PAIN MANAGEMENT

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OBJECTIVE

Geek

• A performer often billed as a wild man
  whose act usually includes biting off the
  head of a live chicken or snake (Merriam Webster’s
  Dictionary 10th Edition)

THE PROBLEM

• 116 million Americans suffer chronic/persistent pain (Institute of Medicine’s Committee on Advancing Pain Research publication “Relieving Pain in America” 2011)
  - Direct medical costs AND loss of productivity - $560 – 635 billion per year
  - Conflicting problems of untreated pain AND opioid abuse ADDS to this overall cost
• Morbidity secondary to pain twofold greater in patients over 60
• Seen in 40-85% of patients in long term care facilities
• One month before death, 66% report pain frequently or all the time
• In chronic/persistent non-cancer patients 50% respond to treatments with reduction in pain of 30% (ref #73)

PAIN IN AMERICA

• Phone survey-Hart Research Associates July 2003 (1,004 adults)
• 76% personally/family member/friend suffer from chronic pain-57% personally
• Pain types
  - Back pain – 20%
  - Arthritis/joint pain – 19%
  - Headaches/migraines – 17%
  - Knee pain – 17%
  - Shoulder pain 7%
• Every age group affected
  - 18-34 -- 54%
  - 35-49 -- 56%
  - 50-64 -- 63%
  - 65+ -- 17%
PAIN IN AMERICA

• 75% make lifestyle adjustments
  – 20% Disability from work, 17% change jobs, 13% help with daily living, 13% move to another home
• 90% did seek professional help
  – Rx 69% (58% effective)
  – Chiropractic Tx 54% effective
  – Surgery 32% (54% effective)
  – Physical therapy 48% (48% effective)
  – OTC medications 79% (41% effective)
  – Other Tx 20% (40% effective)
• 72% physicians supportive, 51% of bosses supportive
• 57% would be willing to pay an extra $1.00 a week in taxes to pay for more pain research

DEFINITION OF PAIN

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

ALTERNATIVE DEFINITION OF PAIN

Pain is whatever the patient says/feels it is, existing whenever he or she says/indicates it does.

TYPES OF PAIN

• ACUTE
  – Follows injury
  – Generally disappears when injury heals
  – Well-defined temporal onset
• CHRONIC
  – Persists beyond expected healing time
  – Cause may be hard to define
• CANCER
  – Definable cause
  – Can be acute, recurrent, or chronic

CHARACTERISTICS OF ACUTE AND CHRONIC/PERSISTENT PAIN

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>ACUTE PAIN</th>
<th>CHRONIC/PERSISTENT PAIN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relief of Pain</td>
<td>Highly Desirable</td>
<td>Highly Desirable</td>
</tr>
<tr>
<td>Dependence &amp; Tolerance</td>
<td>Unusual</td>
<td>Common</td>
</tr>
<tr>
<td>Physiological Component</td>
<td>Usually Not Present</td>
<td>Often a Problem</td>
</tr>
<tr>
<td>Organic Cause</td>
<td>Common</td>
<td>Often Not Present</td>
</tr>
<tr>
<td>Family &amp; Environment Involvement</td>
<td>Small</td>
<td>Significant</td>
</tr>
<tr>
<td>Sleep Problems</td>
<td>Unusual</td>
<td>Common</td>
</tr>
<tr>
<td>Treatment Goal</td>
<td>Cure</td>
<td>Rehabilitation &amp; Acceptance</td>
</tr>
</tbody>
</table>
IF WE CANNOT ASSESS PAIN, WE WILL NEVER BE ABLE TO RELIEVE PAIN.

Betty R. Ferrell, Ph.D.

ASSESSMENT OF PAIN

• Careful history
  — Believe the patient and family
  • When you dislike patients, pain is taken less seriously (ref #77)
  — Assess the nature of the pain
  — Acute pain
    — Distinct onset, short duration, physical signs
  — Chronic/Persistent pain
    — Long duration, long-standing functional impairment
    — Consider neuropathic pain

ASSESSMENT OF PAIN

• CONSIDER ONSET, WHAT MAKES PAIN BETTER OR WORSE, LOCATION, DESCRIPTION, SEVERITY, AND DOES PAIN MOVE?
• Consider multiple pain types and/or sites.
• Assess psychosocial status
  — Emotional, Social, Cultural
• Assess functional status.

