Pain in End of Life Care: Barriers, Principles and Goals

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OBJECTIVES

Participants will learn:
1. Barriers and stigmas related to end of life pain control.
2. The key differences and appropriate medications used to treat varying pain ailments.
3. Use of evidence based medicine to develop and implement patient-specific treatment modules to manage end of life pain.

The Basics

- Palliative care consists of treatment and support to improve QUALITY OF LIFE for the patient and their families, by reducing suffering.
- In a cross-sectional, stratified random national survey of seriously ill patients, recently bereaved family members, physicians, and other healthcare workers, over 70% of each group identified freedom of pain as the most important attribute of care (P < 0.001).
What is Pain?


The Numbers

- In 2014, 14.5% of the US population is aged 65 or older
- Estimated that 45-85% of this population experiences pain, much of it undertreated, which can cause unwanted effects
- 76-90% of hospice patients have pain documented
- Cost for repeat hospitalization and physician visits can be staggering
- Over 50% of patients die in the hospital though some may prefer to die at home

Richard

Richard is an 84 yoM, with end stage Alzheimer’s. With great thought and deliberation, the family has elected hospice care. Despite use of appropriate medications for his agitation, Richard continues to lash out and retract from patient care. His healthcare team continues to titrate his agitation/anxiety medications, and at times, IM administration is given, yet nothing is effective.

WHAT ARE WE MISSING?
Never forget that the patient is a fellow creative in pain, not a mere vessel of disease

Prayer of Maimonides

**What is the concept of pain?**
- Pain is a symptom; observed and explored in pursuit of a diagnosis vs.
- Pain is a symptom; observed and treated as a means of comfort

**Competing models**
- Curative: Dichotomizes the physical and mental; physical vs.
- Palliative: "Bodies do not suffer; persons do"

Hospice can be crucial in improving quality of life, but too many people are admitted with days to weeks left
- ‘Don’t give up hope’

### Model of Healthcare

<table>
<thead>
<tr>
<th>CURATIVE</th>
<th>PALLIATIVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analytic and rational</td>
<td>Humanistic and personal</td>
</tr>
<tr>
<td>Solve/ cure diagnosis</td>
<td>Appeal to symptom management</td>
</tr>
<tr>
<td>Pursuit of a riddle</td>
<td>Pursuit of comfort</td>
</tr>
<tr>
<td>Scientific objectivity</td>
<td>Patient’s subjectivity</td>
</tr>
<tr>
<td>Terminal diagnosis: end of a journey</td>
<td>Terminal diagnosis: beginning of a new challenge</td>
</tr>
<tr>
<td>Death = enemy</td>
<td>Death = end</td>
</tr>
<tr>
<td>Physician failure: not curing</td>
<td>Physician failure: not respecting patient’s way to die</td>
</tr>
</tbody>
</table>

Based on the model of healthcare relationship, this could lead to a failure to identify pain as priority.

**Richard**

After making the appropriate diagnosis of pain related agitation, Richard has been started on MS Contin 15mg PO BID with morphine IR 15mg Take ½-1 tab PO q4h PRN pain. After 4 days, the patient has responded to treatment, but continues to have shortness of breath, outbursts of yelling (especially upon assisted care) and sweating. Despite using 4 tabs of morphine 15mg/24 hours, the doctor feels uncomfortable increasing the dose of MS Contin or PRN dose of morphine.
What are we teaching in healthcare schools? Limited at best
- Passed on from one generation to the next, virtually unchanged despite numerous advances and theories
- Cultivation and propagation of ignorance
- Balance of ‘good physician’ with ‘good patient’

Widespread lack of knowledge to nursing and pharmacy school
- Medical and geriatric texts say very little about pain management
- Few psychometric instruments have yet to be standardized for evaluation of pain in elderly

With the lack of knowledge, comes the fear of prescribing opioids
To avoid regulatory scrutiny, clinicians under-prescribe to stay ‘under the radar’
Physician’s duty: to prevent drug diversion vs. managing pain
- Acute vs. chronic pain
  - Acute pain: short PRN medications
  - Chronic pain: use of sustained release medications for an extended amount of time, which may require frequent titration
### Ethical Question
- **Moral authority & responsibility to treat pain as a true symptom**
- **Healthcare professionals that purposely avoid to manage pain effectively due to lack of skill or fear may be in a violation of ethics**
  - Initiating new medication
  - Lowering doses
  - Using less effective analgesics, when not indicated

