Opiates, NSAIDS and the ANTI's, Oh My!

Pharmacologic Pain Management for the Advanced Practice Nurse

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Via Christi Hospitals Wichita

Objectives

• Become familiar with the pain pathway
• List the action sites for the major classification of medications used in evidence-based pain management
• Identify the principles and rationale for multimodal therapy
• Describe tools to individualize dosing of opiates and non opiates for pain management

Objectives

• Determine equianalgesic dosing among opiates
• Recognize patients presenting with acute versus persistent pain and the treatment modalities for both
• 9 in 10 Americans regularly suffer from pain
• Most common reason individuals seek care
• 25 million US patients acute pain injury/surgery
• 50 million US patients persistent pain
• Persistent pain most common cause LTD

1/3 of us severe persistent pain at some time

Undertreated pain is bad,
Poorly treated pain may be worse

What is pain?
NORMAL pain processing
• Nociception refers to the process by which information about tissue damage is conveyed to the CNS
• Serves to warn and protect from further injury

ABNORMAL pain processing
• Neuropathic refers to pain that is sustained by the abnormal processing of stimuli from the PNS or the CNS or both
• Reflects a pathophysiology that serves no useful purpose
Acute Pain

- Acute pain
  - Follows injury to the body
  - Generally disappears when the bodily injury heals
  - In the first hours, may be associated with objective physical signs
  - If cause is uncertain, diagnosis is priority
  - Symptomatic pain treatment during workup

American Pain Society definition

Types of Pain: Nociceptive Somatic

- Well-localized
- Dull, achy in quality
- Usually musculoskeletal in origin
- Usually responsive to opioids/nonopioids
- May also respond to steroids, short term muscle relaxants, antispasmodics, some antidepressants
- Examples: Post-operative pain, Sprains, Broken bones, Bone metastasis, Arthritis, Muscle strains, Diabetic Foot Ulcers
Types of Pain: Nociceptive *Visceral*

- Involves solid organs
- Poorly localized
- Dull, achy, crampy in nature
- May refer to other areas
- Usually responds to opioids/non opioids
- May respond to steroids, antispasmodics
- Examples: Pancreatitis, Constipation-related, Bowel obstruction, Cancer in the liver or brain

**Persistent Pain**

- Previously called Chronic Pain
  - Common reason for seeking health care
  - Pain that serves no protective purpose
  - Pain that extends beyond the period of healing
  - Pain that disrupts sleep and normal living
  - Pathology often does not explain the presence or extent of the pain

Types of Pain: Neuropathic

- May be peripheral, central, sympathetically-maintained
- Sharp, shooting, stabbing, burning in nature
- First line of treatment, pregabalin, TCA's gabapentin and lidocaine
- Second line of therapy capsicain and opioids
- Examples: Post-herpetic neuralgia (shingles), Sciatica, Pain from strokes, Trigeminal neuralgia, Phantom limb pain, Peripheral neuropathy from diabetes, HIV or chemotherapy, MS, persistent pain after surgery/trauma
Pain

- Acute pain is a symptom
- Persistent pain is a disease
- Mixed pain is not uncommon in persistent pain
  - Diabetic Swollen feet and ankles with peripheral neuropathy

Multimodal Analgesia

- Use of two or more classes of analgesics
- Target different pain mechanisms in PNS or CNS
- Thoughtful rational combination
  - Maximize pain relief
  - Prevent analgesic gaps
  - Allow for lower doses of each
  - Potential for fewer adverse effects
Multi modal NOT poly pharmacy

• Polypharmacy suggests irrational, less effective, less safe regimes
• Avoid two different short acting opiates
• Avoid PO and IV medication for pain
• Avoid opiate only regimes

NSAIDS/APAP

• Unless contraindicated, this should be your first line of defense against pain
• Decrease synthesis of prostaglandins
• Analgesic (anti inflammatory NSAID)
• Contraindication high risk ETOH, cardiac, renal or GI
• Increasing age decrease use
• Cochrane meta analysis together better

• www.empr.com MPR resource center
  – Charts
  – List of NSAIDs by class
  – Usual doses
APAP

