Opioids for Chronic, Non, Cancer Pain

- Most state regulations changed (1998 for WA) from prohibition of use to use without dosing guidance
- Change in policy most likely due to 1) low grade studies (eg, Portenoy) supporting rarity of true addiction, 2) advocacy Re under treatment, 3) disciplinary fatigue
Portenoy and Foley
Pain 1986; 25: 171-186

- Retrospective case series chronic, non-cancer pain
- N=38; 19 Rx for at least 4 years
- 2/3 < 20 mg MED/day; 4> 40 mg MED/day
- 24/38 acceptable pain relief
- No gain in social function or employment could be documented
- Concluded: “Opioid maintenance therapy can be a safe, salutary and more humane alternative…”
Workers’ Comp Guidelines-2000
Principles for Prescribing Oral Opioids

- Single prescribing physician
- Single pharmacy
- Lowest possible dose
- Appearance of misuse of medications
- RTW emphasis
- Track pain and function
- No concomitant use of benzodiazepines or sedative-hypnotics
“I understand that this doctor may stop prescribing opioids or change the treatment plan if:

A. I do not show any improvement in pain from opioids or my physical activity has not improved.
B. My behavior is inconsistent with the responsibilities outlined in #1 above.
C. I give, sell or misuse the opioid medications.
D. I develop rapid tolerance or loss of improvement from the treatment

Also includes permission to conduct random urine drug screen
Earliest report of prescription-opioid related deaths


Washington Workers’ Compensation Opioid-related Deaths, 1995-2002
WA Workers' Compensation Opioid-related Deaths 1995-2007

Opioid-related Death

- Definite
- Probable
- Possible

Years:
- 1995
- 1996
- 1997
- 1998
- 1999
- 2000
- 2001
- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
Figure 1: Yearly Trend of Scheduled Opioids in WA
Figure 3: Trend of Schedule II Opioids
Morphine Equivalent Dose

Average MED (mg/day)
Prescription Opiate Deaths

Number of deaths

0 100 200 300 400 500 600


Definite  Possible
Hospitalizations for Prescription Opiate Overdose, WA 1987-2007

- Total
- Overdose in Primary Diagnosis
- Accidental Poison Ecode Present
- Alcohol Diagnosis Present
- Abuse or Dependence Diagnosis Present
Table 4. Most Frequent Suspect Drugs in Death and Serious Nonfatal Outcomes, 1998-2005

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Rank/Deaths</th>
<th>Drug Class</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Death outcome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>1/5548</td>
<td>Opioid analgesic</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>2/3545</td>
<td>Opioid analgesic</td>
</tr>
<tr>
<td>Clozapine</td>
<td>3/3277</td>
<td>Antipsychotic</td>
</tr>
<tr>
<td>Morphine</td>
<td>4/1616</td>
<td>Opioid analgesic</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>5/1393</td>
<td>Analgesic</td>
</tr>
<tr>
<td>Methadone</td>
<td>6/1258</td>
<td>Opioid analgesic</td>
</tr>
<tr>
<td>Infliximab</td>
<td>7/1228</td>
<td>DMARD</td>
</tr>
<tr>
<td>Interferon beta</td>
<td>8/1178</td>
<td>Immunomodulator</td>
</tr>
<tr>
<td>Risperidone</td>
<td>9/1093</td>
<td>Antipsychotic</td>
</tr>
<tr>
<td>Etanercept</td>
<td>10/1034</td>
<td>DMARD</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>11/1033</td>
<td>Antineoplastic</td>
</tr>
<tr>
<td>Acetaminophen-hydrocodone</td>
<td>12/1032</td>
<td>Combination analgesic</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>13/1005</td>
<td>Antipsychotic</td>
</tr>
<tr>
<td>Rofecoxib</td>
<td>14/932</td>
<td>NSAID</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>15/850</td>
<td>Antidepressant</td>
</tr>
</tbody>
</table>
What’s Causing the Deaths?
My Opinion

- Dramatically increasing avg daily doses not proven to be associated with improved outcomes, and are most likely related to increased tolerance
- Tolerance for euphoric effects likely precedes tolerance for respiratory depression
Central sleep apnea and ataxic breathing related to chronic opioid use

  - Retrospective cohort
  - N=60 on chronic opioids matched to N=60 not on opioids by age, sex and BMI
  - Dose response between opioid MED and apnea/hypopnea, obstructive apnea, hypopnea, and central apnea indices
  - 92% prevalence of ataxic or irregular breathing during NREM sleep at ≥ 200 mg MED
Newly submitted study

- 9000 enrollees large pre-paid health plan on opioids at least 3 months
- Dramatic increase (24 fold) in risk of combined morbidity/mortality at 100 mg/day MED
What’s causing the deaths?
A CDC opinion

“It has been difficult to determine the extent to which increases in opioid-related deaths have been due to specific prescribing practices, improper taking of the medication by patients, diversion of the drug from the patient to someone else, or other means”.