### Debunking the Current Legal Myths

<table>
<thead>
<tr>
<th>Myth</th>
<th>Reality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forgoing life-sustaining treatment without capacity requires evidence</td>
<td>A surrogate may delegate decisions; few states require 'clear and convincing evidence'</td>
</tr>
<tr>
<td>Withholding artificial nutrition/fluids is illegal</td>
<td>May be withheld if patient refuses or a surrogate may delegate decisions</td>
</tr>
<tr>
<td>Risk management personnel must be consulted prior to termination of life-sustaining treatment</td>
<td>No legal requirement (may be location specific policy)</td>
</tr>
<tr>
<td>Advance directives must be particularly stated</td>
<td>May be used, even if all legal formalities not met; oral statements made by patient may suffice</td>
</tr>
</tbody>
</table>

### Debunking the Current Legal Myths

<table>
<thead>
<tr>
<th>Myth</th>
<th>Reality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criminally prosecuted, if healthcare professional prescribes/ administers high doses of medication for symptom management resulting in death</td>
<td>Healthcare worker has not committed murder or assisted suicide</td>
</tr>
<tr>
<td>No legal permissible options to ease suffering/hasten death for terminally ill patient</td>
<td>While physician-assisted suicide illegal in most states, terminal sedation is not</td>
</tr>
<tr>
<td>1997 Supreme Court decisions outlawed physician-assisted suicide</td>
<td>Legal in Oregon; each state is free to legalize or prohibit it</td>
</tr>
</tbody>
</table>
The healthcare team has now decided to increase the MS Contin to 45mg PO BID and morphine IR 15mg Take 1-2 tabs PO q4h PRN pain. Before initiating this regimen, the family now intervenes, and does not want ‘this much morphine’ for their elderly father.

**Richard**

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**Family Limitation**

- Fear of ‘hospice’ or ‘morphine’
- Admission of hospice is equivalent to giving up
- Willing to try invasive techniques or tests to ‘keep dad comfortable’ or to cure
- Cultural sensitivity
- Family’s discord can lead to a misrepresentation of pain (or other symptoms)
- Assuming the role of caregiver

**When is it too much?**

- Irrational belief regarding addiction, dependence & tolerance
  - Outliers define practice
  - Opiophobia
- The difference between dependence that develops to opioid analgesics vs. the dependence that characterizes addiction
- Need for higher doses is likely related to the progression of disease
- Fewer than 1/20,000 patient prescribed opioids become addicted
- Recent hydrocodone rescheduling to Schedule II
Study of Family Caregivers

- Use of The Barriers Questionnaire
  - 62-100% of caregivers reported some type of concern
    - Subscales:
      - Fear of opioid side effects
      - Fear of Addiction
      - Belief that increased pain signifies disease progression and therefore hesitation to report pain
      - Fear of injections
  - Most caregivers who were older and less educated believed that reporting pain may distract the physician from ‘curing’ the cancer
    - Good patients do not complain

Corrective Actions

- Barriers:
  - Current continuum of the healthcare model
    - Educating health care facilities of the GOALS of end of life care (comfort vs. cure)
  - Change in the patient
    - Clear & timely discussion about pain management, aging process & what to expect with the patient with respect and dignity

Corrective Actions (con’t)

- Limitation of proper end of life pain management in school
  - AMA secured a project: Physicians on End-of-Life Care (EPEC)
  - A push towards EOL modules in all healthcare classroom & residency study
- Fear of regulation scrutiny
  - Obtain clear guidance from federal & state regulatory agencies
  - Establish policies & protocols
  - Motivate truly caring clinicians to organize & challenge regulatory scrutiny
Corrective Actions

- Barriers (con’t)
  - Family limitations
  - Grief or family counseling
  - Educational pamphlets & discussion
    - Recent study found that 35% of hospice patients & 20% of families reported receiving inadequate emotional support. Same study found >30% of families had concerns regarding the information that was supplied to them.
  - Irrational beliefs regarding addiction, dependence, & tolerance
  - Insightful pain management
  - EDUCATION!

