Substance Use Disorders: It's a Tough Row to Hoe

NARTC Fall Meeting

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History of Opioids



The "Pod of Pleasure"







<complex-block>

OTC Opiates





Opioids

- Naturally Occurring
 - Opium, Tincture of Opium (Laudanum), Camphorated Tincture of Opium (Paregoric), Morphine, Codeine
- Semi-Synthetic
 - Hydromophone (Dilaudid), Oxycodone (Percocet, Oxycontin), diacetylmorphine (heroin), Hydrocodone (Vicodin, Zohydro)
- Synthetic
 - Meperidine (Demerol), pentazocine (Talwin), methadone (Dolophine), propoxyphene (Darvon)



Opioids

- Opioids
 - Narcotic pain reliever
 - Side effects: sedation, constipation, itching, nausea, respiratory suppression, dependence, addiction, death
 - Indicated for:
 - Short-term acute pain
 - Postsurgical
 - Acute injury
 - Very limited evidence for
 - Chronic non-cancer pain



America Loves Opioids

- Americans are 4.6% of the world's population, but we consume:
 - -80% of the global opioid supply
 - -99% of the global hydrocodone supply
 - -2/3 of the world's illegal drugs



Size of the Problem

- Between 1999 and 2010,
 - # of rx of controlled prescription drugs jumped 400%
 - # of overdose deaths increase 400%
 - Between 2010-2013 heroin OD deaths doubled
 - In 2012 OD exceeded car accidents in preventable cause of death
 - In 2015 Heroin OD exceeded gun homicide in preventable cause of death
- Controlled prescription drugs (i.e. opiates, stimulants, sedatives, and tranquilizers) are now the 4th most abused substances in America
 - Behind marijuana, alcohol, and tobacco
 - 2012 NSDUH survey showed lifetime non-medical use of psychotherapeutics = 20% of the US population (48 million adults)
 - Opioids are the most common prescription drugs of abuse



Who Prescribes Opioids

- According to 2013-2014 CDC data:
 - 40% of opioid prescriptions come from primary care physicians
 - 39% come from emergency department physicians



Opioid Sales 2001-2012

SALES OF OPIOIDS

\$3.97 billion

2012

2001

\$8.34 billion

Up 110%

Increasing use of opioid meds





Overdose Deaths



Opioid Overdose



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Source of Pain Relievers by Non-medical Users



Past Year Non-medical Users of Pain Relievers = 12.4 million Source: SAMHSA, 2009 National Survey on Drug Use and Health (September 2010)



A Brief History of Pain Guidelines

- 1992 Agency for Health Care Policy and Research (AHCPR)
 - Acute Pain Management Guidelines
- 1997 American Society of Anesthesiologists and American Academy of Pain Medicine
 - Clinical guidelines for management of chronic pain
- 1998 Federation of State Medical Boards
 - Model Policy for the Use of Controlled Substances for the Treatment of Pain.
- Each of these guidelines emphasizes that doctors should be free to prescribe opiates <u>without worrying about sanctions</u>.



The Infamous Article

Cited by 1500+ scientific articles

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients' who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,² Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare inmedical patients with no history of addiction.

> JANE PORTER HERSHEL JICK, M.D. Boston Collaborative Drug Surveillance Program Boston University Medical Center

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Opioid Beliefs vs. Reality

Belief

- Sedating
- Good for all pain conditions
- Non-addicting if prescribed and monitored
- Pain is the 5th vital sign

Reality

- Activating after some period of time
- Indicated for acute but not chronic pain in most
- Rates of aberrant use in chronic prescribing 15-45%
- Pain is subjective and cannot be tested. However, functional restoration can be measured



Opioid Beliefs vs. Reality

Belief

- Improve Sleep Quality
- Impossible to stop once started
- Will get people back to work
- Nobody should take opioids because of risks

Reality

- Decrease sleep quality
- Majority of patients taper off opioids without problem
- Early use is associated with increased disability
- Majority of patients use opioid therapies responsibly and to good effect



Opioid Receptor Changes

- Chronic opioid exposure (addiction or therapeutic) causes brain changes
 - Opioid receptors increase
 - Brain stops producing enough endorphins and dopamine (manages pain and motivation)
 - Brain chemistry disrupted until chemicals are replaced or brain recovers
 - OUD is much like Type 2 Diabetes



