MALIGNANT AND TERMINAL PAIN

Mario Milch, MD
Kaiser Permanente Hospice and Palliative Medicine
Metro Los Angeles

PAIN

ACUTE
1. A complex constellation
   unpleasant sensations
   perceptual experiences
   emotional experiences
2. Associated with responses
   autonomic
   psychological
   emotional
   behavioral

PAIN

CHRONIC
1. Pain that persists a month (or more)
   beyond usual course of acute disease or injury healing time
2. Pain associated with chronic pathology
   that is continuous or recurrent for months or years.
Patients want it to stop but often we can just make it tolerable.

Pain is what the patient says it is: have patient rate it.

**PAIN SCALE**

- 0: No pain
- 1-3: Mild
- 4-5: Discomforting
- 6-7: Distressing
- 8-9: Horrible
- 10: Worst possible pain

**NON-VERBAL CLUES**

- Sleeping-calm-relaxed
- Grimacing with movement
- Moaning with movement
- Restless
- Constant moaning without stimuli

Keep high level of suspicion!
**PAIN HISTORY**

- Site(s)
- Intensity (0-10)
- Duration (constant-intermittent-incident)
- Type-quality
- What makes it better and worse
- Effect on lifestyle-function-mood-activity
- What has been tried

**PAIN PERCEPTION**

- Unique to each individual-possibly genetically determined
- Psychosocial factors
- Cultural factors
- Subjective but essential to determine effectiveness of treatment

**TYPE**

- NOCEPTIVE
  - Somatic
  - Visceral
- NEUROPATHIC
- MIXED
**DIFFICULT PAIN**

- Advanced cancer: 70% have pain
- Difficult to control in 10%

Responds poorly to opioids
Episodic-incident pain
Non-physical factors-psychosocial distress

**ADDICTION**

1. A psychological phenomenon
2. Drug craving
3. Overwhelming concern with obtaining
4. Aberrant behavior such as drug selling or hoarding
5. Unsanctioned dose escalation
6. Euphoria or sedation may be sought after effect

Adapted from Twycross, McQuay

**PSEUDOADDICTION**

1. Pain incompletely and inadequately controlled
2. Behavior pattern may resemble addiction but motivation is pain relief, not secondary effects
3. “Watching the clock”
DEPENDENCE

1. A physical phenomenon
2. Abstinence syndrome would develop if drug abruptly withdrawn or an antagonist added
3. Taper dosages before discontinuing drug
4. Do not coadminister antagonist or agonist-antagonist drugs

Twycross, McQuay

TOLERANCE

1. A physical phenomenon
2. Effectiveness or duration of analgesia is reduced over time, necessitating higher dosages
3. In long-term therapy, need for escalation of dosages usually slows, and then trends downwards

W.H.O. ANALGESIC LADDER

• **STEP 1: Mild pain**
  Non-opioids; adjuvants
• **STEP 2: Moderate pain**
  Weaker opioids; non-opioids; adjuvants
• **STEP 3: Severe pain**
  Stronger opioids; non-opioids; adjuvants
NON-OPIOIDS

- ACETAMINOPHEN
- MODIFIED SALICYLATES: 500-1500 mg q 12
  - choline magnesium trisalicylate (Trilisate)
  - salsalate (Disalcid)

NSAID’s

- Non-selective
  - nabumetone (Relafen) 1-2 gm daily
  - etodolac (Lodine) 200-400 mg bid-tid
- COX 2 inhibitors: no effect on platelets
  - not for sulfa allergic pts.
- Significant short and long term side effects:
  - GI - Renal-Hepatic-Fluid retention-CHF

WEAKER OPIOIDS

Usually combined with acetaminophen or aspirin
- CODEINE: max. dose 360 mg/ 24 hrs.
- HYDROCODONE: 1 VICODIN = 9 mg MS
- PROPOXYPHENE: about same strength as acetaminophen
- TRAMADOL (ULTRAM): opioid agonist; norepinephrine & serotonin reuptake inhibitor. Max. dose: 400 mg/d
MEPERIDINE (DEMEROL)

- **ADVANTAGES**
  - Lipophilic, therefore quick acting
- **DISADVANTAGES**
  - Weak narcotic
  - Short duration
  - May cause euphoria-dissociation
  - Toxic metabolite: normeperidine - risk of seizures and psychosis

AGONIST-ANTAGONIST OPIOIDS

- NALBUPHINE (NUBAIN)
- PENTAZOCINE (TALWIN)
- BUTORPHENOL (STADOL)
  - May cause withdrawal sm. when added to opioid agonists
  - DO NOT USE!!

MORPHINE

- Gold standard for moderate to severe pain
- Been around for a few thousand years
- Many dosages with variable duration
- Many routes of administration: PO, IM, SQ, IV, SL or buccal, rectal, inhaled, epidural, intrathecal
**OXYCODONE**

- 30 mg MS= 20-30 mg oxycodone
- Immediate release: tabs 5-15-30mg liquid 1mg/ml; 20 mg/ml
- Sustained release: 10-20-40-80 q 8-12 hrs.
- Not available parenteral

**METHADONE.**

- Effective for about 8 hrs.
- May have NMDA blocking activity
- Trial dose: 2.5 mg
- MS 30=20mg acute; 2-4mg chronic
- Blood levels can build up to toxic levels-titrate slowly (q 3-5 days)

**WHY SWITCH TO A FENTANYL (Duragesic) PATCH?**

- ADVANTAGES
  - Doesn’t have to be swallowed and is long acting
- DISADVANTAGES
  - Variable absorption, dependent on fat depots; takes 12-24 hours to get an adequate blood level
  - Requires short acting opiate for rescue pain
- MS 100mg=fentanyl 200mg
HYDROMORPHONE (Dilaudid)