- Risk of adverse events is low
- Use with caution
  - Malnourishment
  - Recent fasting
  - Alcohol use
  - Liver disease
  - Concomitant use other hepatotoxic drugs
  - >65 Probably not at all >80

NSAIDS

- At equipotent doses, efficacy similar
- Individual responses highly variable
- Toxicities probably more entire class
- Fail NSAID of one class, trial of NSAID of another class reasonable
  - Trial at max anti inflammatory dose
  - Trial length 14 days

NSAIDS

- IV Calador & Ketorolac
- Long acting vs short acting
- Drug interactions (many more use calculator)
  - Highly protein bound drugs (not ASA)
    - Phenytoin
    - Warfarin
- Don’t forget topical NSAID
  - Low serum concentration
  - Voltaren, Pennsaid, Flector Patch
### Adjuvant Analgesics

- Primary indication other than pain
- Analgesic for some painful conditions
- More accurately
  - non traditional pain relievers
  - Co Analgesics
- Can be used as primary or as “add on” therapy
- Effective for both nociceptive and neuropathic

### TCA

- Modulate at the descending pathway
- Depression
- Effective, affordable SE may limit
- Elavil (amitriptyline)

### SNRI

- Synaptic Reuptake Blockers Serotonin Norepi
- Modulate at the descending pathway
- Fibromyalgia, diabetic neuropathy, neuropathy, chronic musculoskeletal pain
- Central pain Parkinson disease
- Duloxetine (Cymbalta)
SSRI
• Selective Serotonin Reuptake Inhibitors
• Paxil, Prozac
• Not as much analgesic efficacy as SNRI
• Probably advocate for TCA and SNRI

AED
• Anti convulsant drugs
• Analgesic specific mechanisms not known
• Have some effect on inhibiting the release of the excitatory neurotransmitters

AED
• Gabapentin (Neurontin) Post herpetic neuralgia
• Lyrica (pregabalin) Fibromyalgia, DNP, Spinal cord injury nerve pain
• Topamax (topiramate) Migraine
• Tegretol (carbamazepine) Trigeminal Neuralgia
Local Anesthetics

- Relieve pain by blocking sodium channels
- Significant anti-inflammatory effects
- Post herpetic shingles
- Lidocaine patches

Capsaicin

- Naturally occurring constituent of chili pepper
- Inhibits the release of substance P
- Inhibits the release of other inflammatory neurochemicals (soup)
- Post herpetic neuralgia pain

Qutenza

- 8% Capsaicin
- APRN must be trained, prepared to treat hypertension, excruciating pain, nausea
- Topical anesthetic to area to be treated
- Wear nitrile gloves, do not touch face mucous membranes!
- Apply patches for 60 minutes
- One treatment can relieve pain for 3 months
Metanx

- Medical food under medical supervision
- Active forms of common B vitamins
- Thought they improve blood flow to small arteries
- B6 supplementation >100mg daily may cause neuropathy. Metanx contains 35 mg

Non Pharmacologic

Not considered therapy by the National Center for Complementary and Alternative Medicine (NCCAM) patients may find them helpful

Treatments for pain include:

- Acupuncture
- Chiropractic
- Distraction
- Counseling, Therapy

Non Pharmacologic

- Guided Imagery
- Heat Therapy and Cold Therapy
- Hypnosis
- Music Therapy
- Physical Therapy
- Relaxation
- Transcutaneous Electrical Nerve Stimulation (TENS) -
Emu Oil

• Important to be odor free
• Apply 2-3 times per day to painful joints
• Used for years in Australia for painful skin and joints

Exercise is Medicine
Motion is Lotion

• Exercise and physical activity are effective non-pharmacologic therapeutic interventions for pain
• One resource Exercise is Medicine
• Assess and review every patient's physical activity program at every visit

One size does not fit all!