Fingerhut, CDC, 2008
More often accidental deaths involving opioid analgesics are due to abuse or misuse of opioids and not due to the therapeutic use of opioids for chronic pain.
Narcotic Maker Guilty of Deceit Over Marketing

“Pleaded guilty …to criminal charges…”
“Purdue Pharma agreed to pay $600 million in fines..”
“…misled doctors and patients when it claimed the drug was less likely to be abused than traditional narcotics.”
“Overall, the evidence supporting long-term analgesic efficacy is weak”

“The putative mechanisms for failed opioid analgesia may be related to (rampant) tolerance or opioid-induced hyperalgesia”

“The premise that tolerance can always be overcome by dose escalation is now questioned.”
Ballantyne, cont’d
Re: longer term clinical trials

• Good results from case series, but..
• “A review of the open-label follow-up studies (from RCTs), however, has shown that 56% of patients abandon the treatment because of lack of efficacy or side-effects.”
• Many trials use ‘enrichment”-select out non-responders pre-trial
Ballantyne: Re: effect on function and QOL

- “Epidemiological studies are less positive, and report failure of opioids to improve QOL in chronic pain patients.”
  - “…it is remarkable that opioid treatment of long-term/chronic non-cancer pain does not seem to fulfill any of the key outcome opioid treatment goals: pain relief, improved quality of life and improved functional capacity.”
No clear case definition—true incidence unknown (addiction > craving)

“After a decade or more of acceptance that therapeutic opioid use was unlikely to result in addiction (5%)... A systematic review published in 1992 (Fishbain et al, Clin J Pain 1992; 8: 77-85) reporting addiction rates of up to 18.9% failed to penetrate... educational materials...”
Agency Medical Director’s Opioid Dosing Guideline

- http://www-dev.agencymeddirectors.wa.gov/opioiddosing.asp#CME

- http://www-dev.agencymeddirectors.wa.gov
AMDG Opioid Dosing Guideline

- Developed during 2006 by 15 clinical pain specialists in collaboration with the AMDG
- It is an Educational Pilot
- We will conduct formal evaluation of impact during Spring-Summer, 2008
- Plan to reconvene clinical group Fall, 2008 to review evaluation and plan next steps
Opioid Dosing Guideline

- **Part I** - If patient has not had clear improvement in pain AND function at 120 mg MED, “take a deep breath” if needed, get one time pain management consultation (certified in pain, Neuro, Physiatry)
- **Part II** - guidance for patients already on very high doses above 120 mg MED
Other Important Considerations

- May want to use urine tox screen
- Are there other important comorbid issues—e.g., past history substance abuse, **current smoking**
Innovations

- Opioid dosing calculator for MED
- 2 HRs free online CME (Category I)
- Educational pilot, not a new standard or regulation
# Opioid Dose Calculator

**Optional:**
- **Patient name:**
- **Today's date:** October 9, 2007

**Instructions:**
Fill in the mg per day* for whichever opioids your patient is taking. The spreadsheet will automatically calculate the total morphine equivalents per day.

<table>
<thead>
<tr>
<th>Opioid (oral or transdermal)</th>
<th>mg per day*</th>
<th>Morphine equivalents</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>fentanyl transdermal (in mcg/hr)</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>hydrocodone</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>hydromorphone</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>methadone</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>up to 20mg per day</td>
<td></td>
<td>0</td>
</tr>
</tbody>
</table>

**21 to 40mg per day**
Since doses at or below 40mg per day are below the threshold for pain management consultation, no opioid conversion calculations are necessary for this dosing range (assuming no other opioids are being taken).

<table>
<thead>
<tr>
<th>mg per day</th>
<th>Morphine equivalents</th>
</tr>
</thead>
<tbody>
<tr>
<td>41 to 60mg per day</td>
<td>0</td>
</tr>
<tr>
<td>&gt;80mg per day</td>
<td>0</td>
</tr>
<tr>
<td>morphine</td>
<td>0</td>
</tr>
<tr>
<td>oxycodone</td>
<td>0</td>
</tr>
<tr>
<td>oxymorphone</td>
<td>0</td>
</tr>
</tbody>
</table>

**TOTAL daily morphine equivalent dose (MED) =** 0

*Note: All doses expressed in mg per day with exception of fentanyl transdermal, which is expressed in mcg per hour*
Opioid Dosing Guideline Evaluation

- Subgroup of expert clinicians will advise evaluation
- Preliminary eval ideas:
  - Degree of diffusion, including geographic distribution of "hits" on website
  - Survey of primary care physicians to determine acceptability and utility of guideline
  - Opioid dosing patterns
  - Deaths
AMDG – Opioid Dosing Guideline

Gdline Downloads
What’s next?

- The AMDG opioid dosing guidelines are an educational pilot, not a new standard
- By March, 2009, evaluation of guideline implementation completed
- Reconvene pain expert advisory group
New Guidelines—will they help?

- **Utah**
  - Requested by statute
  - Great tools, e.g., screening instruments for past substance abuse
  - No specific recommendation on dose-risk/benefit may be problematic at or above 120-200 mg/day

- **APS/AAPM—In press**
  - Evidence-based guidelines
  - High dose Rx at or above 200 mg/day MED
Must solve access problem

- Only 13 certified (pain) specialists agreed to be “go to” consultants on the AMDG website.
- Not a single pain specialist in Spokane willing to see the “120” patients with chronic pain.
- Heat on this point (When is a pain doctor a drug pusher? Tina Rosenberg, NYT Sunday Magazine, June 17, 2007).
- Considering advanced training for primary care docs to become qualified to mentor each other.
- Have successfully “beta tested” telemedicine consults with pain specialists and primary care MDs.
Proposed Prevention Measures-CDC Congressional Testimony-3/11/08

- Get the most out of state prescription drug monitoring programs
- Modify patient behavior with insurance mechanisms
- Screen for drug misuse in EDs
- Provide practice guidelines for primary care
- Make painkillers tamper resistant
Conclusions

- Dramatically increasing doses and deaths occurred rather quickly after law changes
- Guidelines with “best practices” have been around for years with little effect
- Focus on dosing is most likely method to prevent high doses associated with severe morbidity and mortality
Early opioids and disability in WA WC

Spine 2008; 33: 199-204

- Population-based, prospective cohort
- N=1843 workers with acute low back injury and at least 4 days lost time
- Baseline interview within 18 days (median)
- 14% on disability at one year
- Receipt of opioids for > 7 days, at least 2 Rxs, or > 150 mg MED doubled risk of 1 year disability, after adjustment for pain, function, injury severity
THANK YOU!

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