Opioid Addiction: Hospital Presentations and Management

Richard Ries MD
rries@u.washington.edu
Harborview Medical Center and the University of Washington
Seattle, Washington

Len Paulozzi MD MPH
CDC Atlanta Georgia

Ries Conflict of Interest Statement
- Dr Ries is on Speaker’s bureaus for
  - Janssen, Reckitt-Benckiser, and Alkermes
- Dr Ries has Grant funding from:
  - NIH- NIDA-NIAAA
  - Contingency Management Alcohol in Mentally Ill
  - Brief Interventions of Drug Abuse in Prim Care
  - PTSD-- Exposure +/- Sertraline
  - CM for Alcohol in Native Am Indians
  - RCT of Injectable Naltrexone is Severe Alc
  - DOD- Suicide Prevention grant

Mary presents with serious multiple fractures after an auto crash

- 32 y o w female with history of minor traumas (twisted ankle, back spasms), ER scripts 2 years ago for 5 days of oxycodone
- Stabilized fractures of L femur and tibia, L wrist, abrasions, but post stabilization on standard opioid pain control, complains of pain, shows sweating, diarrhea, feels cold and shakes, blood pressure elevates
- Further info from family finds pt is prescribed oxycodone for chronic back pain, also xanax for anxiety, often appears sleepy, they think she might have a drug problem, and may be taking too much medication or maybe not as prescribed

Motor vehicle traffic, poisoning, and drug poisoning (overdose) death rates
United States, 1980-2010

Paulozzi - CDC NCHS Data Brief, December, 2011, Updated with 2009 and 2010 mortality data
Drug overdose deaths by major drug type, US, 1999-2010

- Opioids
- Heroin
- Cocaine
- Benzodiazepines

Oxycodone Involvement in Drug Abuse Deaths: A DAWN-Based Classification Scheme Applied to an Oxycodone Postmortem Database Containing Over 1000 Cases*

Authors: Cone E.J.; Fant R.V.; Rohay J.M.; Caplan Y.H.; Ballina M.; Reder R.F.; Spyker D.; Haddox J.D.

Of 1014 cases:
- 30 (3.3%) involved oxycodone as the single reported chemical entity; of these,
- The vast majority (N = 889, 96.7%) were multiple drug abuse deaths

The most prevalent drug combinations were oxycodone in combination with benzodiazepines, alcohol, cocaine, other narcotics, marijuana, or antidepressants.
Exhibit 2: Past Year Initiation of Non-Medical Use of Prescription-type Psychopharmaceutics, Age 12 or Older: In Thousands, 1965 to 2005

While Opiates have grown fastest, Benzos are not far behind

Source: SAMHSA, OAS, NSDUH data, July 2007

Benzo’s the Hidden Drug

• While there are hundreds of recent articles on Prescription Opiate problems-

• Most literature on Benzo Abuse/Dependence is > 10 years old

• Toxicology studies of Opiate deaths usually find Benzo’s too – respiratory depression is additive.

• Sales of Benzo’s are also increasing dramatically

• Simple Tox screens often miss Clon - and Alprazolam

Source Where Pain Relievers Were Obtained for Most Recent Nonmedical Use among Past Year Users Aged 12 or Older

<table>
<thead>
<tr>
<th>Characteristic Where Respondent Obtained</th>
<th>Pct.</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of substance abuse</td>
<td>78.3</td>
</tr>
<tr>
<td>Other mental illness</td>
<td>42.7</td>
</tr>
<tr>
<td>Nonmedical route of administration</td>
<td>22.4</td>
</tr>
<tr>
<td>Previous overdose</td>
<td>16.9</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Source Where Friend/Relative Obtained

<table>
<thead>
<tr>
<th>Characteristic Where Friend/Relative Obtained</th>
<th>Pct.</th>
</tr>
</thead>
<tbody>
<tr>
<td>One Doctor</td>
<td>80.7%</td>
</tr>
<tr>
<td>More than One Doctor</td>
<td>3.3%</td>
</tr>
<tr>
<td>Free from Friend/Relative</td>
<td>7.3%</td>
</tr>
<tr>
<td>Bought/Took from Friend/Relative</td>
<td>4.9%</td>
</tr>
<tr>
<td>Drug Dealer/Stranger</td>
<td>1.6%</td>
</tr>
<tr>
<td>Other</td>
<td>2.2%</td>
</tr>
</tbody>
</table>

Note: Totals may not sum to 100% because of rounding or because suppressed estimates are not shown.

