The Rising Tide of Prescription Opioid Use Disorders and Current Treatment Options

Michelle R. Lofwall, MD
UK Dept of Psychiatry
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Outline for Today’s Talk

• Past & current state of affairs
• Underlying principles of treatment
• Maintenance medications
Not a New Problem

- Abused 100’s of yrs
- Late 1800’s marked ↑ in use
  - Prescribed & OTC (no labels required)
- 1898 Heroin marketed as cough suppressant and non-addictive substance
- Pure Food and Drug Act 1906
- Harrison’s Narcotic Act 1914
  - Tx no longer in mainstream medicine
- Drug Abuse Treatment Act of 2000
  - Tx back into mainstream medicine
Opioids: Current state

- **Heroin**
  - Approximately 1 million heroin dependent

- **Prescription opioids (PO)**
  - NSDUH 2007: community dwelling age 12 & ↑
  - 0.5 million with PO abuse
  - 1.2 million with PO dependence

Opioid Abuse: DSM-IV Criteria (1+)
1. Failure to fulfill responsibilities
2. Using in physically hazardous situations
3. Legal problems
4. Social/interpersonal problems

Opioid Dependence: DSM-IV Criteria (3+)
1. Take larger amounts or use longer than intended
2. Cannot cut down
3. ↑ time spent to get, use and recover
4. Give up or ↓ other important parts of life
5. Ongoing use despite problems
6. Tolerance
7. Withdrawal
Number of NEW Nonmedical Users of Pain Relievers: 1965-2002

Thousands of New Users

- All Ages
- 18 & Older
- Under 18

Number of NEW Nonmedical Users of Psychotherapeutics: 1965-2000

Millions of New Users

- Pain relievers
- Tranquilizers
- Stimulants
- Sedatives

SAMHSA - National Household Survey Data
Number of NEW Nonmedical Users Ages 12 or Older: 2007

Nonmedical Use of Pain Relievers in Past Year Aged 12 or Older by Substate Region: 2002-2004
Appalachia Prescription Opioid Injection Drug Use

- Cross sectional study
- N = 184 adults in rural Appalachian Kentucky
- Inclusion criteria
  - self-reported use of any prescription opioid past 30 days (medical or non-medical)

Results

Sample of all non-medical users (n = 184)

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<tbody>
<tr>
<td>Female</td>
<td>45.1%</td>
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<tr>
<td>Caucasian</td>
<td>98.4%</td>
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<tr>
<td>Lifetime IDU of prescription opioids</td>
<td>44.3%</td>
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<tr>
<td>Current IDU of prescription opioids</td>
<td>15.0%</td>
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<tr>
<td>Hep C +</td>
<td>6.3%</td>
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Sample of only current IV prescription opioid users

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<tbody>
<tr>
<td>Hep C+</td>
<td>14.8%</td>
</tr>
<tr>
<td>Needle sharing</td>
<td>&gt;25%</td>
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<tr>
<td>Sharing works</td>
<td>42.1%</td>
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PO Dependence vs. Heroin Dependence

- PO more likely use oral & intranasal route
- Heroin more likely IV
  - Poor tx response associated with use by IV route
- 1 randomized study
  - Better tx outcomes with bup if PO than heroin
- Eastern KY
  - High rates of sharing works and IV drug use

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Principles of Opioid Dependence Treatment

- Addiction is chronic relapsing medical disorder
- The longer the treatment - the better the outcome
- Treatment works
- Treatment is more than just a medication
- Treatment is more than relieving/treating opioid withdrawal
  - Remember Lexington Narcotics Farm in 1950s – PHS
- Treatment must enter into mainstream treatment to meet current demand

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Maintenance Medications: 3 Types/3 Diff Axn

- Full opioid agonist
- Partial opioid agonist
- Opioid antagonist

Naltrexone: Mechanism of Action

- Opioid antagonist
  - Occupies mu-opioid opioid receptor AND does not activate it
- High affinity for this receptor
  - Block the effects of opioids (high efficacy) AND
  - Knock off other opioids with less affinity
- Preventative or “insurance” medication
- Start 7 days after no opioid
  - Target 50 mg daily
Naltrexone: Side Effects

- Opioid withdrawal symptoms
- Elevated liver function tests in package insert but typically in cases where supratherapeutic doses were given (>300mg/day) in studies for obesity and was more likely in older individuals
- Concerns about blockade of endogenous opioids and sequelae of depression have not been evident clinically

Naltrexone Pros/Cons

- **Pros**
  - No abuse ability
  - Any physician can prescribe
  - Helpful in highly motivated populations with something to lose