• Each person pain needs differ
  – Genetic differences
  – Previous experience with opiates
  – Smokers require more opiates
    • Nicotine blunts pain perception
    • Abrupt dc for admission pain medication needs
    • Permanent neurophysiological changes are probable
  – Very old, very young - start low, go slow, but go!
  – Pain intensity
Opiates

- Remember modulation (inhibition) of pain involves the release of dozens of neurochemicals by PNS & CNS
- Opiates bind to opioid receptor sites and mimic the actions of the endogenous opioid compounds
- Opioid also block the release of the presynaptic neurotransmitters like substance P

Opiates

- Short term versus long term
- Expect a 30% reduction in pain at most
  - So clearly should not be your only treatment
- For persistent non cancer pain, >100 mg morphine equivalent daily refer
- Long term opiates ↑ rate aberrant behaviors
  - Not in osteoarthritis

No codeine for children
Avoid in breast feeding women

- Dependent on hepatic metabolism CYP2D6 for conversion to morphine
- Wide genetic variability so analgesic and adverse effects are unpredictable
- Slow metabolizers ineffective analgesia 10%
- Ultra rapid metabolizers excessive morphine toxicity 30%
Morphine

- Gold standard
- Used for equianalgesia (morphine equivalents)
- IV/PO/SUBQ/PR/IO
- Hydrophilic slow onset, long duration
- Toxic metabolites M3G M6G
  - Delirium, myoclonus
- More sedating than Fentanyl or Dilaudid
- Histamine release itchy nose

Combination Opioids for Mild to Moderate Pain

All scheduled now
- Hydrocodone (Lortab, Vicodin) CII
- Oxycodone (Percocet, Percodan) CII
- Propoxyphene (Darvocet)
- Tramadol (Ultram, Ultrace) CIV

Single-Agent Opioids

- Used for moderate to severe pain
- No maximum dose
- Can be given by many different routes
- Long-acting forms available for chronic pain
- Morphine
- Hydromorphone
- **Meperidine**
- Methadone
- Oxycodone
- Fentanyl
- Oxymorphone
- Tapentadol
**Hydromorphone**

- Less sedating than other opioids
- Less nausea and vomiting
- Slightly shorter duration than morphine
- No problematic metabolites

**Equianalgesia**

- Patient on IV Morphine 2 mg every 4 hours
  - What is the PO dose?
- Patient on IV Dilaudid 2 mg every 4 hours
  - What is the PO dose?

**First Pass Effect**

Morphine 3:1
Hydromorphone 5:1
I am allergic to ........

- Demerol, Tylenol, Percocet, Morphine, Lortab, Codeine, Norco, Motrin, Darvocet, and Insulin.

The only thing that really works for me is
Online Equianalgesic Converter

- [http://www.globalrph.com/opioidconverter2.htm](http://www.globalrph.com/opioidconverter2.htm)

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Constipation

- **Most common side effect**
- **Never** develop a tolerance
- Always use bowel program with any opioids
- **Treatment**
  - increase fluids and fiber (in food)
  - increase activity
  - administer stimulant / laxative regularly
  - MUSH with NO PUSH

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Pain Management

- Even with limited resources, care should be guided by an understanding that pain is influenced by biomedical, psychological, and social/environmental factors, and treatment should be evidence-based and safe. To whatever extent possible, treatment should be multidisciplinary and aimed at alleviating pain, as well as improving patient physical function and psychological distress.
Be Prudent

- Don’t prescribe if you don’t know
  - Know why you chose each of the meds you used
  - Be sure the patient/family knows
- Educate yourself
  - % of patients with pain as presenting DX?
  - Show that % of education offerings attended

Protocol Requirements

- What does your protocol specifically say?
  - Does it say you can prescribe an opiate for a SORE THROAT?
  - If it does, how would you defend that?
- Don’t make changes to your practice without making sure your protocol is changed FIRST!

Protocol Requirements

- Disease or injury = class of drugs
- Loose-leaf notebook OR published protocols
- Kept at APRN principal workplace
- Cover page containing the following data:
  - names, telephone numbers, and signatures of APRN and responsible MD who authorized
  - date protocol was adopted or last reviewed; and
  - Must be reviewed at least annually
Legal Requirements

- Each written prescription must have
  - APRN name, address, phone
  - MD name, address, phone
  - Signature of the APRN with the letters A.P.R.N.
  And for a controlled substance
  - Contain the DEA number of the APRN

Without this, the pharmacy should not fill the prescription. This is OUR law!

