Pain Management and Practice

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Pain Treatment Today

- Wherever pain is treated, a market can be expected to grow vying for access to controlled substances for misuse.

- All pain management in our society goes on against a backdrop of addiction, diversion and misuse.

- All stakeholders (practitioners, patients, regulators, insurance companies, pharmaceutical companies) need to develop realistic strategies for the use of pain medicines in a drug abusing world.
New* Illicit Drug Use in the US: 2006

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Numbers in thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain relievers</td>
<td>2150</td>
</tr>
<tr>
<td>Marijuana</td>
<td>2063</td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>1112</td>
</tr>
<tr>
<td>Cocaine</td>
<td>977</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>860</td>
</tr>
<tr>
<td>Stimulants</td>
<td>845</td>
</tr>
<tr>
<td>Inhalants</td>
<td>783</td>
</tr>
<tr>
<td>Sedatives</td>
<td>267</td>
</tr>
<tr>
<td>LSD</td>
<td>264</td>
</tr>
<tr>
<td>Heroin</td>
<td>91</td>
</tr>
<tr>
<td>Phencyclidine</td>
<td>69</td>
</tr>
</tbody>
</table>

*Past-yr initiates for specific illicit drugs among persons aged ≥12 yrs

Responsibility of Healthcare Providers

- **Acknowledge**: Rx drug abuse is real – not isolated or purely media hype
- **Evaluate**: Conduct medical evaluation + risk hx before starting opioids
- **Recognize limitations**: Available time, psychiatric expertise, setting, resources, etc.
- **Obtain**: Consultations as needed
- **Employ**: Rational pharmacotherapy
- **Comply**: with state/federal guidelines
The Pendulum Rarely Stops in the Middle

Avoidance
- “Will not prescribe opioids for any reason”
- Driven by fear of regulatory action or being “burned”

Balance
- Rational pharmacology
- Driven by continued prescribing with close monitoring

Widespread Use
- “Less than 1% will ever become addicted”
- Prescribing without recognition of dangers
Embracing Common Definitions

- Tolerance
- Physical Dependence
- Pseudoaddiction
- Substance Abuse
- Addiction
Identifying Addiction – The 4 C’s

- **C**ontinued use of drug despite harm
- Loss of **C**ontrol re: taking the drug
- **C**ompulsive use of the drug
- **C**ravings for the drug

**Note**: Tolerance and physical dependence do not play a defining role.
Protecting Medical Practice
Documentation

Poor documentation is a stumbling block to good pain management:

- Review of 520 randomly selected visits at an outpatient oncology practice:
  - quantitative assessment of pain scores was virtually absent (<1%)
  - qualitative assessment of pain occurred in only 60% of cases (Rhodes, et al, 2001)

- Review of medical records of 111 randomly selected patients who underwent urine toxicology screens in a cancer center:
  - documentation was infrequent: 37.8% of physicians failed to list a reason for the test
  - 89% of the charts did not include the results of the test (Passik et al, 2000)
Screening Tools

A Rational First Step for Safety
Assessment of Addiction Risk

- **Measures for Screening for Addiction Risk**
  - STAR/SISAP
  - CAGE AID
  - Opioid Risk Tool (Emerging Solutions in Pain)
  - SOAPP (see painedu.org)

- **Psychiatric Interview Assessment of Risk**
  - Chemical
  - Psychiatric
  - Social/Familial
  - Genetic
  - Spiritual
Screening Instruments

- Several clinical tools are available that estimate risk of noncompliant opioid use\(^1,^2,^3\)

- The results determine how closely a patient should be monitored during the course of opioid therapy\(^3\)
  - *Scores implying a high risk of abuse are not reasons to deny pain relief*\(^3\)

Opioid Risk Tool (ORT)

Mark each box that applies:    

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Family history of substance abuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2. Personal history of substance abuse</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Alcohol</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>3. Age (mark box if between 16-45 years)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4. History of preadolescent sexual abuse</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>5. Psychological disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADO, OCD, bipolar, schizophrenia</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Scoring totals: __________    __________

