**Fundamentals of Pain Management**

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I have no conflicts of interest to report

**PALLIATION**

The physician's duty is to cure when possible, relieve suffering often, comfort always.

(Great quote, but needs updating. It is a responsibility of every member of the team to provide comfort!)

**Pain Management Objectives**

- Pain Assessment
- Pain treatment
  - Non-pharmacologic
  - Pharmacologic
- Issues of Opioid Use

**Pain Assessment**

- Acute
- Chronic Non-Malignant
- Chronic Malignant

**Pain Assessment**

Components of pain

- Physical
- Psychological
- Spiritual
Pain Assessment
- Pain is a symptom obtained by history taking. (patient report) [0-10 scale good for intra-patient assessment]
- Tenderness is a sign – does not always accompany pain
- Non verbal patients - Grimacing restlessness, agitation (PABS)
- Pain - exhaustion - sleep - pain

Pain Assessment
- 0-10 !!!
- It’s only good for the individual
- Regulatory assessment (Joint Comm)
  - Assess regularly: “5th vital sign”
  - Intervene if VAS =>5
  - Reassess after intervention
  - Document
  - Is “4” OK?
  - What if intervention didn’t work?

Pain Assessment
Type/Quality of pain
- Somatic: dull/aching, well localized: fracture, laceration/incision, bone met, muscle strain
- Visceral: dull, sharp, colicky. May be localized or referred: gastritis, stones
- Neuropathic: burning, (lancinating), numb: zoster, spinal disc, DM

Pain Pathophysiology
- Acute pain
  - identified event, resolves days–weeks
  - usually nociceptive
- Chronic pain
  - cause often not easily identified, multifactorial
  - indeterminate duration
  - nociceptive and / or neuropathic

Nociceptive Pain
- Direct stimulation of intact nociceptors
- Transmission along normal nerves

Nociceptive Pain
- Tissue injury apparent
- Management
  - Non-pharmacologic
  - Non-opioids (NSAIDS, APAP, etc)
  - Opioids
Neuropathic Pain

- Disordered peripheral or central nerves
- Compression, transection, infiltration, ischemia, metabolic injury

Pain Management

- Don’t delay for investigations or disease treatment
- Unmanaged pain → nervous system changes
  - permanent damage
  - amplify pain
  - chronic pain
- Treat underlying cause (e.g., radiation for a neoplasm)

Central Pain Syndromes

- Psychological component
- Genetic component
- Behavioral therapies
- Opioids overused and largely ineffective

Neuropathic Pain

- Pain may exceed observable injury
- Described as burning, tingling, shooting, stabbing, electrical, numb

Management

- Anti-convulsants (e.g. gabapentin, pregabalin)
- TCA’s (side effect issues)
- SNRI (e.g. duloxetine)
- opioids
- ?ketamine

Non-Pharmacological Treatments

- Physical Therapy
- Heat
- Acupuncture
- Relaxation, Biofeedback, Imagery
- Counseling, Psychotherapy
- TENS
- Chiropractic
Non-Opioid Analgesics

- Acetaminophen
- ASA
- NSAIDS
- 17 compounds in clinical use in U.S.
- Ketorolac (Toradol)
- COX-2 inhibitors (1 currently on market)
- Tramadol (Ultram)
- Lidocaine Patch (Lidoderm)
- Capsaicin
- Topical NSAIDs

Acetaminophen - Concerns

- Acetaminophen is ubiquitous in OTC and prescribed medications. (cold, sleep, pain remedies)
- Maximum recommended dose is 4gm/day.
- Lower max dose in active alcohol drinkers and in setting of liver disease
- FDA – lower APAP in hydrocodone/APAP
  - Mcneil Co. changed label on “Tylenol ES to recommend max 3 gm/day

Other Analgesics/Techniques

- Anti-depressants
- Anti-convulsants
- Corticosteroids
- Nerve blocks
  - anesthetic
  - lytic
- Epidural, intra-thecal
  - opioids
  - local anesthetics

WHO Analgesic Ladder for Cancer Pain Management

- Pain - Non-opioid +/- adjuvant
- Pain persisting or increasing – low-dose opioid +/- non-opioid +/- adjuvant
- Pain persisting or increasing – increase dose of opioid +/- non-opioid ........
- Freedom from pain

Rational Use of Opioids

"Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium."

