Pain Management in Palliative Care

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50th Annual Scientific Meeting
Florida ACP

09/07/2018
Disclosure

• I have no financial relationships to disclose.
Objectives

At the end of this lecture, the learner should be able to:

1. Define pain.
2. Evaluate a patient with a complaint of pain.
3. Describe the different types of pain.
4. Explain the basic principles of the pharmacokinetics and pharmacodynamics of opioids commonly used in Palliative Care.
5. Address common misconceptions and barriers concerning pain management in Palliative Care.
6. Differentiate between dependence, addiction and pseudoaddiction.
What I will not be talking about

• Chronic pain management.

• The new opioid law (HB21).

• Details of interventional procedures.

• Palliative Sedation for refractory pain.

• Therapy for opioid addiction.
What is Palliative Care?

• Definition: The active **total care** of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms and of psychological, social and spiritual problems is paramount.

• Its goal is the achievement of the best quality of life for patients and families.

Tough Questions:

• What is the **hardest** pain to bear?

• What is the **easiest** pain to bear?
Definition of Pain

• Unpleasant sensory and emotional experience.

• Associated with actual or potential tissue damage.

• Subjective.

• Complex biopsychosocial event.

Concept of Total Pain

• Physical pain
• Psychological / emotional pain
• Spiritual or existential pain
• Social or Interpersonal pain

– Interdisciplinary team is vital in assessment and management!

Prevalence

- Seen in many end stage diseases
- Common in cancer
  - 70–90% in latter stages of illness
  - 33-70% in patients receiving treatment

Evaluation of Pain

• History

• Examination

• Investigations- Imaging, Organ function assessment.

• Multidimensional approach frequently needed.
History

• PQRST...

• O- Onset
• P- Position
• Q- Quality *
• R- Radiation
• S- Severity *
• T- Timing *
• A- Associated features
• A- Aggravating Factors*
• A- Alleviating Factors *
Classification of Pain

• NOCICEPTIVE
  – Somatic
    • (Well localized/ aching/ gnawing/sharp/ movement)
  – Visceral
    • (less localized/ usually constant/ may be referred)

• NEUROPATHIC
  • Burning, distributed along path of nerves/ roots
  • Assoc. with
    – Dysthesia (numbness and tingling),
    – Hyperalgesia (exaggerated response)
    – Allodynia (pain from stimuli which should not normally cause pain).