MEDICATION HISTORY

• All medications used in the past six months
  — Dose
  — Duration of use
  — Frequency of use
  — Reason for use
  — Perception of efficacy
• Social drug use (Do not forget alcohol)
• What worked, how well they worked, what did not
• Side effects
• Allergies
• Nonprescription drug use
• Nutritional supplements
• Alternative therapies

PAIN TREATMENT PLAN DEVELOPMENT

• Develop treatment plans using assessment tools and, whenever possible, include patient and family input.
• Remember in chronic pain it is unrealistic in most cases to expect COMPLETE relief of pain.
• Do systematic and ongoing reassessments with functional end points in mind.
• Change the plan as needed.
• Document the plan and all changes.
• The process should never end.

Trends

• Acute procedural pain (surgery, labor and delivery) well addressed (ref #71)
• Chronic pain continues to be inadequately addressed (40% report ineffective treatment) (ref #71)
  — A subpopulation exists where opioids do not help and may make overall situation worse
• Analgesic ADEs and errors large problem
• Recognition/perception that prescription opioids are a large part of illicit drug use problem
**Pendulum Swings**

- Under-treatment of cancer pain (1960-1970’s)
- Development of sustained release opioids (1980’s)
- Development of devices that allowed patients to deliver own opioids (1980’s)
- Better definition of addiction (1980-1990’s)
- Use of opioids in chronic pain (1990-2010’s)
- Pain 5th vital sign, emphasis on pain control
- Guidelines for use of opioids (2001-2010)
- Better defined use of opioid in non-cancer pain? 2010-2015
- ?????

**NEWS STORIES ABOUT OPIOIDS**

- CDC Director calls painkiller overdoses an epidemic (State WV Journal 11/2, The Oregonian 11/2, CBS Evening News 11/1, Los Angeles Times 11/2, NPR 11/2, HealthDay 11/2, Medscape 11/2)
  - “More Americans now die from overdosing on painkillers than from overdosing on heroin and cocaine combined”...
  - “deaths linked to opioid pain relievers such as OxyContin, Vicodin, and Opana have become an epidemic...the rate of deaths has more than tripled in the past decade” CDC Director Thomas Frieden

- Misuse of Opioids Doubles Over Five-Year Period (CDC MMWR 2010; 59:1071-2)
- Patients receiving higher doses of opioids at higher risk of overdose (Ann Intern Med 2010; 152(5):359-62)
- Among patients receiving opioid prescriptions for pain, higher doses were associated with increased risk for over overdose death (JAMA. 2011, 305(13): 1315-1321)
  - Risk clear what about solution?

- APM AND APS believe Rx of opioids should be extension of good professional practice
  - Evaluation of patient-physical exam, pain history, pain impact on patient, review of previous diagnostic studies, drug history, coexisting diseases/conditions
  - Treatment plan consideration of all aspects of treatment (behavioral, physical therapy, noninvasive techniques, physical and psychosocial support, and medication)
- If opioid trial selected risks should be explained to patient and family, and informed consent OR signed agreement obtained
- NO TRIAL WITHOUT COMPLETE ASSESSMENT OF PAIN COMPLAINT

**Evidence of Opioid Misuse**

- More Americans now die from overdosing on painkillers than from overdosing on heroin and cocaine combined
- Deaths linked to opioid pain relievers such as OxyContin, Vicodin, and Opana have become an epidemic
- The rate of deaths has more than tripled in the past decade

**Perfect Storm** of increasing pain and increasing opioid misuse, abuse and diversion (ref #74)
TREATING CHRONIC NONCANCER PAIN WITH OPIOIDS