Pain Evaluation

- Begins with recognizing, evaluating & monitoring pain
- Achieving pain control requires knowledge and skills on pharmacologic, behavioral, social & communication strategies
- Frequent communication with the family seeks to address medical progress & to adjust plan of care or goals

Pain Scale

<table>
<thead>
<tr>
<th>Pain</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face</td>
<td>☹</td>
<td>😞</td>
<td>😐</td>
<td>😐</td>
<td>😐</td>
<td>😐</td>
<td>😟</td>
<td>😠</td>
<td>😡</td>
<td>😡</td>
<td>😡</td>
</tr>
</tbody>
</table>

Accessed through fpnotebook.com
### Pain Scale

**Nonverbal Pain Scale, based on Faces, Legs, Activity, Cry, Consolability Scale**

<table>
<thead>
<tr>
<th>Categories</th>
<th>0</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face</td>
<td>No particular expression or activity</td>
<td>Occasional grimace, tearing, frowning, unrelaxed forehead</td>
<td>Frequent grimace, tearing, frowning, unrelaxed forehead</td>
</tr>
<tr>
<td>Activity (movement)</td>
<td>Lying quietly, normal position</td>
<td>Seeking attention through movement or sound, carded</td>
<td>Reaching for an object, uncontrolled movements</td>
</tr>
<tr>
<td>Gait</td>
<td>Lying quietly, no positioning of hands or arms of body</td>
<td>Sprawling areas of the body, total</td>
<td>Rigid, still</td>
</tr>
<tr>
<td>Phasic (vital signs)</td>
<td>Stable vital signs</td>
<td>Change in any of the following: * HR &gt; 200 * BP &gt; 150/95</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>Baseline</td>
<td>* HR &gt; 10 above baseline or 15% * BR &gt; 20 above baseline or 20%</td>
<td></td>
</tr>
</tbody>
</table>

**Critical Care Pain Observation Tool**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial expression</td>
<td>No move or broken observed</td>
<td>0</td>
</tr>
<tr>
<td>Bones</td>
<td>Absent, rigid</td>
<td>0</td>
</tr>
<tr>
<td>Head movements</td>
<td>Absent movements</td>
<td>0</td>
</tr>
<tr>
<td>Body movements</td>
<td>Absent movements</td>
<td>0</td>
</tr>
<tr>
<td>Muscle tension</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Evolvement by passive tension</td>
<td>Weakness, rigidity</td>
<td>0</td>
</tr>
<tr>
<td>Compliance with ventilator</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Compliment with ventilator</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Total score</td>
<td>0-4</td>
<td></td>
</tr>
</tbody>
</table>

### The Changing Patient

- May be more sensitive to severe pain
- Delays
- Decreased tolerance
- Evolving physiology that occurs with aging
  - Structure, biochemical and functional changes in the peripheral nervous system
    - Decrease in fibers
    - Reduction of neurotransmitter systems
    - Slowing in nerve conductivity
  - Changes in drug metabolism
    - Renal/hepatic
  - Volume of distribution
The Changing Patient\textsuperscript{2, 11}

- Cognitive impairment
- Multiple co-morbidities, therefore many medications
- Atypical presentation of pain
  - May choose not to report pain due to fear of involuntarily hospitalization, subject to invasive procedures or could be intimidated by their clinician
- Older patients could be misinformed about pain management and analgesics

Treating Pain in the Elderly

- According to the American Geriatric Society\textsuperscript{11}
  - Use the least invasive route of administration
  - Choose sustained release medications
  - Introduce one agent at a time; start low & titrate slowly
  - Allow a sufficient interval to assess the validity of the pain medication
  - Treatment should be monitored & adjusted accordingly
  - Switch opioids as necessary

World Health Organization: Step Wise Approach\textsuperscript{12}

[Diagram showing the step-wise approach for pain management in elderly patients]
Types of Pain