# Pain Severity Assessment Tools

<table>
<thead>
<tr>
<th>Descriptor Differential Scale (DDS) (Alert and nonimpaired adults)</th>
<th>Self-report in 12-item questionnaire</th>
<th>Good reliability and is sensitive to even small changes in pain intensity(^\text{11}) (^\text{12})</th>
<th>Easy for patients to use but requires some training for health care team to interpret</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discomfort in Dementia (DS-DAT) (Adults with dementia or Alzheimer’s disease)</td>
<td>Observational 9-item tool for completion by staff over 5-minute assessment period</td>
<td>Inter-rater variability exists in 3 of the 9 items</td>
<td>Requires staff training to administer accurately</td>
</tr>
<tr>
<td>Edmonton Symptom Assessment System (Palliative care patients, typically end-of-life cancer patients)</td>
<td>Twice-daily assessment using 8 visual analog scales to be completed by patient alone or by patient with assistance (from nurse or family member)</td>
<td>Validation evidence is not robust(^\text{12})</td>
<td>Data from the 8 scales are transferred to a graph; the sum of all scores is the “symptom distress score” Has been translated into several languages</td>
</tr>
<tr>
<td>FACES (Wong-Baker) (Pediatric patients [age 3 to 7] treated for acute pain in emergency department)</td>
<td>Self-report using 6-item ordinal scale made up of 6 faces showing no pain (smiling face) to worst pain imaginable (grimace)</td>
<td>Validated with good agreement between FACES and visual analog scale(^\text{13})</td>
<td>May also be used for adults when there is a language barrier</td>
</tr>
<tr>
<td>Loeskenze-Allognctional index (1987, 1991, 1997) (Adult pain patients with circadian types of pain)</td>
<td>Self-report in 10-item questionnaire that puts pain in temporal context, pain at night, upon rising and situations (pain standing, pain walking, and so on)</td>
<td>Validated</td>
<td>Easy to administer, takes about 10 minutes, and is well suited for pain that fluctuates over course of day</td>
</tr>
<tr>
<td>Mankowski Pain Scale (Developed for endometriosis patients but used with other types of chronic pain)</td>
<td>Self-report on 0 to 10 scale with descriptions to help better quantify pain (for example, 5=“pain that can’t be ignored for more than 30 minutes; mild painkillers reduce this pain about 3 or 4 hours”)</td>
<td>Validated for chronic pain patients (not just endometriosis patients)(^\text{14})</td>
<td>Developed by Andrea Mankowski, a chronic pain patient</td>
</tr>
<tr>
<td>McGill Pain Questionnaire (MPQ) (Adults with various pain syndromes)</td>
<td>Self-report, 20 items grouped as sensory, affective, evaluative, and miscellaneous; patients score each 0 to 5. The Pain Rating Index (PRI) is the sum of the rank values</td>
<td>Validated and designed to better capture the subjective experiences of pain patients(^\text{15})</td>
<td>Also rates the Present Pain Index (PRI) as a separate scale (0–5)</td>
</tr>
<tr>
<td>Neck Pain and Disability Scale (NPDS) (Adults with cervical pain syndromes)</td>
<td>Self-report of 20 items as visual analog scales with descriptors, describing different aspects or behaviors associated with the neck</td>
<td>Reliable, internally consistent, correlates well with other scales(^\text{16})</td>
<td></td>
</tr>
<tr>
<td>Numerical Rating Scale (NRS) (Adult and pediatric pain patients)</td>
<td>Self-report on scale of 0 to 10 with 0 meaning “no pain at all” and 10 “the worst pain imaginable”</td>
<td>Reliable, validated, widely used</td>
<td>Minimal training required, easy for patients to understand; measures pain intensity only</td>
</tr>
</tbody>
</table>

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Pain Severity Assessment Tools

• Limitations:
  – May not express true severity, impact
  – Numerical, verbal ratings may be inconsistent
  – Observer bias: patient should do own assessment if possible
  – Comprehensive tools too long for very ill patients
Pharmacological Options

• Non Opioid Analgesics

• Adjuvant Drugs

• Opioid Analgesics

Non Opioid Analgesics

• **Acetaminophen**
  – < 4 g /day; central and peripheral action; caution liver Dz

• **NSAIDs**
  – Peripheral and central action.; GI /renal toxicity;
  – Increased risk of GI bleeding
  – Consider GI protection

• **Tramadol**
  – Synthetic analgesic with opioid/ non opioid properties
  – Centrally acting
  – Pro drug → O-desmethyltramadol
  – 5-10% of the population don’t metabolize it → little/ no analgesic effect
  – Can be regarded as “Double strength Codeine”
Adjuvant Drugs

• **Corticosteroids**
  – bone pain/tissue edema/ spinal cord compression/ ↑ICP

• **Tricyclic antidepressants**
  – neuropathic pain; side effect profile/ watch elderly

• **Anticonvulsants**
  – Neuropathic pain. Watch liver function and bone marrow suppression

• **Bisphosphonates**
  – Bone pain, MM, Breast cancer, osteoporosis with past fracture

• **Muscle relaxants**
  – Side effects- sedation and anticholinergic side effect profile

• **Anesthetics**
  – Ketamine- Controversial

Opioids

• **Weak**
  – Codeine
  – Propoxyphene
  – Hydrocodone

• **Strong**
  – Morphine
  – Oxycodone
  – Fentanyl
  – Methadone
  – Meperidine
  – Sufnetanil
  – Alfentanil

• **Partial agonists**
  – Buprenorphine
WHO Pain Ladder

Pain score 1-3
- Non-opioid
  ± Adjuvant

Pain score 1-3
- Opioid for mild to moderate pain
  + Non-opioid
  ± Adjuvant

Pain score 4-6
- Pain persisting or increasing
- Opioid for moderate to severe pain
  ± Non-opioid
  ± Adjuvant

Pain score 7-10
- Freedom from cancer pain

Pharmacokinetics of Opioids

• Morphine and codeine are relatively poorly absorbed from the GI tract.