• AAPM AND APS believe Rx of opioids should be extension of good professional practice
  – Consultation as needed
  – Pain specialist, psychologist, pharmacist
  – Periodic review of treatment efficacy
    • Assess functional state of patient, continued analgesia, side effects, quality of life, indications of medication misuse, urine drug screens
  – Documentation
    • Reason for opioid, overall treatment plan, periodic review

TREATING CHRONIC NONCANCER PAIN WITH OPIOIDS

• Signs of drug seeking behavior (DEA)
  – Unusual behavior in waiting room
  – Extremes in dress (way over or under dressed)
  – Comes in at irregular hours (on call doc only)
  – Must be taken care of NOW
  – Reluctant or unwilling to provide reference information, no regular physician
  – Travelling through town, visiting relative, no permanent address
  – Uses child or elderly person when seeking pain medications
  – Pressures care giver with guilt

TREATING CHRONIC NONCANCER PAIN WITH OPIOIDS

• Evaluate risk factors for abuse
  – Personal history of alcohol or drug abuse
  – Family history of alcohol or drug abuse
  – Younger age and presence of psychiatric conditions
  – Use of screening tools
    • Screener and Opioid Assessment of Patients with Pain (SOAPP version 1 or SOAPP-R)
    • Opioid Risk Tool

TREATING CHRONIC NONCANCER PAIN WITH OPIOIDS

• Watch for diversion
  – Patients continually trying to fill Rx early despite dose agreements
  – Frequent reports of lost or stolen Rx
  – Use multiple pharmacies and multiple prescribers
  – Is noncompliant with other treatments
  – Unusual quantity
  – Quantity looks altered
  – Reports allergies to all other drugs

Risk Evaluation and Mitigation Strategies (REMS)

• FDA approved class-wide REMS for long acting opioids (2012)
  – 1) Prescriber training (provided by manufacturer and not mandatory)
  – 2) NEW Medication Guides (www.er-la-opioridrems.com)
  – 3) REMS implementation responsibility falls on pharmaceutical companies
  – 4) Administrative requirements

Petition Letter to FDA

(Pain and Palliative Care PRN, List serve, posted Richard Wheeler, 8/1/12)

• 37 Physicians (Physicians for Responsible Opioid Prescribing)
  • Strike the term “moderate” from the indication for use of opioids in non-cancer pain
  • Add maximum daily dose, equivalent to 100mg of morphine for non-cancer pain
  • Add maximum duration of 90 days for continuous (daily) use for non-cancer pain
  • Response (Professionals for Rational Opioid Monitoring and Pharmacotherapy)
Dr. Jeffry Fudin (posted 1/23/2013)

- IT IS NOT OK TO:
  - Drink alcohol with opioids
  - Use someone else's medication
  - Take more medication than instructed

BALANCING NEWS STORIES ABOUT OPIOIDS

- “Taking legal, FDA approved opioid medications as prescribed, under the direction of a physician for pain relief, is safe and effective, and only rarely leads to addiction. When properly used, these medications rarely give a “high”—they give relief. And, most importantly, they allow many people to resume their normal lives”

Dr. James Campbell, Professor of Neurosurgery at Johns Hopkins Medical Center, past president Of the American Pain Society, and Chairman of The American Pain Foundation (ref 53)

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OPIOID ANALGESICS

- Pharmacologic activity depends on affinity for opiate receptors.
- Agents do not eliminate pain, but decrease its unpleasantness.
- Some variability in onset and duration of action.
- Key to effective use is individualization and proper titration

OPIOID ANALGESIC ADVERSE EFFECTS

- Mood changes (minimized with careful titration)
  - Dysphoria (may be seen as agitation in elderly)
  - Euphoria or paradoxical excitement
- Cognitive disturbances (minimized with careful titration)
- Somnolence (minimized with careful titration)
  - Drowsiness
  - Inability to concentrate; apathy
  - Increase in falls