Administration

- On initial visit
- Prior to opioid therapy

Scoring

- 0-3: low risk (6%)
- 4-7: moderate risk (28%)
- > 8: high risk (> 90%)

## Screening Instrument for Substance Abuse Potential (SISAP)

<table>
<thead>
<tr>
<th>Question</th>
<th>Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) How many alcoholic drinks/day?</td>
<td>Men: ≥ 5 drinks/day or ≥ 17/wk</td>
</tr>
<tr>
<td>2) How many alcoholic drinks/week?</td>
<td>Women: ≥ 4 drinks/day or ≥ 13/wk</td>
</tr>
<tr>
<td>3) Use of marijuana/hashish in last year?</td>
<td>Admission of recent use</td>
</tr>
<tr>
<td>4) Have you ever smoked cigarettes?</td>
<td>Persons who are younger than 40 years and smoke</td>
</tr>
<tr>
<td>5) What is your age?</td>
<td></td>
</tr>
</tbody>
</table>

Screener and Opioid Assessment for Patients in Pain (SOAPP)

- 14-item, self-administered form, capturing the primary determinants of aberrant drug-related behavior
  - Validated over a 6-month period in 175 chronic pain patients
  - Adequate sensitivity and selectivity
  - May not be representative of all patient groups
- A score of $\geq 7$ identifies 91% of patients who are high risk

Ongoing Assessment Tool

Or: What Elements Should Be Documented on a Consistent Basis?
Documentation: The 4 A’s

- Analgesia (pain relief)
- Activities of Daily Living (psychosocial functioning)
- Adverse effects (side effects)
- Aberrant drug taking (addiction related outcomes)

Passik and Weinreb, 1998; Passik, Kirsh et al, 2004; 2005
### Analgesia

If zero indicates "no pain" and ten indicates "pain as bad as it can be," on a scale of 0 to 10, what is your level of pain for the following questions?

1. What was your pain level on average during the past week? (Please circle the appropriate number)

<table>
<thead>
<tr>
<th>No Pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Pain as bad as it can be</th>
</tr>
</thead>
</table>

2. What was your pain level at its worst during the past week?

<table>
<thead>
<tr>
<th>No Pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>Pain as bad as it can be</th>
</tr>
</thead>
</table>

3. What percentage of your pain has been relieved during the past week? (Write in a percentage between 0% and 100%) ____________

4. Is the amount of pain relief you are now obtaining from your current pain relievers enough to make a real difference in your life?
   - Yes
   - No

5. **Query to clinician:** Is the patient's pain relief clinically significant?
   - Yes
   - No
   - Unsure
# Activities of Daily Living

Please indicate whether the patient’s functioning with the current pain reliever(s) is Better, the Same, or Worse since the patient’s last assessment with the PADT.* (Please check the box for Better, Same, or Worse for each item below.)

<table>
<thead>
<tr>
<th>Item</th>
<th>Better</th>
<th>Same</th>
<th>Worse</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Physical functioning</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>2. Family relationships</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>3. Social relationships</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>4. Mood</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>5. Sleep patterns</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>6. Overall functioning</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

* If the patient is receiving his or her first PADT assessment, the clinician should compare the patient’s functional status with other reports from the last office visit.
### Adverse Events

1. Is patient experiencing any side effects from current pain relievers?  
   - Yes  
   - No

**Ask patient** about potential side effects:

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Nausea</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Vomiting</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Constipation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Itching</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Mental cloudiness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Sweating</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Fatigue</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h. Drowsiness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>j. Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Patient's overall severity of side effects?  
   - None  
   - Mild  
   - Moderate  
   - Severe
### Potential Aberrant Drug-Related Behavior

*Please check any of the following items that you discovered during your interactions with the patient.*  
Please note that some of these are directly observable (e.g., appears intoxicated), while others may require more active listening and/or probing. Use the “Assessment” section below to note additional details.