• Bioavailability further reduced by metabolism in gut wall and liver.

• All opioids are bound to protein but to different degrees (Fentanyl 80-86%; Morphine 20-35%).

• Most opioids have large volume of distribution.

• Fentanyl and Methadone are most lipophilic.

# Pharmacokinetics of Opioids

<table>
<thead>
<tr>
<th>Kinetic Parameters (Chart)</th>
<th>oral bio-availability (avg)</th>
<th>onset of effect</th>
<th>average half life (hr.)</th>
<th>plasma protein binding</th>
<th>typical duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>codeine</td>
<td>70-90%</td>
<td>45-60m</td>
<td>prodrug</td>
<td>7.25%</td>
<td>4-6h</td>
</tr>
<tr>
<td>pethidine</td>
<td>40-80%</td>
<td>20-40m</td>
<td>3-5h</td>
<td>60-80%</td>
<td>2-4h</td>
</tr>
<tr>
<td>morphine</td>
<td>30-40%</td>
<td>30-45m</td>
<td>2.4h</td>
<td>35%</td>
<td>3-4h</td>
</tr>
<tr>
<td>oxycodone</td>
<td>60-80%</td>
<td>45-60m</td>
<td>3.5h</td>
<td>45%</td>
<td>4-6h</td>
</tr>
<tr>
<td>hydrocodone</td>
<td>60-80%</td>
<td>45-60m</td>
<td>3.5h</td>
<td>unknown</td>
<td>4-6h</td>
</tr>
<tr>
<td>hydromorphone</td>
<td>24%</td>
<td>30m</td>
<td>2.6h</td>
<td>8.19%</td>
<td>2-3h</td>
</tr>
<tr>
<td>oxymorphone</td>
<td>10%</td>
<td>20-40m</td>
<td>1.3h</td>
<td>10-12%</td>
<td>3-4h</td>
</tr>
<tr>
<td>levorphanol</td>
<td>~50%</td>
<td>20-40m</td>
<td>11-16h</td>
<td>40%</td>
<td>4-8h</td>
</tr>
<tr>
<td>methadone</td>
<td>80%</td>
<td>60-90m</td>
<td>22h</td>
<td>80-90%</td>
<td>6-12h</td>
</tr>
<tr>
<td>fentanyl</td>
<td>~10-15%</td>
<td>10-20m</td>
<td>3.5h</td>
<td>85%</td>
<td>1-2h</td>
</tr>
<tr>
<td>buprenorphine</td>
<td>~10-15%</td>
<td>60m</td>
<td>36h</td>
<td>96%</td>
<td>4-12h</td>
</tr>
<tr>
<td>tramadol</td>
<td>70%</td>
<td>60-90m</td>
<td>6-7h</td>
<td>20%</td>
<td>4-6h</td>
</tr>
<tr>
<td>tapentadol</td>
<td>30-40%</td>
<td>30-45m</td>
<td>4.5h</td>
<td>20%</td>
<td>2-4h</td>
</tr>
</tbody>
</table>

Demaree, R Accessed from Pinterest at [https://www.pinterest.com/robertdemaree/opioids/?lp=true](https://www.pinterest.com/robertdemaree/opioids/?lp=true) on 07/16/18
Pharmacokinetics of Opioids

• Metabolized to more hydrophilic compounds predominantly through glucoronidation.

• Most metabolites are less active than parent compounds but some are more active e.g. morphine is a metabolite from codeine and morphine-6-glucuronide from morphine.

