**OPIOID USE IN CHRONIC NON-CANCER PAIN**

The Past, Present and Future

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**OBJECTIVES**

At the end of this presentation the participants should be able to:

- Identify causes of widespread use of opioids for CNCP
- Discuss present implications of opioid misuse
- Utilize strategies to ensure appropriate use of opioids for CNCP

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**THE PAST...**

- **Opium**
  - Available in US before 1800s
  - Recommended for numerous conditions

- **Morphine**
  - Opium derivative, discovered in 1804
  - Manufactured legally from domestic/imported poppy seeds
  - Invention of the hypodermic needle in 1870s increased use

- **Heroin**
  - Discovered in 1874
  - Bayer Pharmaceuticals marketed heroin as a cough suppressant in 1898
  - Used as treatment for tuberculosis, pneumonia
  - Commonly prescribed into 1920s

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**ADDITION TO OPIOIDS RARE?**

- **Porter et al**
  - Evaluated records of 39,946 patients to determine addiction rates
  - Results
    - 11,882 patients received at least one opioid
    - 4 cases of addiction in patients with no history of drug abuse
      - 2 Meperidine, 1 Percodan®, 1 hydromorphone

  - Conclusion
    - Addiction rare in patients with no history of drug abuse

- **Perry et al**
  - Evaluated indication, course, safety, efficacy
  - Retrospective review of 38 patients
  - Regimens included oxycodone, methadone, codeine
  - Results
    - 50% treated for > 4 years, 15% treated for > 7 years
    - 67% prescribed < 20 mg morphine equivalents per day
    - 10% prescribed > 40 mg morphine equivalents per day
    - 63% experienced adequate pain relief
    - No toxicity reported
    - Management difficult in 2 patients, both with history of drug abuse

  - Conclusion
    - Therapy is safe, beneficial, more humane

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**DISCLOSURE**

- I have no actual or potential conflicts of interest to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation.

- American Pain Society (APS) first introduced idea in 1995
- Elevated level of importance for better management
- Adopted by the Veterans Health Administration and The Joint Commission
- Pain assessments routine in hospitals and clinics
- HCAHPS Scores
- Contributed to increased opioid prescribing
- Some prescribers lack training to treat pain
- Writing a Rx is efficient


HCAHPS = Hospital Consumer Assessment of Healthcare Providers and Systems

Mularski et al.

- Evaluated impact of “Pain as the 5th Vital Sign” initiative
- Retrospective medical records review at a single Veteran Affairs medical center
- Compared 300 pre-initiative and 300 post-initiative visits

Results and conclusion

- Effective pain management a part of quality medical practice
- Causes of inadequate pain control:
  - Deficient pain management knowledge
  - Inadequate understanding of addiction
  - Fear of sanctions, investigations
- First adopted 1998
- Created to clarify the Board’s stance on pain control
- Ease physician hesitation
- Improve management of pain

Overview
- Opioids may be essential for chronic pain
- Management based on knowledge and research
- Utilize both pharmacologic and non-pharmacologic treatments
- Promptly assess and treat pain
- Increase quantity and dosing frequency based on pain duration and intensity
- Tolerance and physical dependence normal, not same as addiction
- Prevent drug diversion
- Do not fear disciplinary action if prescribing controlled substances for legitimate medical purpose in usual course of practice

Purdue Pharma introduced OxyContin® in 1996

- Marketing strategy
  - Hosted all expense paid conferences
  - Targeted top opioid prescribers
  - Bonuses for sales reps
  - Coupon program
  - Branded promotional items
  - Minimized addiction risk

- ↑ Sales from $48 million in 1996 to $1.1 billion in 2000
- ↑ Rx from ~670,000 in 1997 to 6.2 million in 2002

OxyContin® most abused drug by 2004
- First reported in 1999
- 68% of oxycodone extracted from crushed tablets
- Swallowed, inhaled, injected
- Criminal charges for misbranding
- “Less addictive and less subject to abuse and diversion than other opioids”
- Purdue Pharma and 3 executives plead guilty in 2007
- Paid $634 million in fines
Committee on Finance sends letters requesting documentation in 2012

Recent investigative reporting from the Milwaukee Journal Sentinel/MedPage Today and ProPublica revealed extensive ties between companies that manufacture and market opioids and non-profit organizations such as the American Pain Foundation, the American Academy of Pain Medicine, the Federation of State Medical Boards, the University of Wisconsin Pain and Policy Study Group, and the Joint Commission.