- Respiratory depression (minimized with careful titration)
- Nausea and vomiting (tolerance usually develops)
- Increased sphincter tone
- Urinary retention
- Histamine release
- Pruritus
  - Rarely, exacerbation of asthma
Sentinel Event Alert
Safe Use of Opioids in Hospitals
(The Joint Commission, Issue 49, August 8, 2012)

- Opioids rank among the agents most frequently associated with adverse events
  - 16% of all reported in British study
- Joint Commission Sentinel Event Database
  - 47%, wrong dose
  - 29%, improper monitoring
  - 11%, other (e.g. excessive dosing, medication interactions)

OPIOID ANALGESIC ADVERSE EFFECTS

- Decreased gastrointestinal motility and secretion
  - Unlike most other adverse effects that are transient or are avoided with careful titration, this IS TO BE EXPECTED!
  - Methylaltrexone (Relistor) sub-q (Block receptors in GI tract)
  - Use an aggressive bowel regimen
    - Lots of fluid
    - Plenty of dietary fiber
    - Stimulants
    - Stool softeners
    - by themselves are often ineffective
    - Bulk-producing laxative ??

OPIOID ANALGESIC ADVERSE EFFECTS

- Risk for respiratory depression may be higher than previously reported
  - Higher risk patients
    - Sleep apnea
    - Morbid obesity
    - Older age
    - Newly prescribed
    - Long time users
    - Drug interactions with other sedative like drugs
    - Smokers

- Tolerance – a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug’s effects over time.
  - Always a possibility
  - Easily confused with change in pain status
  - May be minimized with regular dosing
  - Increase dose to achieve effective analgesia

OPIOID ANALGESIC ADVERSE EFFECTS

- Physical Dependence – a state of adaptation that is manifest by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.
  - Rarely seen with short-term use
  - Slow wean will prevent withdrawal symptoms
    - determined by length of time on therapy and why on therapy

- Addiction – a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.
  - Inability to take meds as Rx’d, frequent lost/stolen Rx, Doc shopping, isolation, intoxication
  - No single event is diagnostic of addictive disorder, diagnosis is pattern of behavior over time
OPIOID ANALGESICS

- Equianalgesic dosing
  - Can use reference guides (better tables being developed)
  - Use only as a guide
  - Individual titration and constant reassessment a must
  - What-How well-How long-End Point

Opioid Conversion Chart

  (Whose “slide rule” are you using????)
  Terry Baumann e-mail tbaumann@mhc.net

THE PROBLEM (McPherson - Demystifying Opioid Conversion Calculation – 2010)

- Ask 15 experts – get 15 answers
- We can agree
  - Patients switch from one opioid to another
  - Patients switch from route to another
  - Patients switch from formulation to another
  - Conversion charts are often based on:
    - Anecdotal information
    - Unidirectional information
    - Single dose studies
    - No regard for patient variability

Other Opioids and Conversions

- Need to know
  - What is being treated
  - How is patient doing on present dose
  - How long has the patient been on present dose
  - What are the other drugs used to treat the patient
  - What is the end point

Case Studies

- 77 YO female
- “Cancer” Pain
- Taking 10, oxycodone 5mg/acetaminophen 325mg daily
- Physician wants to switch to fentanyl patch
- Check table = 25 mcg/hr every 72 hours
- Correct?

Case Studies

- Compression Fracture
- Terminal COPD
- Long standing lymphoma
- Severe pain (10/10) when moves, otherwise pain 2/10
- Was on 1-2 tablets a day until resent visit to daughter
- No other pain medications
- New dose?
Case Studies

- Low back pain (10 years)
- Terminal COPD, history of breast cancer 15 years ago
- Pain on scale 5/10
- Has taken the same amount of oxycodone/acetaminophen with very little change for 6 months
- Taking no other pain medications
- New dose?

Case Studies

- Aggressive breast cancer with metastasis, new low back pain, pain in right leg
- Pain scale 9/10 most of time
- Taking 1-2 oxycodone/acetaminophen 5/325 until two weeks ago with pain 3/10, two days ago patient on 6 of above, yesterday 10
- Patient also on lorazepam and ibuprofen
- New Dose?