Sleep Apnea

- Sleep Apnea is a dose dependent side effect of opioids
 - Overall prevalence 24%
 - Methadone Maintenance 30%
 - MME > 200 >90%
 - Benzodiazepines and hypnotics increase rate
- Can interrogate CPAP/BiPAP to establish adherence



Opioid-Induced Hyperalgesia

- Associated with long-term use of opioids
- Increasing sensitivity to noxious and benign stimuli
- Tolerance (loss of body's own pain control mechanisms) and opioid-induced hyperalgesia (sensitization of pain pathways) are separate phenomena but clinically similar
- Prevalence rates 15-35% in opioid treated chronic pain



Opioids and Disability

- >40% of people receiving SSDI are taking opioid pain medication
- >20% of people receiving SSDI are on chronic opioid prescriptions
- Depression rates of 38% in chronic opioid users



Morphine Equivalents

- High dose opioids
 - Morphine Milligram Equivalents (MME)
 - –>100 MME increases overdose deaths ninefold



Morphine Milligram Equivalents

Comparing opioids is like comparing cars. They will all get you from 0-60mph but at very different rates Calculating morphine milligram equivalents (MME)

OPIOID (doses in mg/day except where noted) **CONVERSION FACTOR** Codeine 0.15 Fentanyl transdermal (in mcg/hr) 2.4 Hydrocodone 1 Hydromorphone 4 Methadone 1-20 mg/day 4 8 21-40 mg/day 41-60 mg/day 10 ≥ 61-80 mg/day 12 Morphine 1 Oxycodone 1.5 Oxymorphone 3

These dose conversions are estimated and cannot account for all individual differences in genetics and pharmacokinetics.



How much is too much?

Low Risk		Moderate Risk		High Risk	
Morphine Milligram Equivalent		Morphine Milligram Equivalent		Morphine Milligram Equivalent	
(MME) < 50 mg/day		(MME) < 90 mg/day		(MME) ≥ 90 mg/day	
Morphine	< 50 mg/day	Morphine	< 90 mg/day	Morphine	≥ 90 mg/day
Hydrocodone	< 50 mg/day	Hydrocodone	< 90 mg/day	Hydrocodone	≥ 90 mg/day
Oxycodone	< 30 mg/day	Oxycodone	< 60 mg/day	Oxycodone	≥ 60 mg/day
Hydromorphone	< 12.5 mg/day	Hydromorphone	< 22.5 mg/day	Hydromorphone	≥ 22.5 mg/day
Oxymorphone	< 15 mg/day	Oxymorphone	< 30 mg/day	Oxymorphone	≥ 30 mg/day
Fentanyl patch	≤ 12 mcg/hr	Fentanyl patch	≤ 37 mcg/hr	Fentanyl patch	≥ 50 mcg/hr
			(25+12)		
Methadone	< 10 mg/day	Methadone	≤ 20 mg/day	Methadone	> 20 mg/day

**This is not intended to be used for dosing conversions from one opioid to another.



How much is too much?





Suffering Relief vs. Functional Restoration

- Suffering
 - State of being
 - Individual mindset
 - "Pain is inevitable, suffering is optional"
 - Easy to treat
 - Keep upping the dose of opioids

- Functional Restoration
 - Should be the goal of pain management
 - Acute pain may be "curable"
 - Chronic pain (lasting longer than 6 months) should be managed
 - Opioids poor choices for chronic non-cancer pain



Suffering Relief vs. Functional Restoration

- Large retrospective worker's comp claims study found:
 - 8443 claimants
 - 21% received at least one early opioid rx
 - Higher doses associated with avg. 69 more days disability
 - Risk for surgery 3x greater in high dose
 - Risk for continuing opioids 6x greater
 - 67% of patients using opioids for 90 days continue to use them long-term (>2 years)



Opioid Rx Regional Variability

Percentage of providers giving Opioid prescription in first 2 weeks after date of injury for simple back strain



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Prescription Drug Monitoring Programs (PDMP)