The Joint Commission

In 2003, the GAO report pointed to Purdue’s partnership with the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) as possible means for Purdue to have facilitated its access to hospitals to promote OxyContin. The report revealed that Purdue funded over 20,000 pain-related educational programs through direct sponsorship or financial grants in addition to funding the JCAHO pain management programs.

Specifically, the Sentinel reported that the Federation of State Medical Boards, with financial support from opioid manufacturers, distributed more than 160,000 copies of a model policy book authored by FSMB’s chief medical advisor and the director of the University of Wisconsin Pain and Policy Study Group. In a letter to the Joint Commission, the group said the book “failed to point out the lack of science supporting the use of opioids for chronic, non-cancer pain.”

Dr. Portenoy, New York pain specialist

Advocated use of opioids to treat CNCP

Past president of American Pain Society

Comments from Wall Street Journal interview

“Did I teach about pain management, specifically about opioid therapy, in a way that reflects misinformation? Well, against the standards of 2012, I guess I did.”

“I gave innumerable lectures in the late 1980s and 1990s about addiction that weren’t true.”

“Clearly, if I had an inkling of what I know now then, I wouldn’t have spoken in the way that I spoke. It was clearly the wrong thing to do.”

Data about the effectiveness of opioids does not exist.

Do they work for five years, 10 years, 20 years?

We’re at the level of anecdote.

Became most prescribed drug in 2009

Reclassified as Schedule II in 2014

No longer most prescribed

Superseded by levothyroxine in 2014

3-fold increase from 2001 to 2013

Florida

61% increase from 2003 to 2009

National

9/11/2015

3
**HEROIN EPIDEMIC**

- Heroin in FL
  - Cause of death in 98.7% of cases involving drugs
  - Deaths increased by 102.9% compared to 2013
  - May have been taken with other drugs
  - 90% of deaths classified as accidental
  - Occurrences increased by 119.7% compared to 2013

- Heroin use is part of a larger substance abuse problem

**HEROIN IN FL**

- High unemployment, low income, lack of education
- Majority of cases linked to oxymorphone abuse
- Feb 2015
  - 26 confirmed cases
  - 4 preliminary positive
  > 80% Hepatitis C coinfection
- September 2015
  - 181 confirmed cases
  - 0 preliminary positive

**FDA WARNED ENDO PHARMACEUTICALS**

- Manufactures Opana® (oxymorphone)
- Introduced new abuse deterrent formulation
- Requested FDA to rule old formulation unsafe
- FDA denied request
  - New formulation harder to crush and more difficult to inject
- Endo denies Opana® at fault for outbreak
- Blames generic formulations

**ADDICTS CAN SUE PHARMACISTS?**

- 29 patients of Mountain Medical Center, West Virginia
  - 8 law suits against 3 pharmacies
  - Alleged pharmacists aware of the "pill mill”, filled controls too early and for excessive time periods, filled contraindicated and "synergistic" combinations
  - One of three pharmacists sentenced
  - 6 months federal prison, 1 year supervised release, $500,000 in fines

- Mobogenie.com
- 2015

- Indiana State Department of Health 2015.
**Florida’s PDMP**
- Created in 2009, operational in 2011
- Provide safer prescribing, decrease abuse and diversion
- Collects prescribing and dispensing data on Schedules II to IV
- Information reported within 7 days
- Cannot accept funds from pharmaceutical companies

**Overview**
- Evaluated effect of new legislation on opioid prescribing and use
- Study period, July 2010 to September 2012
- Florida as intervention state, Georgia as control state

**Results**
- 480 million prescriptions associated with 2.6 million patient, 431,890 prescribers, 2829 pharmacies
- 7.7% of prescriptions were opioids
- ↓ 1.4% in opioid prescriptions
- ↓ 2.5% in opioid volume
- ↓ 5.6% in morphine milligram equivalents per transaction