Be Prudent

- Obtain informed consent
- Risk tool reasonable even for short term use
- Make sure patients/family understand the dangers of opiates around children, pets and other adults

<table>
<thead>
<tr>
<th>Opioid Risk Tool</th>
<th>Mark each box that applies</th>
<th>Item score if female</th>
<th>Item score if male</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Family history of substance abuse</td>
<td>Alcohol</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Illegals drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prescription drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Personal history of substance abuse</td>
<td>Alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Illegals drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prescription drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Age (mark box if 15-45)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4. History of preadolescent sexual abuse</td>
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</tbody>
</table>
Moderate Risk patients should be seen frequently, consider pill count
High Risk patients probably need to be referred to Pain Specialist
unless you have special knowledge/training/experience

Be Prudent

- A NICE treatment agreement
  - It is a two way street
  - Respect the patient, their life may have changed in
every aspect.
  - Be sure every member of your staff is on board
  - Should be done at the start of EVERY persistent
pain treatment plan NOT as punishment for
transgression

Never Set Limits when you are Angry

- Don’t say “No early refills will be granted”.
- Instead say “Running out of your medicine early is a complicated matter that can be confusing to your medical team. It could mean your pain is poorly controlled, it could mean you are losing control over how you use your medications, it could mean someone is borrowing or stealing your medicines.
What will you be held to?

- Clearly list the treatment goals you and the patient have set
- Discuss the OA yourself, don’t put it in a stack of papers you send out or have the clerk give
- Consider making it a three way agreement with the pharmacist involved as well

Be Prudent

- Urine drug screen for all scheduled and randomly
  - Everyone every 6 months
  - Deck of cards
  - Understand the results!!
- Patient (and you) are able to show objective measure of compliance to family, friends, employer
- Explain this in the opioid agreement

Document

- Diagnosis with appropriate differential
- Conduct both pre- and post-intervention assessments of pain level and function
- Prescribe an appropriate trial of opioid therapy, with adjunctive medication
- Reassess pain score and level of function
Document

- Regularly assess the "4 As" of pain medicine: analgesia, activity, adverse effects, and aberrant behavior
- Periodically review pain diagnosis and comorbid conditions, including addictive disorders
- Record initial evaluation and each follow-up visit

Plan ahead

- What will you say when someone wants more opiate than you want to prescribe?

Pain Management is an Art

- Treat patients the way you want to be treated
- Pain treatment is a trial
- If no improvement in function, no point in pain medication
  - Set your function goals, who will verify?
- An opiate alone is never the answer
- >100 mg Morphine equivalent Pain Specialist
- Fentanyl patch or Methadone ??
Best Practice

- Fewer than one third of physicians are following current recommendations and giving exercise advice to patients with osteoarthritis or sciatica, according to a balanced factorial experiment among 192 primary care physicians in the United States.
- Generally, newer physicians had greater adherence to current recommendations


Methadone Guideline

- Methadone Safety: A Clinical Practice Guideline From the American Pain Society and College on Problems of Drug Dependence, in Collaboration With the Heart Rhythm Society
- Published, April 2014
- Available on APS website.
- Never prescribe alone
Persistent Pain Guideline

- Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain
- The Annals of Internal Medicine recently published a systematic review and appraisal of guidelines for use of opioids to treat chronic pain.
- Of the 13 guidelines evaluated, only two received high scores on both ratings systems, this APS publication was one

American Pain Society

- APS planning to publish Post operative pain guideline before the end of the year
- APS planning to update Principles of Analgesic Use in the Treatment of Pain this year

National Guidelines

Neuropathic Pain

• Treatment guidelines exist
• American Academy of Neurology
• International Association for the Study of Pain
• European Federation of Neurological Societies

Neuropathic Pain

• Series of Meta Analysis and Systematic Reviews of Pharmacologic Therapies showing pregabalin, lidocaine plasters and opiates as most effective

INCORRECT Beliefs

• Physical or behavioral signs of pain (e.g., abnormal vital signs, grimacing, limping) are more reliable indicators of pain than patient self-report.
• Elderly or cognitively impaired patients cannot use pain intensity rating scales.
• Pain does not exist in the absence of physical or behavioral signs or detectable tissue damage.
INCORRECT Beliefs

• Pain without an obvious physical cause, or that is more severe than expected based on findings, is usually psychogenic.