- The National All Schedules Prescription Electronic Reporting (NASPER) Act, was signed into law on August 11, 2005.
 - Authorized \$60 million to establish or improve state-run Prescription Drug Monitoring Programs (PDMP) which analyze prescription data
- PDMP can identify individuals, physicians, or pharmacies that have unusual patterns suggesting drug diversion, abuse, or doctor shopping
- Operational in 49 states, Guam, and Washington D.C.
 - Missouri only one without
- California requires PDMP query prior to prescribing controlled substances



Benzodiazepines

- Benzodiazepines
 - Sedative, anti-anxiety, sleep aid
 - Side effects: sedation, slowed reaction time, confusion, incoordination, dependence, addiction
 - Good evidence for:
 - Panic Disorder
 - Generalized Anxiety Disorder
 - Very limited evidence for
 - Posttraumatic Stress Disorder



Benzodiazepine Examples

- Short Acting (2-20 hours)
 - Lorazepam (Ativan), Alprazolam (Xanax)
- Intermediate Acting (10-30 hours)
 - Diazepam (Valium)
- Long Acting (30-100 hours)
 - Clonazepam (Klonopin)
- Very Long Acting
 - Flurazepam (Dalmane)



Benzodiazepines



Benzodiazepines and Opioids a Risky Combination

Opioid Overdose Deaths Involving Benzodiazepines



Opioid Risk Tool

Female	Male
1 2 4	3 3 4
3 4 5	3 4 5
1	1
3	0
2 1	2 1
	Female

*0-3 Low Risk *4-7 Moderate Risk *≥ 8 High Risk



Universal Precautions

- "At Risk" Definition varies
- Therefore:
 - Universal Precautions
 - Like HIV/HCV
- Assume universal risk
- Naloxone with all opioids
 - Don't need rx



49 CFR Part B.II.219.103

• §219.103 Prescribed and over-the-counter drugs.

(a) This subpart does not prohibit the use of a controlled substance (on Schedules II through V of the controlled substance list) prescribed or authorized by a medical practitioner, or possession incident to such use, if—

(1) The treating medical practitioner or a physician designated by the railroad has made a good faith judgment, with notice of the employee's assigned duties and on the basis of the available medical history, that use of the substance by the employee at the prescribed or authorized dosage level is consistent with the safe performance of the employee's duties;

(2) The substance is used at the dosage prescribed or authorized; and

(3) In the event the employee is being treated by more than one medical practitioner, at least one treating medical practitioner has been informed of all medications authorized or prescribed and has determined that use of the medications is consistent with the safe performance of the employee's duties (and the employee has observed any restrictions imposed with respect to use of the medications in combination).

(b) This subpart does not restrict any discretion available to the railroad to require that employees notify the railroad of therapeutic drug use or obtain prior approval for such use.



FRA Drug Testing

- Cannabis, cocaine, amphetamines, opiates, phencyclidine
- Post-Accident
 - Barbiturates
 - Benzodiazepines
- Companies can test for additional drugs



FRA Drug Testing Metabolic Pathways

Known metabolites

Pattern observed in patients receiving chronic opiate therapy



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FRA Drug Testing What's Missing?

- Z-drugs
 - Zolpidem (Ambien), Zaleplon (Sonata)
- Muscle Relaxants
 - SOMA, Baclofen, Flexeril
- Cannabinoid Receptor Analogues
 - Spice, K2
- Other sedating medications
 - Many
 - Antihistamines, gabapentinoids



FRA Drug Testing What's Missing?

- Opioids
 - Tests for morphine, codeine, and 6-MAM (heroin metabolite)
 - Medical Review Officer
 - Presence of a legitimate prescription will result in positive drug test being negative
- Recommendation
 - Routinely employ expanded drug testing panels



Opioid Use Disorder Treatment

- Medication Assisted Treatment (MAT) is gold standard
- Very good outcomes with:
 - Methadone Maintenance
 - Buprenorphine Maintenance
- Marginal evidence for Naltrexone (opioid blocker) both oral and injected
- Detoxification is of limited-long term efficacy and associated with risks (overdose)



Summary

- There are no "good" or "bad" medications
- Risks are dose dependent
- Treatment works!
- There are other drugs to be concerned about
 - Benzodiazepines
 - Muscle Relaxants
- Drug Testing
 - Consider expanded panels



THANK YOU!



QUESTIONS?



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