- Nociceptive Pain
  - Muscle, tissue or organ pain
  - May or may not radiate
  - Patient may describe as dull, aching, or throbbing
- Neuropathic Pain
  - Nerve pain
  - Shooting, stabbing, radiating
- Bone pain
  - Inflammatory pain
  - Pain with movement

Pharmacological Options

- Pharmacologic treatment by type of pain
  - Nociceptive: NSAIDS, opioids, combination
  - World Health Organization (WHO) guidelines
  - Morphine (#1 recommended for severe pain)
  - Neuropathic
    - Anticonvulsants
    - Antidepressants
    - NMDA Antagonist: Methadone
  - Bone pain:
    - Anti-inflammatory
    - Decrease osteoclast activity

Mild Nociceptive Pain

- Arthritis, 'old age aches', mild headaches
- Acetaminophen
  - Max 3,000mg per day in the elderly
  - Liver impairment
- NSAIDS
  - Cox 1&2 mixed
    - Ibuprofen, Naproxen, Meloxicam
  - Cox 2 Inhibitors
    - Celecoxib
  - Renal/ cardiac/ GI concern
**Moderate- Severe Nociceptive Pain**

- **Moderate**
  - Tramadol
  - Opioid/Non-opioid combinations
    - Hydrocodone/APAP
    - Oxycodone/APAP
  - Watch APAP content

- **Severe**
  - Pure opioid
  - IR and ER
    - ER formulations should be used for chronic nociceptive pain

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**Clinical Considerations**

- Routes of administration:
  - Orally: NSAIDS, opioids, others
  - Topically: Lidocaine, Capsaicin cream/lotion, Fentanyl TD patch
  - Rectally: Acetaminophen supp, Methadone, Morphine SR tabs, most orally administered IR opioids

- Patient-specific parameters
  - Body composition (height, weight, skin turgor, SC tissue)
  - Renal/Hepatic function
  - Environment of care, ambulation status
  - Is anxiety contributing?

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**Opioids in Pain Management**

- Three receptor groups in the CNS and peripheral tissues
  - All have supraspinal & spinal analgesia
  1. Mu receptor: Euphoria, Miosis, sedation, constipation, respiratory depression, addiction, hormonal changes
  2. Kappa Receptor: Diuresis, sedation, miosis, dysphoria, psychomimetic effects, respiratory depression, constipation
  3. Delta Receptor

- All opioids are effective for managing nociceptive pain
- Methadone is the most effective opioid for neuropathic pain
### Opioid Kinetics

- Peak concentration in plasma after:
  - PO administration: 60 minutes
  - SC/IM administration: 30 minutes
  - IV administration: 6 min
- Half-life at steady state:
  - PO / PR / SC / IM / IV: 3-4 hours
- Steady state is attained after 4-5 half-lives
- Duration of effect of “immediate-release” formulations:
  - 3-5 hours PO / PR
  - Shorter with parenteral bolus
- Notable exception to the rule: Methadone

### Clearance

- All opioids conjugated by liver
- 90%–95% excreted in urine
- Renal failure & severe hepatic failure:
  - Lower doses and/or less frequent dosing intervals suggested
  - Avoid morphine in patients with oliguria & anuria

### Renal Function

- **CrCl = 10-30ml/min**
  - Oxycodone
  - Methadone
  - Hydromorphone
  - Fentanyl
  - Buprenorphine
  - **Morphine
- **CrCl < 10ml/ml**
  - Oxycodone
  - Methadone
  - Fentanyl
  - Buprenorphine
- **CrCl = 30-40ml/min**
  - Oxycodone
  - Hydromorphone
  - Methadone
  - Fentanyl
  - Buprenorphine
  - **Morphine
- **CrCl >40ml/min**
  - Oxycodone
  - Morphine
  - Hydromorphone
  - Methadone
  - Fentanyl
  - Buprenorphine
  - **Morphine**
**Morphine**

- WHO: Gold standard for acute pain/SOB
- Variety of dosage forms (solution, ER, IR)
- May be used acutely in end stage patients (prognosis ~ 7 days) with severe renal impairment
- Oral: rectal bioavailability is approximately equivalent