Thomas Sydenham
(17th century)
Opioids

1. Analgesia
2. Sedation
3. Respiratory Depression (RARE)

(These effects occur in this order!)

Think PCA

Opioids

- Tolerance – need higher dose of drug to get same previous effect.
  (In cancer patients, increased need often due to increased disease)
  A cancer patient on 300 mg/day morphine wide awake; me – not likely.
- Physical Dependence – defined by abstinence/withdrawal syndrome
- Psychological dependence = addiction

Opioids - Addiction

- Non-medicinal use
- Use despite negative physical, social, legal consequences
- Pre-occupation with obtaining the substance
- Not likely in cancer patients

Morphine

- Conjugated in liver.
- Morphine glucuronides are active.
- Excreted in urine.
- Decrease dose with renal impairment.
- May want to titrate dose down near end of life because of renal shut-down.
- Do NOT use long-acting/slow-release morphine in renal failure or dialysis patient
- Some concern re: immunosuppression

Hydromorphone

- More potent than morphine
  IV Morphine:Hydromorphone ratio = 7:1
- Oral or IV
- Safer in renal disease
- Mostly hepatic metabolism
- No long acting version available yet
**Hydrocodone**
- Only oral
- Coupled with Acetaminophen or NSAID
- About equipotent with morphine
- The most commonly prescribed opioid (Vicodin, Lortab, Norco, others)

**Codeine**
- Oral
- Coverts to morphine
- Effect ceiling (about 60 mg)
- Side effect ceiling higher than effect ceiling.

**Fentanyl**
- Much more potent than morphine/hyromorphone
- Oral (lollipop, orally dissolving tabs)
- IV - less hemodynamic effects than morphine
- Transdermal – generally change every 72 hours; 80% of original dose remains in the “used” patch. *Flush! (or sharps container)*

**Meperidine**
- Limited use
- Toxic metabolite – normeperidine
- Seizures, hallucinations, bronchospasm, Death.
- Some hospitals have eliminated from formulary
- APS Guidelines – procedure related pain; <48 hrs.; <600mg; not for chronic or prolonged post-op pain.
- Forget about it!

**Methadone**
- Unique opioid
- Intrinsically long half-life – can be problematic
- Multiple pain receptor activity (mu, delta, NMDA, serotonin and norepi reuptake)
- Inexpensive
- Probably best opioid for neuropathic pain
- Conversion ratio varies inversely with higher morphine doses
- Hepatic metabolism

**Conversion ratio of Morphine po to Methadone po**

<table>
<thead>
<tr>
<th>Daily MS po dose (mg)</th>
<th>Conversion ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 100 mg</td>
<td>3:1</td>
</tr>
<tr>
<td>101 - 300 mg</td>
<td>5:1</td>
</tr>
<tr>
<td>301 - 600 mg</td>
<td>10:1</td>
</tr>
<tr>
<td>601 - 800 mg</td>
<td>12:1</td>
</tr>
<tr>
<td>801 - 1000 mg</td>
<td>15:1</td>
</tr>
<tr>
<td>&gt; 1000 mg</td>
<td>20:1</td>
</tr>
</tbody>
</table>
Methadone

Cautions:
- Get supervised experience
- LONG half-life
- Only titrate every four days
- High doses – torsades de pointes (QT prolongation)

Opioids

Impediments to Effective Use

Opioids - Impediments
- Side effects – know them; control them
- Addictions - <6% of pain patients
- What about the previously addicted patient?
- My license – new CME requirements
  Know what you are doing, document
- Societal stigmas
- What would my mother think?