1 The Other category includes the sources: “Wrote Fake Prescription,” “Stole from Doctor's Office/Clinic/Hospital/Pharmacy,” and “Some Other Way.”
Opioid Abstinence Syndrome

- Symptoms: craving, anxiety, irritability, restlessness, nervousness, insomnia, rhinorrhea, lacrimation, nausea, abdominal cramps, myalgias, arthralgias

- Signs: tachycardia, hypertension, mydriasis, piloerection, diaphoresis, tremor

- Depending on opioid abused, starts within 4-6 hours, full intensity at 24 to 72 hours, can last for 7-14 days—
  - Eg oxycodone vs methadone

- Though less medically dangerous than alcohol or BZP, appears to drive relapse to opioid use at much higher rate.

Clinical Opiate Withdrawal Scale (COWS) 1

- Resting Pulse Rate: (record beats per minute)
  - Measured after patient is sitting or lying for one minute
  - 0 pulse rate 80 or below
  - 1 pulse rate 81-100
  - 2 pulse rate 101-120
  - 4 pulse rate greater than 120

- Sweating: over past ½ hour not accounted for by room temperature or patient activity.
  - 0 no report of chills or flushing
  - 1 subjective report of chills or flushing
  - 2 flushed or observable moistness on face
  - 3 beads of sweat on brow or face
  - 4 sweat streaming off face

- Restlessness Observation during assessment
  - 0 able to sit still
  - 1 reports difficulty sitting still, but is able to do so
  - 3 frequent shifting or extraneous movements of legs/arms
  - 5 Unable to sit still for more than a few seconds

- Runny nose or tearing: Not accounted for by cold symptoms or allergies
  - 0 not present
  - 1 nasal stuffiness or unusually moist eyes
  - 2 nose running or tearing
  - 4 nose constantly running or tears streaming

COWS p2

- GI Upset: over last ½ hour
  - 0 no GI symptoms
  - 1 stomach cramps
  - 2 nausea or loose stool
  - 3 vomiting or diarrhea
  - 5 Multiple episodes of diarrhea or vomiting

- Tremor observation of outstretched hands
  - 0 No tremor
  - 1 tremor can be felt, but not observed
  - 2 slight tremor observable
  - 4 gross tremor or muscle twitching

- Yawning Observation during assessment
  - 0 no yawning
  - 1 yawning once or twice during assessment
  - 2 yawning three or more times during assessment
  - 4 yawning several times/minute

- Anxiety or Irritability
  - 0 none
  - 1 patient reports increasing irritability or anxiousness
  - 2 patient obviously irritable anxious
  - 4 patient so irritable or anxious that participation in the assessment is difficult

- Gooseflesh skin
  - 0 skin is smooth
  - 3 piloerection of skin can be felt or hairs standing up on arms
  - 5 prominent piloerection

- Total scores with observer’s initials
  - Score:
    - 5-12 = mild;
    - 13-24 = moderate;
    - 25-36 = moderately severe;
    - more than 36 = severe withdrawal

- Pupil size
  - 0 pupils pinned or normal size for room light
  - 1 pupils possibly larger than normal for room light
  - 2 pupils moderately dilated
  - 5 pupils so dilated that only the rim of the iris is visible

- Bone or Joint aches if patient was having pain previously, only the additional component attributed
  - to opiates withdrawal is scored
  - 0 not present
  - 1 mild diffuse discomfort
  - 2 patient reports severe diffuse aching of joints/muscles
  - 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort

- Gi Upset: over last ½ hour
  - 0 no GI symptoms
  - 1 stomach cramps
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Medically Supervised Opioid Withdrawal

- Methadone substitution and taper - not advised

- Clonidine
  - α-2 adrenergic agonist
  - Acts on autoreceptors in locus coeruleus to decrease noradrenergic output
  - Major side effect hypotension
  - Push dose until withdrawal sx abate or diastolic BP <60
  - Use adjunctive benzodiazepines, anti-emetics, antidiarrheals

- Buprenorphine

Key Medications in Acute Opioid Withdrawal

- Buprenorphine/Naltrexone
  - 16 mg x 1
  - 16 mg, 8 mg, 4 mg
  - 16 mg maintenance to outpt

- Sedation
  - Gabapentin 400 tid – 800 tid esp if BZPs involved
  - Mirtazapine 7.5 or 14 mg (more is less sedative)
  - Tizanidine to 4-12 mg tid (muscle spasm and sedation)
  - Quetiapine 200 - 400 HS esp if agitated/psychotic
  - Olazapine 10 mg hs

- Autonomic stabilization
  - Clonidine .1 tid to 1 mg tid over time
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Opioids + Benzos

- Short acting Opioid and Long acting Benzo (Clonazepam or Diazepam)
- Classic opioid WD, migrating to hyperadrenergic autonomic + anxiety and possible seizures
- Though not published, using combination of Bup + anticonvulsant covers this
  - Gabapentin 400 tid, or 600 tid helps both

For those with Severe Opioid Dependence ----Withdrawal only (Detox) ---vs. Maintenance vs ----Block ?