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**But I’m allergic to Morphine??**

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**Structural Classes of Opioids**

<table>
<thead>
<tr>
<th>OPIOIDS</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine*</td>
<td></td>
<td>Fentanyl***</td>
<td>Methadone***</td>
</tr>
<tr>
<td>Codeine*</td>
<td></td>
<td>Meperidine***</td>
<td>Propoxyphene***</td>
</tr>
<tr>
<td>Oxymorphone**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydromorphone**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocodone**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine**</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Natural  
**Semi-Synthetic  
*** Synthetic
Semi-Synthetic Opioids\textsuperscript{12,13}

- Oxycodone
  - Available as ER and IR formulations
  - May be a viable option for a ‘morphine’ allergy, or renal impairment
  - Oxycodone ER cannot be given PR
  - $ (IR tabs); $$$ (concentrated solution and ER formulation)

Semi-Synthetic Opioids\textsuperscript{12,13}

- Hydromorphone
  - Available as ER and IR formulations
  - Tends to be 2\textsuperscript{nd} line therapy for breakthrough pain
  - Kinetics allow it to be dosed a bit further apart (ie q6h, versus q4h)
  - Oral: rectal bioavailability approximately equal
  - FDA dosing interval for rectal HM is 6 hours
  - $$$
- Oxymorphone (Opana\textregistered)
  - $$$
- Buprenorphine
  - Available as a patch and IV
  - $$$

Routine Oral Dosing\textsuperscript{16}

- Long acting opioid agents
  - Improve compliance, adherence
  - Calculate TOTAL daily dose from PRN, convert opioid (as needed), adjust for incomplete cross tolerance, and dose q8h, q12, or q24h (product specific)
  - Don’t crush or chew tablets
  - Once steady state is achieved, can titrate dose
Breakthrough Pain

- Use immediate-release opioids
  - 5%-15% of 24-hour dose (typically derived from oral morphine equivalents) every 2-4h
  - Can adjust dose daily (both routine and PRN)
    - mild / moderate pain ↑ 25%-50%
    - severe / uncontrolled pain ↑ 50%-100%
- Do NOT use extended-release opioids

SAMPLE Equianalgesic Dosing

<table>
<thead>
<tr>
<th>GENERIC NAME</th>
<th>TRADE NAMES</th>
<th>SC/IV/24 hr</th>
<th>ORAL/24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine Sulfate</td>
<td>Roxanol, MS Contin, MSIR</td>
<td>10 mg</td>
<td>30 mg</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>OxyContin, Roxicodone, Oxyfast, Percocet, Roxicet, Tylox</td>
<td>-</td>
<td>10-30 mg</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Opioid</td>
<td>3 mg</td>
<td>1.5 mg</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Vicodin, Lorcet, Lortab</td>
<td>-</td>
<td>20 mg</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td></td>
<td>1 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>Codeine</td>
<td></td>
<td>130 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>Mepiphanate</td>
<td>Darvocet</td>
<td>75 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Ultram</td>
<td>-</td>
<td>50 mg</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>Nucynta</td>
<td>-</td>
<td>100 mg</td>
</tr>
<tr>
<td>Fentanyl Injection</td>
<td>Sublimaze</td>
<td>300 mcg</td>
<td>-</td>
</tr>
<tr>
<td>Fentanyl Buccal Tablet</td>
<td>Actiq</td>
<td>-</td>
<td>1000 mcg</td>
</tr>
<tr>
<td>Fentanyl Transdermal</td>
<td>Duragesic</td>
<td>see chart below</td>
<td>see chart below</td>
</tr>
</tbody>
</table>

Incomplete Cross Tolerance

- Occurs when switching from one opioid to another
- Likely due to subtle differences in the molecular structure or the interaction of receptors
- May be a difference in equianalgesic dosing and ratio
- Start with about 75% of the published dose of the new opioid to compensate
- 75% is an estimate, and should be based on the patient’s individual traits and current status (ie pain crisis vs. being comfortable)
JJ is a 75 year old female with end stage breast CA and mets to the lungs. She reports pain 8/10, & is ‘hurting’ all over. She has mild renal insufficiency, with no liver impairment. She weighs about 150lbs, with no problems swallowing. She has been taking Percocet 5mg/325mg at least 5x daily for the last couple of days.