• Some metabolites like morphine-3- glucuronide and hydromorphone-3-glucoronide cause neurotoxic side effects (myoclonus and confusion)

Pharmacokinetics of Opioids

• Metabolites are excreted in the urine so they may accumulate in renal failure.

• Methadone is the exception as it is metabolized via the Cytochrome P450 system and the major route or excretion is fecal.

• Oxycodone, fentanyl and methadone have no active final metabolites.
Pharmacodynamics

- Opioids bind to opioid receptors in the CNS (thalamus, periacqueductal grey matter and dorsal horn of the spinal cord.)
- Receptors also in lungs, myenteric plexus of the GI tract and other areas where their function is not clear.
- The μ receptor → Analgesia/ resp depression
- The δ receptor → GI Motility/ mood behaviour/CVS/ convulsant effects
- The κ receptor → sedation, dysphoria, miosis
EOL PROFESSIONALS present

MORPHINE SIDE EFFECTS

CONFUSION
DECREASE DOSE or
ADD ANTIPSYCHOTIC

SEDATION
20-60%

BLURRED VISION
Stimulation of Edinger-Westphal nucleus causing pupillary constriction

HALLUCINATION

DRY MOUTH
Anticholinergic stimulation
USE MOVEMENT ABLATION

NAUSEA and VOMITING
Stimulation of chemoreceptor trigger zone increased sensitivity decreased gastrointestinal motility
USE TARGETED ANTIEMETICS

ITCH
Try antihistamine or switch to oxycodone

URINARY RETENTION
Decreased bladder tone decreased urine contraction decreased voiding reflex
MAY NEED INDWELLING CATHETER

CONSTITUTION
40-45%

ENDOCRINE
SEXUAL DYSFUNCTION

FATIGUE DEPRESSION
OSTEOPOROSIS

IMMUNE RESPONSE

MYOCLONUS

©TheVil propulsion @ericpress

Practical Points

• Think of q 4 hourly dosing prn when opioid naïve. Don’t start with long acting agents.

• Schedule if pain is expected to be constant.

• Starting dose for oral morphine? 5-10mg po.

• Smaller doses for frail, elderly and organ dysfunction.

• Opioids are all not dose equivalent.
### Equianalgesic Opioid Dosing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Equianalgesic Doses (mg)</th>
<th>Parenteral</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td></td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td></td>
<td>0.3</td>
<td>0.4 (sl)</td>
</tr>
<tr>
<td>Codeine</td>
<td></td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Fentanyl</td>
<td></td>
<td>0.1</td>
<td>NA</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td></td>
<td>NA</td>
<td>30</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td></td>
<td>1.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Meperidine</td>
<td></td>
<td>100</td>
<td>300</td>
</tr>
<tr>
<td>Oxycodone</td>
<td></td>
<td>10*</td>
<td>20</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td></td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Tramadol</td>
<td></td>
<td>100*</td>
<td>120</td>
</tr>
</tbody>
</table>

*Not available in the US

McPherson ML. Demystifying Opioid Conversion Calculations: A Guide For Effective Dosing. Amer Soc of Health-Systems Pharm, Bethesda, MD, 2010. Copyright ASHP, 2010. Used with permission. NOTE: Learner is STRONGLY encouraged to access original work to review all caveats and explanations pertaining to this chart.
## Practical Points

<table>
<thead>
<tr>
<th>daily morphine dose range</th>
<th>methadone conversion ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30mg</td>
<td>2/1</td>
</tr>
<tr>
<td>30-99mg</td>
<td>4/1</td>
</tr>
<tr>
<td>100-299mg</td>
<td>8/1</td>
</tr>
<tr>
<td>300-499mg</td>
<td>12/1</td>
</tr>
<tr>
<td>500-999mg</td>
<td>15/1</td>
</tr>
<tr>
<td>&gt;1000mg</td>
<td>20/1</td>
</tr>
</tbody>
</table>

More on Methadone

- Can be used in renal impairment.
- Neuropathic and somatic pain relief.
- Only long acting liquid opioid.
- Long half life.
- Check QTc
Practical Points

• Consider long acting agents when patient consistently needs short acting initial regimen (at least 4 short acting doses a day.)