• Comparable stimuli produce the same level of pain in all individuals (i.e., a uniform pain threshold exists).

INCORRECT Beliefs

• Prior experience with pain teaches a person to be more tolerant of pain.

• Analgesics should be withheld until the cause of the pain is established.

• Noncancer pain is not as severe as cancer pain.

INCORRECT Beliefs

• Patients who are knowledgeable about pain medications, are frequent emergency department patrons, or have been taking opioids for a long time are necessarily addicts or “drug seekers.”

• Use of opioids in patients with pain will cause them to become addicted.
INCORRECT Beliefs
• Patients who respond to a placebo drug are malingering.
• Neonates, infants, and young children have decreased pain sensation.

Opioid Induced Sedation
• Beware the Basal!
• Cocktails belong only in a bar!
• Unless the diet order is NPO, pain medication should be delivered by the cheapest, easiest, least dangerous way-Per Os

Opioid Induced Sedation
• Respiratory rate, depth and regularity is the best assessment of the sleeping patient
• Never depend upon an intermittent SpO2
• Snoring is always a warning sign
  – Respond immediately
  – Reposition
## POSS Intervention

<table>
<thead>
<tr>
<th>POSS</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>8: Sleep, easy to arouse</td>
<td>Acceptable; no action necessary; may increase opioid dose if needed</td>
</tr>
<tr>
<td>7: Awake and alert</td>
<td>Acceptable; no action necessary; may increase opioid dose if needed</td>
</tr>
<tr>
<td>6: Slightly drowsy, easily aroused</td>
<td>Acceptable; no action necessary; may increase opioid dose if needed</td>
</tr>
<tr>
<td>5: Frequently drowsy, arousable, drifts off to sleep during conversation</td>
<td>Unacceptable; stop basal rate. If patient has no basal rate, reduce PCA bolus dose by 50%. Notify managing MD. Monitor POSS, respiratory status, and pain rating every 15 minutes until POSS is less than 3.</td>
</tr>
<tr>
<td>4: Somnolent, minimal or no response to physical stimulation</td>
<td>Unacceptable; or respiratory depression (respiratory rate 8/minute or less): Stop PCA pump, stimulate patient, support respirations as needed, call rapid response team, have managing physician notified, give IV dilute Naloxone (0.4mg of Naloxone per 10 ml normal saline) 0.5ml over 2 minutes; repeat this dose until POSS is less than 4 and respirations are more than 8. Monitor POSS, respiratory status, and pain rating every 15 minutes until POSS is less than 3 for more than one hour.</td>
</tr>
</tbody>
</table>

## References

American Society of Pain Management Nursing position statement on pain assessment in patients who cannot self-report:


## Reference


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Reference


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References


Opioids Polymorphism

or

Why some patients have more pain than others
Known Genetic Differences

- OPRMI-A118G & COMT
  - Consumed less morphine with PCA
  - Less nausea and vomiting
- Polymorphism at A118
  - More headaches
- Single-nucleotide polymorphism at GCHI
  - Makes certain women more sensitive to early labor pain as cervix dilates

Known Genetic Differences

- COMT haplotype GCGG
  - Higher pain scores, use more opiates, higher HR
- Oxycodone after quinidine inhibited CYP2D6
  - Decreased peak effect of opiate
- Oxycodone after ketoconazole inhibited CYP3A
  - Dramatic increase in medication efficiency and oxycodone toxicity

Great Information!

- Fundamentals of Pain Management: An Interdisciplinary Primer
- American Pain Society
- Online session recordings 2014 course
- 16 sessions
Online Learning

• Medscape Education Pain Learning Center
• Department of Pain Medicine and Palliative Care at Beth Israel Medical Center (New York) has online CME available (IOA)
• Virginia Commonwealth University School of Medicine Online access can be purchased

Online Learning

• McGill University is offering an online Graduate Certificate in Chronic Pain Management for health professionals who wish to enhance their knowledge and learn the latest developments in the assessment and treatment of chronic pain conditions.
• 15 hours

ASPMN

• Certified Pain Nurse
• Certified Advanced Practice Pain nurse
• ASPMN webinars
• ASPMN/Prescribers Support Opioids