Case #1

- MS Contin 15mg PO BID
- Morphine or Oxycodone 5mg PO q4h PRN pain
- What are some of the side effects we should educate the patient about?

Side Effects

- PLAN ON...
  - CONSTIPATION!
    - Less common
  - Itching
    - caused by opioid-induced histamine release & is often mistaken for an allergy
  - Nausea and vomiting
  - Respiratory depression
    - Tolerance usually develops quickly and sedation occurs BEFORE depression
  - Risk factors
  - Myoclonus
    - With very high doses
  - Hallucinations
Fentanyl

- **Distribution:** Very lipophilic
- **Half-life:** With multiple applications: 13-22 hours
- **Onset of Action:** 12-24 hours
- **Steady state:** 6 days (2 applications)
- **Available:** 12, 25, 50, 75, 100 microgram patch
  Also comes in injectable, lozenge, spray solution
- **Duration:** 72 hours
  Some patients require Q48 hour dosing & increased use of PRN breakthrough pain medication

To Fentanyl or To Not Fentanyl?

**Pros**
- Patch: Apply and forget it
- Variety of dosage forms

**Cons**
- Unpredictable absorption = poor pain control
- Body fat required for adequate absorption
- Elevated temperature causes changes in absorption
- Patches may become dislodged
- Effects may last up to 24 hours after removal
- Not suitable for unstable/acute pain

Fentanyl Dosing

<table>
<thead>
<tr>
<th>Age/Body Composition</th>
<th>Fentanyl patch (mcg/hr)</th>
<th>Morphine PO (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult, normal wt, non-cachectic</td>
<td>100</td>
<td>180-200</td>
</tr>
<tr>
<td>Elderly &amp; thin, non-cachectic</td>
<td>100</td>
<td>120</td>
</tr>
<tr>
<td>Cachectic patient</td>
<td>100</td>
<td>90</td>
</tr>
</tbody>
</table>
Case #2

MR is a 91 year old woman with an end-stage malignancy. She had been maintained on transdermal fentanyl 25 mcg every 3 days. Her pain progressed, & the fentanyl was increased to 50 mcg, and then 75 mcg. Not using anything for BTP. Unfortunately, the recent dosage increases did not appreciably result in pain relief.

MR is 5'4", & weighs 78 pounds, with the ability to swallow tablets and capsules, and the physician would like to switch her to oral long-acting morphine.

What do you think we can recommend?

Case #2

* For elderly, cachectic patient ... 100 mcg/hr
  Fentanyl patch is equivalent to 90 mg morphine
* Pharmacist recommends discontinuing
  Fentanyl patch and starting …
  * MSContin 30mg po BID (for long-acting pain control)
  * Morphine 20mg/mL Take 5-10mg SL q2h PRN breakthrough pain/sob

Methadone

One of the preferred long-acting opioids in end of life care
* Multiple routes of administration
  * PO, SL, PR, PV, SQ, IV, IM
* Unique receptor affinity
  * Most effective opioid for neuropathic pain
  * Less cognitive impairment and euphoria than other opioids
* Appropriate option for patients with renal or hepatic impairment
* Consider for patients with a morphine allergy/intolerance
Methadone Dosing in 5 MINUTES!

5 Minutes to Methadone

The Patient
- Easy to administer – via all routes
- Always double-check drug-drug interactions
- Pharmacist
- Evaluate for CI cardiac factors (fluctuating electrolytes, pacer, noncompliance) & compare risk vs. benefit
- Smoker
- Adipose tissue

The Pain
- OPQRST (Onset, Provocation/Palliation, Quality, Region/Radiation, Severity, Time)
- What total dose of opioid are they currently taking (LA + IR)?
- What does that do to the OPQRST?
Methadone Equianalgesic Dosing Ratio