• Breakthrough dosing should be 10-15% of the Total Daily Dose.

• When converting opioids, look at the total daily dose and convert using the Equianalgesic table.

• Reduce dose by 25%-33% when rotating
Basal vs Breakthrough Analgesia

TIME/ Hrs.

PAIN INTENSITY

OPIOID BLOOD CONC.
Practical Points

• Once the patient can safely swallow, use the oral route.

• I hardly ever recommend transdermal Fentanyl in the Palliative population.

• Always consider Adjuvants.

• Try to understand the patient’s outpatient pain regimen before “starting over” with low dosing on admission.
Non Pharmacological options

• Radiation therapy.

• Relaxation therapy/ Mindfulness.

• PT/ OT.

• Transcutaneous Electrical Nerve Stimulation.

• Accupuncture.

• Interventional – Good immediate relief but long term relief usually lacking.
Opioid Myths

• Opioids hasten death in the terminally ill.
• Injectable morphine works better than oral.
• Strong opioids should be considered only when death is imminent.
• Normal vital signs mean that there is no pain.
• Using opioids in patients with end stage COPD or heart failure will result in respiratory depression.
• Opioid use will lead to addiction.
• The opioids caused AMS/ sedation.

Barriers to pain management

• Patient / family
  – Myths about inevitability of pain.
  – Fears about opioids: addiction, side effects, confusion, effectiveness.
  – Pain management at terminal stage.
  – Culture, religion.
  – Social, economic factors.
Barriers to pain management

• Interdisciplinary team
  – Inadequate education.
  – Fears, myths.
  – Not prioritizing pain management.
  – Failure to manage adverse effects.
  – Inadequate follow-up processes.
  – Limited accessibility to resources.
Barriers to pain management

• System
  – Lack of standards.
  – Lack of priority for pain.
  – Lack of specialized resources.
  – Regulations that restrict opioid use.
  – Fear of legal actions.
Opioid stigma is keeping many cancer patients from getting the pain control they need

By SARA RAY and KATHLEEN HOFFMAN / JULY 8, 2019

History is repeating itself. Twenty years ago, a pain management crisis existed. As many as 70 percent of cancer patients in treatment at that time, or in end-of-life care, experienced unrelieved pain. Identified as a major medical problem, poor pain management became synonymous with poor medical care. In fact, everything about it...
Addiction

• Primary, chronic neurobiological disease with genetic, psychosocial and environmental factors influencing its development and manifestations.

• Characterized by
  – Impaired control over drug use
  – Compulsive use
  – Continued use despite harm
  – Craving

Physical Dependence

- A state of adaptation manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug &/or administration of an antagonist.

Pseudoaddiction

• Syndrome of behavioral symptoms that mimic those seen with psychological dependence, including an overwhelming and compulsive interest in the acquisition and use of opioids.

Management of Opioid Overdose In Palliative Care

• Clinical features
  – RR < 8/min
  – Reduced responsiveness
  – Cyanosis
• Naloxone is rarely used but can be necessary
• Look for an underlying cause
• Unless outright apnea, don’t push an ampoule of Naloxone ➔ pain crisis
• If patient is arousable, pulse oximetry and observation
• If not arousable/ desaturating...
Management of Opioid Overdose In Palliative Care

• Stop the opioid

• Oxygen via facemask

• Dilute 1 ampoule of Naloxone (0.4mg) in 9 ml NS

• Give 1-2 ml of this diluted Naloxone (0.04mg) until more responsive

In Summary

• We defined pain.- It’s complicated!
• You can’t beat a good history and Physical exam.
• Opioids are useful but dangerous in the wrong hands (like Fire!) - Follow the rules and stay safe.
• Dependence / Addiction/ Pseudoaddiction-Know the difference!
• Overdose?- Look for a cause. Gentle reversal with diluted Naloxone.
Thank You!

Questions?