- Withdrawal Only—
  - High Relapse (90+ %) whether fast or slow Detox
  - Relapse incurred Morbidity, Mortality, Cost
  - Not only costly, but ethical?

- Maintenance
  - Bup/Ntx- Training certification fits ACO Prim Care
  - Methadone--- only in Federally certified clinics

- Block – Naltrexone
  - Oral– adherence issues, but OK after long term stabilization
  - Injectable– fits in with “abstinence model”, good at inpt DC

Treatment Retention and more…

Remainig in treatment (nr)

75% retention
75% UTS negative
20% mortality in placebo group
Loss of tolerance and overdose mortality after inpatient opiate detoxification: follow up study.

Strang J, McCambridge J, Best D, Beswick T, Bearn J, Rees S, Gossop M.

Mortality following release from prison.

Harding-Pink D.

Author information

Abstract

. The mortality rate during the first year after release was about 5 deaths/1000 person years, a rate over four times the age-adjusted rate in the general population. The majority of deaths were due to overdose by opiate drugs among young, frequently imprisoned drug abusers, and occurred within the first few weeks after release.

Best Treatment by FAR---

• Prevention -- Prevention – Prevention
• Avoid Opioids in most non-severe syndromes
• Use Opioids like Steroids…aggressively with built in short taper for most acute cases
• The US uses more presc opioids than most of the rest of the world combined

Early opioid prescription and subsequent disability among workers with back injuries: the Disability Risk Identification Study Cohort.

Franklin GM1, Stover BD, Turner JA, Fulton-Kehoe D, Wickizer TM; Disability Risk

- To examine whether prescription of opioids within 6 weeks of low back injury is associated with work disability at 1 year.
- Nearly 14% (254 of 1843) of the sample were receiving work disability
- After adjustment for pain, function, injury severity, and other baseline covariates, receipt of opioids for more than 7 days (odds ratio = 2.2; 95% confidence interval, 1.5-3.1) and receipt of more than 1 opioid prescription were associated significantly with work disability at 1 year.

• CONCLUSION:
• Prescription of opioids for more than 7 days for workers with acute back injuries is a risk factor for long-term disability. Further research is needed to elucidate this association.
Outcomes: Buprenorphine, Methadone, LAAM: Treatment Retention

- 73% Hi Meth
- 58% Bup
- 53% LAAM
- 20% Lo Meth

Study Week

Naltrexone for Opioid Dependence

- Most ideal pharmacologic treatment
- Requires complete withdrawal before initiation or severe withdrawal will be precipitated
- Requires Naloxone challenge test
- Risk of OD if medication stopped
- In general poor patient compliance with oral form but superb treatment for selected patients
- Now available in long acting injection
Injectable Extended-release Naltrexone for Opioid Dependence: a Double-blind, Placebo-controlled, Multicentre Randomised Trial.

Krupitsky E, Nunes EV, Ling W, Illeperuma A, Gastfriend DR, Silverman BL.

FINDINGS:
6 month study of 250 patients randomly assigned to XR-NTX (n=126) or placebo (n=124).

<table>
<thead>
<tr>
<th></th>
<th>XR-NTX</th>
<th>Placebo Inj</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Weeks abstinent</td>
<td>90.0%</td>
<td>35.0%</td>
</tr>
<tr>
<td>Opioid-free days</td>
<td>99.2%</td>
<td>60.4%</td>
</tr>
<tr>
<td>Decreased craving</td>
<td>-10.1%</td>
<td>-0.7%</td>
</tr>
<tr>
<td>Retention days</td>
<td>168</td>
<td>96 days</td>
</tr>
</tbody>
</table>

Two patients in each group discontinued owing to adverse events. No XR-NTX-treated patients died, overdosed, or discontinued owing to severe adverse events.

12 step facilitation ...is a method to help get patients to 12 step meetings and maximize their benefit

- Why get people to 12 step meetings?
  - 20-50% of trauma (med-surg) and psychiatric in and outpts will have current, history or episodic substance problems

- Substance treatment may be unavailable or even if used, 12 step will likely be involved

- Positive effects include not only the group support and socialization, but key psychological/therapeutic content elements.

- Addiction is a chronic potentially relapsing disease....Usual TREATMENT is not usually structured for this BUT AA is

Alcohol Abstinence Rates at 8 Years by Duration of Meeting Attendance in the First Year

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  - The USA uses more presc opioids than most of the rest of the world combined
Your Case Examples:

- 1.
- 2.
- 3.