- Purposeful over-sedation
- Negative mood change
- Appears intoxicated
- Increasingly unkempt or impaired
- Involvement in car or other accident
- Requests frequent early renewals
- Increased dose without authorization
- Reports lost or stolen prescriptions
- Attempts to obtain prescriptions from other doctors
- Changes route of administration
- Uses pain medication in response to situational stressor
- Insists on certain medications by name
- Contact with street drug culture
- Abusing alcohol or illicit drugs
- Hoarding (i.e., stockpiling) of medication
- Arrested by police
- Victim of abuse

Other:

- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
- [ ]
Classifying Assessment Findings

Or: Does Every Problem Indicate Addiction?
Addiction or Something Else?

- Most research on addiction has focused on:
  - Prediction,
  - Assessment,
  - Treatment of substance use disorders

- A vast grey area exists between extremes of compliance (beneficial opioid therapy) and addiction (harmful opioid therapy)

- Patients in this grey area are
  - Not likely to display aberrant behaviors that rise to the level of compulsivity or loss of control
  - Not likely to be driven by cravings in a fashion that would make a clinician concerned about addiction.

Bottlender & Soyka, 2005; Comfort et al, 2003; Dekel et al, 2004; Schuckit et al, 2005
Population of Rx Opioid Users Is Heterogeneous

- "Addicted" (SUD)
- "Substance abusers"
- "Recreational users"
- "Self-Treaters"
- "Adherent"
- "Chemical copers"
- "Substance abusers"
- "Addicted" (SUD)

Nonmedical Users

Pain Patients
Differential Diagnosis of Aberrant Drug-Taking Attitudes and Behavior

- Addiction
- Pseudoaddiction (inadequate analgesia)
- Chemical Copers
- Other psychiatric diagnosis
  - Encephalopathy
  - Borderline personality disorder
  - Depression
  - Anxiety
- Criminal Intent

(Passik & Portenoy 1996)
Management Issues Past Screening
Management of Risk Is a “Package Deal”

- Screening & risk stratification
- Use of PMP data
- Compliance monitoring
  - Urine screening
  - Pill/patch counts
- Education regarding drug storage & sharing
- Psychotherapy & highly “structured” approaches
- Abuse-deterrent formulations
Opioid Prescribing: In & Out of the Box

Dose <180 mg MSO₄ equivalents daily
- Cancer & perioperative pain
- Lack of active psych or substance abuse
- Limited contact with nonmedical users

Pain syndrome in which opioid use controversial

Dose >180 mg MSO₄ equivalents daily
- Active psych disorder or substance abuse
- Contact with nonmedical users
- Younger age

Older age
Methadone Focus

- **History:**
  - Discovered 1938 Hoechst-Am-Main in Germany
    - Question if developed as anti-spasm or analgesic medication
    - Patent 1942
  - Developed after WWII during occupation
    - Eli-Lilly produced Dolophine®
      - “Dolor” for pain, “fin” for end
  - Name derivation:
    - 6-Dimethylamino-4, 4-diphenyl-3-heptanone
Dr. Max Beckmann und Dr. Gustav Ehret in Frankfurt, Main-Höchst sind als Erfinder genannt worden.

I. C. Farbenindustrie Akt.-Ges. in Frankfurt, Main
Verfahren zur Darstellung von basischen Estern


Prinzipien
1. Zwei 4.5 g Salzsäurewasser, die aufgenommen werden, werden in 60 g Wasser gelöst, das mit 30 g Eis und 20 g Natronlauge versetzt wird. Die Lösung wird unter Rühren mit einem Gasmischer durch eine Mischung von 10 g Dehydrat und 100 g Chlorhydrat erwärmt. Die Temperatur wird durch Kühlen oder Anheizen der Lösung der gewünschten Stufe entsprechend angepasst.