<table>
<thead>
<tr>
<th>24 Hour Oral Morphine Equivalent</th>
<th>Morphine: Methadone Ratio per 24 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 mg/24 hr</td>
<td>2:1</td>
</tr>
<tr>
<td>30 - 99 mg/24 hrs</td>
<td>4:1</td>
</tr>
<tr>
<td>100-299 mg/24 hrs</td>
<td>8:1</td>
</tr>
<tr>
<td>300-499 mg/24 hrs</td>
<td>10:1</td>
</tr>
<tr>
<td>500-999 mg/24 hrs</td>
<td>15:1</td>
</tr>
<tr>
<td>1000-1999 mg/24 hrs</td>
<td>20:1</td>
</tr>
<tr>
<td>2000-2999 mg/24 hrs **</td>
<td>30:1</td>
</tr>
<tr>
<td>&gt;3000 mg/24 hrs **</td>
<td>40:1</td>
</tr>
</tbody>
</table>

Methadone Equianalgesic Dosing Ratio

Calculation: total daily methadone dose and administer every 8 to 12 hours.

Storey P, Primer of Palliative Care 3rd ed AAMPM 2004

5 Minutes to Methadone

- Use a well-respected & well-researched dosing conversion, every time
- Convert in phases if Total Daily Dose greater than 300 mg of opioid
- Get a colleague to double-check your conversion
- Don’t forget a IR opioid (morphine, oxycodone, hydromorphone) for BTP

The Conversion

5 Minutes to Methadone

- Daily Methadone Checks x 5-7 days
- We DO expect:
  - The pt to need more BTP medication in the first 1-3 days, while methadone reaches SS
  - Increased sleepiness (especially if has not had pain control in a long time)
- We DON’T expect:
  - A pain crisis (10/10)
  - Sedation or lethargy

The Follow Up
Opioid Assessment

- Assess for:
  - Lack of therapeutic response
    - Up to 30% of patients show poor responsiveness to a given opioid during routine administration
  - Development of adverse effects
  - Change in patient status

- Dose titration is critical to successful therapy and pain control
  - NO SIZE FITS ALL
  - No "MAXIMUM" dose of opioids

**GOAL**: Increase dose until pain relief or intolerable side effects occur

Increasing Opioids

- Evaluate pain intensity rating
  - If mild - moderate pain (<5/10)
    - Increase by 25-50%
  - If moderate - severe pain (>5/10)
    - Increase by 50-100%
  - Can be titrated q24h for unrelieved pain

- Evaluate use of breakthrough analgesic
  - Increase long acting if using > 3-4 BT doses
  - Increase "rescue" dose as baseline dose increases

Case #3

Mrs. Smith is a 92 year old woman with COPD, currently receiving MS Contin 45mg po q12h, plus MS IR 20 mg po q4h prn, taking on average 2 doses per day. She has been on this dose for about 2 weeks, and her pain is well controlled, but she has developed visual hallucinations which she finds quite frightening. She has significant renal impairment (Scr = 2.0 mg/dl) and this adverse effect may be due to accumulation of morphine metabolites. Her physician would like to switch her to long-acting oxycodone.

What information do I need to provide the pharmacist to make this conversion?
Pharmacist will need the following information to make a good patient-specific recommendation:

1. Long-acting medication & dosing: MS Contin 45 mg po q12h = 90 mg/day
2. Breakthrough medication & dosing: MS IR 20 mg po q4h prn (2 doses per day) = 40 mg/day
3. Describe type of pain (to determine whether nociceptive, neuropathic or both)
4. How is patient rating pain on 1-10 scale?
5. Is patient more lethargic or sedated vs. baseline?

Pharmacist recommends converting the patient to:

- Oxycodone ER 40 mg po q12h
- Oxycodone IR 10 mg po q4h prn breakthrough pain

Caregiver calls the nurse 3 days later & says the patient’s pain is getting worse. Describes pain as shooting down her legs & down to her feet. Rating pain at 10/10 before breakthrough dose, pain 6/10 after breakthrough dose. Taking Oxycodone 10 mg every 2 hours, took 10 doses since yesterday.

