
A Brief History of Opiates

• Derivative of the opium poppy (*Papaver somniferum*)

• First documented medical use of opium on Sumerian clay tablets (3400 BCE)
A Brief History of Opiates

• Opium began being widely traded in the 1800s for recreational use

• Morphine was first created in 1803 as an extract from opium resin
A Brief History of Opiates

• Heroin first distilled from morphine in 1874

• Abuse potential of heroin recognized in 1924 and made a controlled substance
Regulation of Opiates

- DEA Drug Schedules
  - five categories
  - based on acceptable medical use
  - takes into account abuse/dependency potential
Regulation of Opiates

- Schedule I - no currently accepted medical use and high abuse potential (heroin)
Regulation of Opiates

- Schedule I - no currently accepted medical use and high abuse potential (heroin)
- Schedule II - high potential for abuse or dependency, but accepted medical use (most opiates)
Regulation of Opiates

- **Schedule I** - no currently accepted medical use and high abuse potential (heroin)
- **Schedule II** - high potential for abuse or dependency, but accepted medical use (most opiates)
- **Schedule III-V** - lower abuse potential, accepted medical use (low dose formulations of opiates)
A Brief History of Opiates

- Ongoing development of opium derivatives
  - morphine/MS Contin
  - oxycodone/Oxycontin
  - Fentanyl (Duragesic)
  - Hydromorphone (Dilaudid)
  - Methadone
A Brief History of Opiates

● Ongoing development of opium derivatives
  ○ Codeine/hydrocodone (Vicodin/Norco)
  ○ Meperidine (Demerol)
  ○ Tramadol (Ultram)
The Opioid Crisis (20th Century)

- In first half of 20th century, pain was considered an existential problem
- Complaints of pain were considered hysterical complaints
- Abuse of heroin led to regulation and increased fear of use of opiates
The Opioid Crisis (1980s)

- Until 1980s, official recommendation was for cancer patients to avoid or wean opiates until their “life could be measured in weeks”
- Studies into the 1990s suggest a fear and avoidance of opiates for any reason by physicians, due to abuse potential
The Opioid Crisis (1980s)

- WHO in 1986 reported undertreatment of post-operative and cancer pain
- Suggested opiates as a valid and effective means to treat
The Opioid Crisis (1990s)

- Studies reported that use of opiates for pain is “unlikely to result in addiction”
- Encouraged use of opiates for acute pain (injuries/illnesses)
The Opioid Crisis (1990s)

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...And chronic pain
The Opioid Crisis (1990s)

- In 1995, the American Pain Society introduced pain as “the fifth vital sign” with help from:
  - The Joint Commission
  - Veterans Administration
  - Pharmaceutical companies

- Not treating any reported pain was labeled as “inhumane”
The Opioid Crisis (2000s)

- Massive increase in prescriptions for opiates for all indications
- Increase in abuse, dependence, addiction and deaths from overdose
- Management of chronic pain did not improve
- Labeled a public health emergency by the CDC in 2017
MORE DEATHS FROM OPIOID ABUSE

American deaths from overdoses of opioid drugs increased 311% from 1999 to 2015.

Annual deaths:

- 1999: 8,048
- 2015: 33,091

SOURCE National Institute on Drug Abuse
George Petras, USA TODAY
Risk of Opiate Overdose

● Greatly increased if medications are combined
  ○ Vast majority of fatal overdoses from opiates also had benzodiazepines and alcohol in their system
● Increased if taking a prescription medication that belongs to someone else
● History of substance abuse
● History of depression
Response to Opioid Crisis

- Monitoring prescriptions via Prescription Drug Monitoring Databases
- Teaching physicians alternative methods of treating acute and chronic pain in the community
- Educating community on risks of opioid medication treatment
- Developing interdisciplinary models for chronic pain programs
Preventing Opioid Overdoses and Related Harms

- Conduct surveillance and research
- Empower consumers to make safe choices
- Build state, local, and tribal capacity
- Support providers, health systems, and payers
- Partner with public safety

[Logo: CDC]
Response to Opioid Crisis

- **NOT** avoiding opiates at all costs
- **NOT** limiting access to appropriate use of opiates in cancer-related pain or end of life symptom management
- **NOT** punishing patients or physicians
Opiates in End of Life Care

- Not anticipating long term, chronic use
- Not anticipating that pain will resolve or stabilize
- Minimal concern for addiction
Opiates in End of Life Care

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- Minimal concern for addiction

What is addiction?
I love the smell of socially acceptable chemical dependence in the morning.