- MS 30 mg PO = HM 7.5 mg PO
  MS 10 mg IM/SC/IV = HM 1.5 mg
- Short acting: 3-4 hrs except
  Dilaudid 3 mg supp. Q 6-8 h

PRINCIPLES OF OPIOID USE

- Anticipate the pain—more effective than chasing it
  Use long acting preparations
  Use IR prior to painful activity
- Breakthrough (rescue) doses as needed (q 1 h) 10-20% of 24hr opioid dose
- If more than 3 rescue doses in 24h, increase long acting dose

- Use adequate doses of one opioid rather than small doses of many opioids
- Reevaluate if no relief: ?constipation
  ?bladder distention
- Opioid rotation
- Think of non-physical factors
POTENTIAL ADVERSE EFFECTS OF OPIOIDS

• MOOD CHANGES
• SEDATION
• CONFUSION
• RESPIRATORY DEPRESSION
• NAUSEA AND VOMITING
• ORTHOSTATIC HYPOTENSION
• URINARY RETENTION
• PRURITUS
• CONSTIPATION

ADJUVANTS

• Corticosteroids
• Anticonvulsants
• Antidepressants
• Neuroleptics
• Local anesthetics
• Antihistamines
• Psychostimulants

KETAMINE

• Affects nociceptive processing - repetitive C fiber activation - NMDA inhibitor
• Side effects: excessive salivation, purposeless movements, behavioral changes
• SQ-IV-PO
• Opioid sparing effect - shifts dose response curve
TOTAL PAIN

• PHYSICAL
• PSYCHOLOGICAL
• SOCIAL
• SPIRITUAL/EXISTENTIAL
  C. Saunders

STAGES AT END-OF-LIFE

• DENIAL
• ANGER
• BARGAINING
• DEPRESSION
• ACCEPTANCE
  Kubler-Ross
PALLIATIVE SEDATION

- For intractable symptoms: pain, dyspnea, existential anguish
- Terminal care meds:
  - Morphine PO or SL or buccal
  - Hyoscyamine (Levsin) or atropine
  - Lorazepam (Ativan) or Haloperidol

CASE STUDY # 1

- R.R.: 11 y.o. Presented 2/00 w/ large mass in L cheek extending intraorally.
- Ewing’s Sarcoma of infratemporal fossa and nasopharynx
- Repeated courses of chemotherapy w/ “some complaints of pain”

CASE STUDY # 1 (Cont.)

- XRT; mucositis w/ inability to eat; TPN; G-tube feedings.
- MS continuous dose w/ supplemental bolus doses for pain of mucositis
  “Most likely patient has a narcotic addiction and attempts to wean him off have resulted in episodes of nausea and vomiting, possibly withdrawal”
• He was transitioned to a fentanyl patch prior to discharge with G-tube narcotics as needed "
• "Will attempt to wean but perhaps will not be successful until post-op and then may require a methadone taper"

• Transferred to Sunset for resection of persistent tumor of the left skull base
• L infratemporal fossa craniotomy and resection; L rad. Maxillectomy; L oral pharyngeal and parapharyngeal resection; upper neck resection; exploration of midneck vasculature; removal of bone graft R humerus

• A week post-op, Psych consult requested because of "agitation, anxiety", aggressive behavior such as pinching the nurses
• CDRP consult requested to address "narcotic dependency" manifested by frequent pushing of call button and requests for bolus doses of morphine, while on continuous dose of 0.4 mg/ hr w/ 0.9 mg q 10 min boluses via PCA.
• Pain is 8-9 out of 10
• Increase continuous dose gradually to 4 mg/hr.
• Continue PCA settings
• Switch to liquid morphine via G-tube q 4 hrs around the clock and q 1 hr prn
• Do not switch to methadone

PAYOFF!!

• Pain rating down to 3-4
• He rings call button much less often, doesn’t pinch nurses, ask for IV boluses
• Slept much better
• Nurses and Pediatric residents much happier and say nice things to pain consultant.
• Transfer summary: “he has developed a narcotic dependency in last few mos due to his pain management”

CASE STUDY # 2

• J.L.- 39 y.o man w/ lung CA w/ spinal mets, dx 1/00 - underwent spinal surgery followed by chemo and XRT
• Pain recurred - admitted to hospital 12/00 for pain out of control - had been on Oxycontin and oxycodone
• Morphine titrated in the E.R under guidance of hospice MD. Increasing gradually to 10 mg/hr IV with pain still 8-10 out of 10
• Hospitalized w/ orders to give MS continuous at 25 mg/hr IV with PCA settings of 5 mg q 10 min.

• Pharmacist calls RN and tells her dose seems too high
• Nurse does not call hospice MD on call
• Nurse calls MOD who, without examining the patient or reviewing the chart, lowers the continuous dose to 2.5 mg/hr and the PCA dose to 0.5 mg q 10 min

• Next morning, patient tells hospice MD his pain was so excruciating that he contemplated suicide
• Patient pain controlled on morphine, 80 mg/hr IV. Goes home on that dose via SQ continuous with CADD pump.
CASE STUDY # 2
(Continued)

• Patient’s pain continues to increase and he is switched to morphine IV via PICC catheter, up to 350 mg/ hr. with inadequate pain control
• He develops some asterixis and confusion
• Started on a ketamine SQ infusion

SUMMARY

PAIN CAN BE CONTROLLED IN MOST PATIENTS
1. Assess pain properly
2. Titrate Rx to positive effect
3. Switch Rx if adverse effect not controlled
4. Use adjuvants