What do you think?
Case #3

- Is patient a candidate for methadone?
  - History of atrial fibrillation or cardiac arrhythmias?
  - Does she have a pacemaker?
  - Risk vs. benefit!
- Any other questions to ask patient?
  - Current smoker?
    - No
  - Approximate weight or BMI information?
    - 5 feet tall, weight 87 pounds

Pharmacist recommendation:
- Discontinue Oxycodone ER
- Start methadone 5 mg po Q8h
  - Recommend to complete methadone checks daily for the first 5-7 days of therapy to monitor for potential side effects.
  - QT prolongation is mentioned in the FDA labeling of this medication. Contact a pharmacist any time a new medication is added to patient's regimen to check for drug interactions
- Increase Oxycodone IR 20 mg po Q2h prn breakthrough pain

Adjuvants

- Neuropathic pain
  - Anticonvulsants: Gabapentin, Valproic acid
  - Antidepressants: Desipramine, Elavil (TCA), Cymbalta (SNRI)
- Pain that is localized/neuropathic pain
  - Creams (ie capsicain)
  - Lidoderm Patch
- Bone pain
  - Anti-inflammatory: NSAIDs, oral steroids
  - Decrease osteoclast activity: Miacalcin NS, Bisphosphonates (IV)
- Pain that is not responding to typical agents
  - Ketamine
Neuropathic Pain - Use of Adjuvants

- Proposed effect by preventing injured neurons from excessive discharge
- Side effects: Sedation, hypotension, dry mouth
- Older agents:
  - Carbamazepine, phenytoin, valproic acid
- Newer agents:
  - Gabapentin, lamotrigine, levetiracetam, oxcarbazepine, zonisamide, pregabalin
  - Gabapentin: Renal dosing

Neuropathic Pain - Use of Adjuvants

TCAs > SNRS > SSRI

- Tricyclic antidepressants (TCA)
  - Inhibition of serotonin and norepinephrine
  - Common side effects: Sedation, dry mouth, constipation, sweating, cognitive impairment
  - Nortriptyline and Desipramine: good choice in elderly due to low side effects
- Serotonin-norepinephrine reuptake inhibitors (SNRI)
  - Venlafaxine and duloxetine
  - Duloxetine with an FDA indication of depression and diabetic peripheral neuropathy

Neuropathic Pain - Use of Adjuvants

- Topical Agents
  - Capsaicin
    - OTC, extract of hot chili peppers
    - Thought to deplete Substance P
  - Lidoderm
    - Blocks sodium channel responsible for spontaneous activity in nerve terminals of local tissue and nerve injury
    - Works in both nociceptive and neuropathic pain
Bone Pain

- Corticosteroids
  - Decrease inflammation
  - Uses: increased cranial pressure, nerve compression, BONE PAIN, soft tissue damage
  - Side effects: GI effects, increased appetite, hyperglycemia, insomnia
- NSAIDs
  - Decrease inflammation
  - GI/ cardiac/ renal issues

Ketamine

- Reserved for refractory pain when typical agents for both nociceptive and neuropathic pain have failed
- Co-analgesic, opioid sparing
- MOA: NMDA receptor inhibitor, agonist at cholinergic/ opioid/ GABA A receptors, and inhibits serotonin/ norepinephrine reuptake and Na+ and K+ channels
- Active metabolite: Norketamine
- Pretreatment with benzodiazepines, or haloperidol may decrease psychotomimetic effects

You Made It! it’s The END

- Common barrier and stigmas associated with end of life pain treatment include the failure to identify pain as a priority, the lack of knowledge by healthcare professionals, legal ramifications, ethical debates, family and patient limitations.
  - EDUCATE your team, your patient, yourself
- Opioids are generally regarded as first line treatment for moderate to severe pain, with adjuvants to help with neuropathic or non-nociceptive pain.
- Start low, titrate slowly and be aware of the side effects of all pharmacological interventions.
We are the Champions!

“The last act of life is dying. Facing our death is an opportunity to bring closure to this journey. Our vision as people should be the humanization of death and its healing properties.”

References


References

15. Lewarne, R. End of Life Pain and Symptom Management: Balancing Clinical Appropriateness with Cost Effectiveness in Your Community. Procare HospiceCare Inservice 2012 (PowerPoint Presentation).


All medication review:
Accessed Lexi-Comp Database; 2014.