Unknown
Tolerance

An adaptive state that develops from repeated drug administration, which results in increasing doses of medicine being needed to give the same result.
Dependence

An adaptive state that develops from repeated drug administration, and which results in withdrawal upon cessation of drug use.
Abuse

A pattern of repeated drug or alcohol use that often interferes with health, work, or social relationships
Addiction

A chronic, relapsing disorder characterized by compulsive drug seeking, continued use despite harmful consequences, and long-lasting changes in the brain.
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Opiates in End of Life Care

- Treatment of pain
- Use of opiates for ancillary effects
- Variety of effective delivery methods
Opiates in End of Life Care

- Few adverse effects, compared to alternatives
  - NSAIDs (ibuprofen, naproxen, aspirin)- limited use in heart disease, gastrointestinal disease and renal failure
  - Steroids (prednisone, dexamethasone)- limited use in gastrointestinal disease, many potential adverse effects
  - Acetaminophen (Tylenol)- limited use in liver disease
  - Adjunct medications (gabapentin, depakote)- many potential adverse effects
Opiate Formulations

- Oral
- Buccal (through cheek/tongue)
- Rectal
- Transdermal (patches)
- IV
- Intramuscular (ouch!)
- Subcutaneous (under the skin)
- Intrathecal (into the space around the spinal cord)
- Inhaled
- Topical and into wound bed
Opiate Formulations

- Long acting
  - Oxycontin
  - MS Contin
  - Fentanyl patches
  - Methadone
- Short acting
  - Oxycodone
  - Morphine
  - Hydromorphone
  - Fentanyl (oral/IV)
Opiate Formulations

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  - Fentanyl patches
  - Methadone
- Short acting
  - Oxycodone
  - Morphine
  - Hydromorphone
  - Fentanyl (oral/IV)

- Continuous (IV/subcutaneous)
  - Morphine
  - Hydromorphone
  - Fentanyl
  - Methadone
Long acting Opiates

- Constant pain
- Frequent use of short acting opiates
- Pain that is worse upon waking
- Pain that is unlikely to decrease suddenly
Short acting Opiates

- Breakthrough pain (with use of a long acting)
- Occasional pain
- Pain that is changing/decreasing (injuries, fractures)
Ancillary Effects of Opiates

- Decreased respiratory drive
- Constipation
- Urinary retention
- Confusion/euphoria
- Opiate toxicity
Decreased Respiratory Drive

- Effect varies from person to person
- Effect varies from drug to drug
- Tolerance can develop
- Dose dependent
Decreased Respiratory Drive

Benefits

- Very effective in treating shortness of breath (not hypoxia)
- Any opiate works (especially short acting)
- More effective than lorazepam at treating air hunger
- Studies mixed at best showing that inhaling opiates better at treating shortness of breath than oral
Decreased Respiratory Drive Treatment

- Naloxone (Narcan) can be used to reverse this (CAUTION!)
- Holding medication also effective
- Pushing fluids, if possible/desired
- Education of patient, family, staff
Constipation

- 100% of patients on opiates develop this
- 100% of opiates cause this
- No tolerance develops
- Not dose dependent
- Slows transit (no “push”)
Constipation

Benefits

- Can be useful in cases where disease causes fast transit
  - some cancers
  - short gut syndrome
  - NOT C. difficile
Constipation Treatment

- Does not respond to fiber, diet, increased water
- Does not respond to stool softeners (docusate/Colace)
- Must use an agent that gives some “push”
  - senna
  - bisacodyl
  - polyethylene glycol
  - Magnesium
- Can also use methylnaltrexone (Relistor)
Urinary Retention

- Effect varies from person to person
- Effect varies from drug to drug
- Tolerance can develop
- Dose dependent
- More common in older patients
- More likely when also using benzodiazepines, anti-psychotics, antidepressants or some hypertension medications
Urinary Retention

Benefits

- Opiates classically used to treat bladder spasms (B&O suppositories)
  - Indwelling catheter use
  - Bleeding in the urinary tract
  - Cancer of the urinary tract
Urinary Retention Treatment

- Indwelling catheter
- Minimize other medications that may cause retention
- Ensure constipation is treated
- Decrease opiate dose
- Rotate to another opiate
Confusion/Euphoria

- Psychomotor depression ("downer")
- Street value of opiates
- Abuse and diversion
- Chemical coping
Confusion/Euphoria

- Varies based on route
  - snorting
  - injecting quickly
- Tolerance develops
- Dose dependent
- Varies based on drug
  - Heroin, hydrocodone more euphoric
  - Fentanyl, hydromorphone euphoric when injected
  - Methadone, morphine, oxycodone less euphoric
Confusion/Euphoria Treatment

- Likely to abate over time (tolerance)
- Encourage fluids
- Rotate to another opiate
- Minimize other medications that may cause confusion
Opiate Toxicity

- Doses escalated quickly
- Started at too high dose
- Progressive renal failure
  - very common at end of life
  - may have to decrease dose to make up for kidneys not clearing
Opiate Toxicity

Symptoms

- Escalating pain
- Hyperalgesia (pain all over)
- Confusion
- Twitching
Opiate Toxicity Treatment

- Decrease dose
- Switch to another opiate
- Fluids
- Lorazepam (for twitching)
History
Opiates at End of Life
Appropriate Use of Opiates
Ancillary Effects of Opiates
Questions?
References

• https://www.deamuseum.org/ccp/opium/history.html
• https://www.who.int/substance_abuse/information-sheet/en/
References

• [https://www.cdc.gov/opioids/strategy.html](https://www.cdc.gov/opioids/strategy.html)