**Conclusion**
- PDMP and pill mill laws yielded modest reductions in prescribing and use
- ↓ greatest in providers and patients with highest baseline prescribing and use

**Walgreens-US alleged record-keeping and dispensing violations under the CSA**
- Jupiter Distribution Center
  - Failed to report suspicious prescription drug orders
  - Allowed retail pharmacies receive at least three times the FL average for controlled substances
- 6 retail pharmacies
  - Received suspicious drug shipments from distribution center
  - Distributed prescriptions to pharmacies even though no legitimate order was received
- Failed to properly mark hardcopy controlled substance prescriptions outsourced to “central fill” pharmacy
- $80 million to settle civil penalty claims

**CVS-US alleged violations of the CSA and record-keeping regulations**
- Created, owned “dummy” DEA numbers
- Filled prescriptions for providers with invalid DEA numbers
- Maintained dispensing records with falsified DEA numbers
- $1.1 million to settle civil penalty claims
WHOLESALE LIMIT SHIPMENTS

- NCPA Survey in 2014
  - Assessed controlled substance shipments over past 18 months
  - ~1,100 pharmacies responded
  - 75% experienced at least 3 delays
  - 67.9% unable to order replacements from alternative suppliers
  - Legitimate patients unable to get opioids

- Is the DEA responsible?
  - Accused of targeting distributors to combat diversion and drug abuse
  - Denies increased regulatory actions against distributors

Legitimate patients unable to get opioids

THE FUTURE...

PRESCRIBER EDUCATION

- Utilize non-pharmacologic therapies
- Initiate non-opioid and adjuvants
- Incorporate interventional treatments
- Opioid prescribing
  - Controlled substance agreement
  - Screening for substance abuse/cessation
  - Use E-FORCSE
  - Track pain and function
  - Track morphine milligram equivalent used daily
  - Avoid use of concomitant sedative-hypnotics

GOT DRUGS?

- Public health, safety concern with unused medications
- National Prescription Drug Take-Back Days
  - DEA collects expired, unused medications
  - 108,000 lbs collected April 2014
  - > 4.1 million lbs collected since 2010
- Secure and Responsible Drug Disposal Act of 2010
  - Enacted after 1st Take-Back Day
  - Certain DEA registrants may become authorized collectors
  - Provides safe and routine disposal

SUBSTANCE ABUSE TREATMENT

- Substance Abuse and Mental Health Program
  - Programs within Department of Children and Families
  - Federal designation from SAMHSA
- Treatment and referral services
  - Available 24 hours a day, 7 days a week
  - Online treatment facility locator
  - Some programs with sliding fee scale for uninsured

ABUSE-DETERRENT FORMULATIONS

- Guidance published by FDA
  - No legal requirements, only recommendations
  - Abuse-deterrent ≠ no abuse risk
  - Abuse-deterrent ≠ tamper-resistant
  - Physical/chemical barriers
    - Prevents chewing, crushing, cutting, grinding
    - Resists opioid extraction
- OxyContin® (oxycodone)
- Hysingla® (hydrocodone)

Public health, safety concern with unused medications

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ABUSE-DETERRENT FORMULATIONS

- Agonist/antagonist combinations
- Added to reduce euphoric effect
- Actives with manipulation of drug
- Taken (morphine-sulfate/naloxone)
- Embed® (morphine-sulfate/naloxone)
- Delivery system
- New molecular entities/products
- Combination
- Novel approaches

EXEMPTION®
- Extended-release oxycodone
- Recently approved by FDA advisory panel
- Details technology
- Contains tiny beads of solution stored in the capsule
- Capsule may be emptied in mouth, feeding tube, or sprinkled on soft food
- Avridi®
- Immediate-release oxycodone
- Needs to be taken on an empty stomach
- Recently denied approval from FDA advisory committee

INCREASE AVAILABILITY OF NALOXONE

KEEP CALM AND CARRY NALOXONE

SUMMARY

- Many factors contributed to the current opioid epidemic
- Non-pharmacologic therapies should be incorporated in current practice
- More safe, effective and abuse-deterrent options for pain management are needed
- Pharmacists play an important role in educating prescribers and monitoring patients

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