Important Opioid Issues

- Morphine
- Fentanyl Patch
- Codeine
- Hydromorphone
- Meperidine
- Methadone
- Schedule II Hydrocodone

MORPHINE

- Metabolism
  - Very little excreted unchanged
  - Morphine-6-glucuronide is renally eliminated
  - decrease dose and careful titrate in patients with renal impairment
- Cardiovascular effects
- IV time to peak 15 minutes – duration 2-4 hours

FENTANYL

- Transdermal patch available
  - q 72 hours
  - 12-24 hours to steady state (deposits in skin)
  - 6 days after increasing dose to steady state
- Chronic nonmalignant pain and cancer pain only
  - Increased body temperature can change the way patch delivers fentanyl

FENTANYL

- Formulation (FDA approved November 1998) Oral Transmucosal Fentanyl Citrate (Actiq)-flavored sugar lozenge for treatment of breakthrough cancer pain
  - Many transmucosal dosage forms now available
  - Lower strength patch (may be better suited for nursing facility patients)
  - Buccal tablets available (not mg to mg same as lozenge)
  - Some Patches can burn patient in MRI
CODEINE

• Moderate pain only
  – Analgesia due to morphine metabolite
  – Antinociceptive actions probably involve codeine
• Many are advocating STOPping its use in Peds
  – In kids with polymorphism in genes coding for CYP2D6 isoenzyme (which transforms codeine to morphine) risk of death increase – ultra-rapid transformation of codeine to morphine
• No better than ibuprofen in reducing pain?
• Works best when combined with acetaminophen or NSAID
• Watch acetaminophen in combination product
• Same propensity as morphine to produce tolerance, dependence, and constipation

CODEINE  Ref 91

• One to 7 of every 100 persons are ultrarapid metabolizers
• FDA’s safety review of codeine - 10 pediatric deaths and 3 overdoses between 1969 and 2012. The children were aged 21 months to 9 years; many were recovering from tonsil or adenoid surgery for obstructive sleep apnea. All received codeine that was within the recommended dose range. Signs of overdose developed within 1 to 2 days.
• The new boxed warning and contraindication state that codeine should not be used for postoperative pain management in children undergoing tonsillectomy or adenotonsillectomy.
• Codeine can be prescribed only for children with other types of pain if the benefits are expected to outweigh the risks
• Children taking codeine should be monitored closely for signs of morphine overdose

HYDROMORPHONE

• More potent than morphine
• Fast oral absorption
  – Favored street drug
• Very soluble
  – Use when need a highly concentrated narcotic solution (intrathecal, subcutaneous)
• Pharmacology very similar to morphine
• ER Hydromorphone (Frazyle) – [REMS]
  – Osmotic release oral release alters pharmacokinetics thus decreasing abuse potential
• IV Dose = POTENTIAL DANGER-DANGER

MEPERIDINE

• Particularly HAZARDOUS in the elderly
  – Normeperidine accumulation can lead to delirium and seizures
  – Contraindicated in renal failure
  – Interaction with MAOIs
• Less potent and shorter duration than morphine
  – If administered, should be at higher doses and more often is not
  – Oral dose usually underdosed
• NO advantages over morphine

METHADONE  Ref 55,56,57

• Longer duration of action than morphine
  – Long half-life (30.4 +/- 16.3 hours) (May range from 8-56 hours)
• Must individually dose because of long unpredictable half-life
• QTc interval prolongation
  – Disclose to all patients
  – Look for history of heart disease, arrhythmias, syncope
  – Pretreatment ECG, follow up 30 days (all patients)
  – Additional ECG follow up > 100 mg day
• QTc 450 ms – 500 ms consider risks vs benefit
• Increased deaths in northern Michigan
• Can be taken orally or by injection
• Inexpensive
  – 100 tablets AWP 40mg OxyContin=$440.82
  – 100 tablets AWP 10mg methadone=$13.74