Opioids - Side Effects
- Nausea
- Sedation (consider methylphenidate)
- Respiratory depression

TOLERANCE DEVELOPS TO ALL

Opioids - Side Effects
- Pruritis - morphine
  Previously thought to be histamine mediated, but NOT allergic
  Treat with opioid antagonist, ondansetron or change opioid
- Constipation
  **No tolerance**
  Prophylax - Laxative (senna) and softener.
  Treatment – bisacodyl, lactulose, polyethylene glycol, enemas
  methylnaltrexone (pretty new)
  sub-Q injection, non-centrally acting
  mu receptor antagonist
Opioids - Side Effects
- Neuro effects – sedation, confusion, delirium;
- High dose - myoclonus can develop and may be a dose limiting effect of morphine
  - May want to add benzodiazepine
  - Switch opioid. Methadone may be best alternative

Hyperlgesia
- Probably involves NMDA receptors (N-methyl-D-aspartate)
- May be related to mechanism of neuropathic pain
- Glutamate and perhaps other excitatory neurotransmitters
- NMDA blockers – Ketamine, methadone

Opioids - Side Effects
- Hyperalgesia
  - Allodynia – Painful sensation from normally non-painful stimulus
  - Hyperesthesia – dramatically increased sensitivity to painful stimulus
  - May want to add benzodiazepine
  - Switch opioid. Methadone may be best alternative

Opioid Pharmacokinetics
- Oral
  - Short acting - almost all opioids
    - oral dose - peak 90 minutes
    - duration 2-4 hours
  - Methadone - intrinsically long acting
    - accumulates with repeat dosing
  - Long acting preps - morphine, oxycodone
    - fentanyl (patch)

Opioid Pharmacokinetics
- Oral
  - Dose escalation - 1-2 hours
    - mild/mod pain - 25% - 50%
    - severe pain 50% - 100%

Opioid Pharmacology
- Oral
  - Maximum dose - none except meperidine or combo with APAP, NSAID
Opioid Pharmacokinetics

Intravenous
- Push - Peaks in 6-10 min. IV; 30 min. subQ/IM
- Continuous - Give a loading bolus at the start and with each increase in basal rate
- Administer bolus slowly

Continuous
- Give a loading bolus at the start and with each increase in basal rate
- Administer bolus slowly

Switching Opioids
- Use conversion table (see handout)
- Allow for incomplete cross-tolerance
- Start with 50 - 75% of published dose (“safety factor”)
- Transdermal Fentanyl - Approx 50 – 130 mg morphine/day -> 25 mcg/hr patch
  (Difficult to calculate in reverse)

Opioids and Chronic Pain

Getting started
- Start with short acting to determine need and tolerance
- Don’t start an opioid naïve patient on long acting first! (How do you know where to start?)
- Mild/elderly w/moderate pain: 2-5 mg morphine every three hours PRN
- Transdermal Fentanyl - Approx 50 – 130 mg morphine/day -> 25 mcg/hr patch
  (Difficult to calculate in reverse)
- If pt has known pre-existing tolerance start higher

Opioids and Chronic Pain

Escalate dose at appropriate interval until pain relief achieved
- For oral – determine 24 hr need after 24-48 hours. This determines long acting daily dose.
- For IV – find effective bolus dose and start continuous at half of bolus.
- Monitor effect and side effects carefully

Opioids and Chronic Pain

- Long acting plus short acting for breakthrough q. 1-2 hrs. (10-20% of 24 hr. oral dose)
- Continuous IV – breakthrough dose is usually about 50% of hourly rate q 10 minutes.
- Observe closely and adjust dose and frequency based on effect and side effects
Opioids and Chronic Pain

- If frequent breakthrough dosing needed, adjust daily long acting/continuous dose.
- Monitor and control side effects
  - constipation - treat proactively
  - nausea - short lived
  - pruritis - ondansetron, opioid antagonist, switch to different opioid
  - resp depression - RARE with proper titration

One long acting

One short acting

Opioid rotation may be needed if high doses are reached and pain not very well controlled

NOTE: doses of morphine required for relief of dyspnea are usually smaller than those used for pain.

Opioids - Withdrawal

- Cruel to let patient withdrawal
- Dilated pupils, piloerection, nasal flaring
- ABDOMINAL PAIN
- Avoid naloxone if at all possible.
- If used – dilute, administer slowly
- Naloxone has short half-life. If used for a patient overdosed on long acting opioid, overdose side-effects will recur when naloxone wears off.

Opioids, Chronic Pain and Ethics

- It's unethical to not treat pain
- Rule of double effect
- Terminally ill patients with good symptom management live longer!
Resources

- American Pain Society
- [www.ampainsoc.org](http://www.ampainsoc.org)

Info for professionals and patients
Guidelines
Several links