2. Das Erhitzen wird so lange fortgesetzt, bis die gesamte Masse in Lösung geht.
• Trade name “Physeptone” for methadone branded under Wellcome company in United Kingdom

• Rec’d for pain and cough, even studied in infants (studies stopped due to respiratory depression in babies)

• Believed to have no addiction risk
Methadone

- **Pharmacokinetics:**
  - Extensive peripheral tissue distribution
  - Racine mixture: RS-methadone
    - R enantiomer opioid activity
    - S enantiomer, NMDA antagonist (weak to moderate), potent inhibitor of 5-
      hydroxytryptamine and norepinephrine uptake
  - Half life = 17-128 hours, average 36 hours
    - Analgesic half-life is much less
Methadone

- **Conversion**:  
  - “No universally safe or effective conversion ration or method currently exists, and because of the large variability in opioid ratios, it is not possible to derive a simple conversion method for rotating to or from methadone” *(Weschules, 2008)*

- Not good for immediate release usage

- Cheap, effective analgesic
  - Must know drug well to use it!
## Opioid Preference and Cost

Number of Instances of Abuse of Specific Drugs Preferred by Addicts, Where the Drug was Obtained, and Cost per Opioid.

<table>
<thead>
<tr>
<th>Opioid:*</th>
<th># of Instances of Abuse (of n = 109):</th>
<th>Purchased from street dealer??</th>
<th>Amount of $ per mg/mcg (mean/range):</th>
</tr>
</thead>
<tbody>
<tr>
<td>OxyContin</td>
<td>65 (60%)</td>
<td>62 (95%)</td>
<td>$1.01/mg (.50-1.50/mg)</td>
</tr>
<tr>
<td>Lortab</td>
<td>40 (37%)</td>
<td>37 (93 %)</td>
<td>$0.82/mg (.50-1.20/mg)</td>
</tr>
<tr>
<td>Percocet</td>
<td>15 (14%)</td>
<td>15 (100%)</td>
<td>$1.11/mg (.20-1.60/mg)</td>
</tr>
<tr>
<td>Methadone</td>
<td>7 (6%)</td>
<td>6 (85%)</td>
<td>$1.05/mg (.80-1.50/mg)</td>
</tr>
<tr>
<td>Morphine</td>
<td>4 (4%)</td>
<td>3 (75%)</td>
<td>$0.73/mg (.25-1.50/mg)</td>
</tr>
<tr>
<td>Lorcoret</td>
<td>3 (3%)</td>
<td>2 (67%)</td>
<td>$0.77/mg (.60-.90/mg)</td>
</tr>
<tr>
<td>Duragesic</td>
<td>3 (3%)</td>
<td>2 (67%)</td>
<td>$0.90/mcg (.80-1.00/mcg)</td>
</tr>
<tr>
<td>Dilaudid</td>
<td>2 (2%)</td>
<td>2 (100%)</td>
<td>$10.00/mg (7.50-12.50/mg)</td>
</tr>
<tr>
<td>Vicodin</td>
<td>1 (1%)</td>
<td>1 (%)</td>
<td>$0.06/mg</td>
</tr>
<tr>
<td>Tylenol #3</td>
<td>1 (1%)</td>
<td>1 (%)</td>
<td>$0.03/mg</td>
</tr>
</tbody>
</table>

* Drug listed as reported by patients (trade names reported when they were specified)

** At least once

Future Horizons

Can Pain Management Be Made ‘Safer’?
Abuse Deterrent Formulation: Questions

- Requirements for “reduced abuse liability” label claim
  - Bioequivalence to existing product?
  - Short-term evaluation of therapeutic efficacy?
  - Long-term studies in susceptible populations?
  - Acceptable risk?

- How much does the barrier approach deter the determined?

- How much do agonist/antagonist compounds retain efficacy & pose serious adversity?

- Will it be possible to retain titratable or rapid onset properties required for some analgesic needs?
Conclusion

- Pain management is under intense scrutiny
- However, chronic pain is still under-treated in this country
- We must use standards of good practice
  - documentation, rational prescribing, opioid agreements, urine screens, etc. to protect ourselves and our patients
  - A growing number of screening tools are becoming available, but more work needs to be done
  - We must not be afraid to ask the difficult questions of our patients about their lives, loved ones, and social circles.