- **Cons**
  - Low acceptance in most patient populations
Methadone: History

• Methadone developed in 1940’s in Germany & used as alternative to morphine during WWII – “dolophine” – dolor – pain
• Dole & Nyswander at Rockefeller University in New York really demonstrated its effectiveness in treating opioid addiction in the 1960s
• Currently, regulated by federal, state and local levels
• Approximately 250,000 people in MMT (Strain, 2006)

Methadone: Mechanism of Action

• Long acting opioid agonist
• Occupies opioid receptor so difficult to get opioid agonist effects with continued illicit use (cross-tolerance)
• Schedule II
• Only methadone clinics can prescribe for addiction
Methadone Maintenance Programs

- Will fail if given as just a medication (stop and drops)
- Combination of pharmacological and nonpharmacological therapies

“Some people became overly converted. They felt, without reading our reports carefully, that all they had to do was give methadone and then there was no more problem with the addict...I urged physicians should see that the problem was one of rehabilitating people with a very complicated problem and that they ought to tailor their programs to the kinds of problems they were dealing with. The strength of the early programs as designed by Marie Nsywander was in their sensitivity to individual human problems. The stupidity of thinking that just giving methadone will solve a complicated social problem seems to me beyond comprehension (Courtwright, 1989, p 338).”

Vincent Dole

Methadone vs. Placebo

100 opioid abusers (Newman & Whitehill 1979)
Inpatient x 2 weeks – 60 mg meth

Methadone Detox by 1mg/day
32 weeks 32 weeks

76% in treatment 10% in treatment
Methadone Dose Matters

Methadone: Benefits

Methadone Maintenance
- Decreases spread of HIV and other infectious diseases
- Decreases violence, theft and property damage
- Improves access to health care and improved general health
- Improves psychological and social well-being
- Improves employment
- Improves childrearing
Methadone: Limitations

- Needs to be prescribed through a methadone maintenance clinic which is heavily regulated
- Comprehensive methadone treatment clinics have difficulty in making clinics financially viable and retaining staff
- Stigma – many patients refuse
- Large variability in methadone treatment programs
- Requires daily visits initially by patients and can be difficult to detox

Buprenorphine: History

- Initially used as an analgesic (in parenteral form - buprenex®)
- Been used in France for over a decade for opioid addiction
Buprenorphine: Mechanism of Action

- Partial agonist/antagonist at mu-opioid receptor
  - Schedule III, good safety profile
- Tight binding, low rate of dissociation
- If opioid is present
  - Bup may induce withdrawal because has high affinity for receptor, but won’t be as bad as naloxone-precipitated withdrawal
- If not opioid is present
  - Typical agonist effects but ceiling is present

Buprenorphine/Naloxone Sublingual Tablets

- US added naloxone (aka: suboxone vs. subutex) to decrease abuse potential of drug
- Two doses: 2/0.5 and 8/2 mg
- Naloxone poor sublingual and oral bioavailability but great IV bioavailability
Comparison of LAAM, Buprenorphine and Methadone for Opioid Dependence

- Enrolled 220 opioid-dependent patients
- Four-arm, flexible dosing, randomized, double-blind, triple-dummy, 17-week clinical trial

Methadone (20 mg po) daily
Methadone (60-100 mg po) daily
Buprenorphine (16 - 32 mg, sl) M-W-F
LAAM (75-115 mg, po) M-W-F


Study Retention

Opioid Positive Urine Specimens

Mean Frequency

Self-Reported Opiate Use

Buprenorphine Office-based Practice

- On-line course
- Special DEA ‘X’ number
- Learn to do it right/P
- DATA 2000 reviewed by Congress
- Continued availability of bup depends in part on physicians documentation & results from ongoing post-marketing studies on its abuse and diversion

Buprenorphine: Side Effects

- Elevated liver function tests
  - Increased slightly with hep C+ (Petry, 2000) but not significantly different compared to methadone maintenance (Lofwall, 2005)
- Opioid withdrawal-like symptoms
  - Insomnia, sweating, low energy, headache, nausea, constipation (Ling, 1998)
- Comparable side effect profile to methadone
Buprenorphine: Benefits

- Highly acceptable to patients
- Outpatient clinics so more anonymity and less intrusive to patients
- Increased access to treatment as long as physicians willing to treat
- Less abuse liability and diversion than methadone
- Similar treatment outcomes as 60 mg methadone
- Reinforcing medication that can easily use to shape other behaviors

Buprenorphine: Limitations

- Not enough treatment providers
- Medication is expensive
- No CLIA-waived buprenorphine test to ensure compliance with medication
Conclusions

• Rising, troublesome public health problem
• Improve screening, prescribe appropriate amounts
• Medical disorder deserving of treatment
• Treatment works
  – Spread the word
  – Destigmatize treatment
• Consider learning more and treating one person with prescription opioid dependence

Resources

www.samhsa.gov
TIP#40 Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction. DHHS Publication NO. (SMA) 04-3939
PCSS.org