METHADONE  Ref 55,56

• Dose ratios to achieve equianalgesia influenced by previous opioid
  – Tolerance to opioids may be dependent on NMDA receptor
  – At high morphine doses, metabolites may produce constant activation of NMDA receptor, requiring more morphine to maintain pain relief
  – Can even see severe myoclonic jerking
• Conversion to Methadone (which has NMDA antagonist activity) and no excitatory metabolites can result in dramatic decrease in the MS requirements as excitatory metabolite effects are blunted and over time decreased
• Has been noted to stop myoclonic jerking
Methadone Conversion

**ORAL MORPHINE EQUIVALENT DAILY DOSE**

<table>
<thead>
<tr>
<th>Mg</th>
<th>Ratio</th>
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<tbody>
<tr>
<td>0-99</td>
<td>4:1</td>
</tr>
<tr>
<td>100-299</td>
<td>8:1</td>
</tr>
<tr>
<td>300-499</td>
<td>12:1</td>
</tr>
<tr>
<td>500-999</td>
<td>15:1</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>20:1</td>
</tr>
</tbody>
</table>

20 mg Oral Oxycodone = 30 mg Oral Morphine

Patient on 100 mg Oxycodone Q12 Hours

Equal to 300 mg Oral Morphine Equivalents (24 hours)

300/12 = 25

Oral Methadone dose = ?

Methadone

• Suggestions when initiating Methadone
  – Carefully note dose and length of therapy of previous opioid use
  – Carefully use NEWER ratios for conversion
  – Note degree of opioid tolerance
  – Carefully consider age, general condition, and medical status of patient
  – Consider concurrent medication
  – Type, severity, and duration of pain
  – Acceptable balance between pain symptoms and analgesia

OXYCODONE AND HYDROCODONE

• Most often seen in combination products with aspirin or acetaminophen
• Use in moderate to severe pain
• Hydrocodone Schedule II
  • Similar efficacy
  • Same pharmacology as morphine

OPIOID ANALGESIC USE

High Risk Patients

• 55 YO white female, 90 kg, admitted for back surgery, 4 year history methadone use, present dose 80 mg BID, non smoker, occasional alcohol use
• Put on hydromorphone PCA post surgery, once on floor pain 15/20, patient in obvious discomfort
• Patient reveals “fired” from pain clinic week before surgery (never told anyone)
• ????

OPIOID ANALGESIC USE

High Risk Patients

• 47 YO white female, 60 kg, recently moved into area from another state, no LMO, 10 year history of low back pain, 20 pack year smoker, occasional alcohol use, in MVA with multiple fractures, Med Red shows no meds
• Put on hydromorphone PCA for 2 days, pain 9/10 most of time, able to ambulate well, converted to hydrocodone 10mg/acetaminophen 325 mg every 4 hours, uses maximum daily dose, pain 9/10 most of time
• Near discharge, patient reveals use of “friends” vicodins daily (several in AM and several PM) before admission
• ????
OPIOID ANALGESIC USE
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- ???

OPIOID ANALGESIC USE
High Risk Patients

- Worked to find LMD to accept patient
- Communicated problem to office (obvious high risk to abuse opioids)
- Sent patient out with limited supply (7 days) opioid and specific visit date with LMD
- Discussed case with multidisciplinary pain clinic
  - Will accept after patient establishes relationship with LMD

OPIOID ANALGESIC USE
High Risk Patients

- Restarted methadone (1/2 dose as IVPIB) and continued PCA, pain controlled within few hours
- Monitoring ??
- Re-established baseline methadone dose (put into system as PRN)
- Over several days convert to oral IR oxycodone and methadone with patient able to participate in all post op activities
- Communicated with patient’s LMD and pain clinic
  - Plan to continue methadone short term with “breakthrough” opioids , pain clinic to guide patient opioid therapy with LMD, with plan for eventual opioid wean
- Struck agreement with patient to accept plan

QUESTIONS

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68. Adopted from “Methadone use in the hospice setting:safe, effective, cost efficient” by McCormick BY, Fisch MJ MD Anderson Cancer Center, Houston Texas


