Pearls and Pitfalls of Pain Management in Palliative Care

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• No disclosures or financial relationships to pharmaceutical companies
• No conflicts of interest
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Learning Objectives
• Understand and apply principles of pain assessment and treatment in the setting of serious illness
• Understand how to safely and effectively prescribe opioid medications
  • Preventing and treating common side effects
  – Understand comfort care medication types and dosing

What Is Palliative Care?

WHO Definition of Palliative Care
• “Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.”

www.who.int/cancer/palliative/definition/en (2016)
Case #1

- 72yo woman with stage 4 non-small cell lung cancer with mets to bone, and chronic lower abd/back pain, fatigue and constipation, admitted for pneumonia
- Home opioids: Hydrocodone/APAP 10/325mg q4h PRN
- Inpatient: has morphine 1mg IV q4h PRN available
- Reports severe pain ("15/10")
  - Watches clock, moans, looks uncomfortable
  - Asks for morphine before 4 hours
- *How should you evaluate and treat her pain more effectively?*

Evaluation of Pain

**Pitfalls of Pain Evaluation**

- Not enough time for comprehensive H&P
- Not listening, or not believing the patient who reports pain
- Focusing more on the pain score than the whole person

**Pain History**

- Pain self-report; intensity and characteristics
- Pain diagnoses, etiology and comorbidities
- Current and past treatments and their effectiveness
- Coexisting psychiatric conditions
- Current or past substance abuse
  - Including alcohol, tobacco, marijuana
- Consider variable pain thresholds/reporting with:
  - Age, gender, race, subculture, socioeconomic status, psychosocial and environmental issues


**Pearl: Assess “Total Pain”**

- Physical, psychosocial, spiritual components
  - Effect of pain on:
    - Work and home function
    - Relationships
    - Sleep
    - Mood
    - Quality of life; enjoyment of life
  - Stressors or contributors to pain:
    - Poor sleep, fatigue
    - Fear, anxiety, denial, anger, depression, loneliness
    - Financial stressors
    - Loss of faith or meaning; spiritual distress

UNIPAC 3; AAHPM 2012

**Is This Patient “Addicted”?**
Addiction

- Consensus Definition (AAPM, APS, ASAM 2001):
  - A primary, chronic, and neurologic disease with genetic, psychosocial, and environmental factors influencing its development and manifestations:
    - Continued use despite harm (adverse consequences)
    - Impaired control over use (compulsive use)
    - Preoccupation with the use for non-pain relief purposes (cravings)
  - Worsens with escalating opioid dosing
  - Risk in those using opioids depends on history of prior substance use disorder
    - None (0.2-4%) vs. drugs (7.5%) vs. EtOH (14.1%)

- Pseudoaddiction
  - Iatrogenic syndrome due to poorly treated pain
    - Misinterpretation of relief-seeking behaviors as drug-seeking:
      - Moaning; trying to convince the doctor the pain is real
      - Clock watching; requests for medication prior to next dose due
      - Complaints of pain are excessive to the given stimulus
    - Symptoms improve with increased analgesic tx
      - Pharmacologically appropriate doses and schedules
    - Physiologic adaptations to chronic opioid therapy
      - Tolerance
      - Physical dependence

DDx Uncontrolled Pain

- Disease progression or treatment complications
  - Metastatic disease: bone or organ compression, destruction or obstruction (neoplasm, infection); increased intracranial pressure
  - Nerve impingement or invasion (R/O cauda equina syndrome)
  - Poor opioid absorption (cachexia, edema, sweating)
  - Tolerance, withdrawal or opioid-induced hyperalgesia
  - Poorly opioid-responsive pain
  - Emotional/spiritual pain, comorbid psychiatric disease
  - Noncompliance due to side effects or poverty

Management of Pain

- Individualized goals of therapy, management plan
  - Focus on improving function and quality of life, not just analgesia
    - "Coping" rather than "Cure"
  - Treat underlying etiology by pain type/severity
  - Treat comorbid depression, anxiety
  - Follow-up and monitor for side effects and efficacy

Pitfall: Underdosing

- Reasons:
  - Fears or biases about opioids
  - Fear of side effects
  - Fear of addiction
  - Fear of regulatory action
  - Lack of understanding of appropriate opioid dose conversions and dosing intervals
- Results:
  - Inadequate pain control
  - Prolonged suffering

Pearls of Pain Management
Treatment by Pain Type

• **Somatic/Nociceptive** (dull ache, deep throbbing)
  – Acetaminophen or NSAIDs (+ opioids if more severe)
  – Bone pain or brain mets: add steroids (+ GI prophylaxis) +
    adjuncts (calcitonin, bisphosphonates)

• **Visceral** (colicky, sharp, transient)
  – Opioids, anticholinergics (oxybutinin, hyoscyamine,
    scopolamine, octreotide)

• **Neuropathic** (shooting, burning, tingling)
  – Anticonvulsants (gabapentin, pregabalin), TCAs, oxcarbazepine,
    carbamazepine
  – SSRI/SNRIs (duloxetine, venlafaxine)

When Are Opioids Appropriate?

• Failure of non-opioid treatments
  – PT/OT, NSAIDs, APAP, heat/ice, behavioral

• Malignant pain (moderate to severe)

• Nonmalignant pain (moderate to severe):
  – Acute pain when benefits > risks
  – Chronic pain if uncontrolled by less potent meds
    • If long-term risks of other medications (e.g. NSAIDs)
      too high to justify benefit
      • If patient without signs of abuse/diversion

Treatment By Pain Severity

(Mild Pain)
  – OTC drugs (Acetaminophen, ASA, NSAIDs)

(Moderate Pain)
  – Lower potency opioids + OTC drugs
  – Codeine q4h or Tramadol, Tapentadol q6h

(Severe pain)
  – Short-acting potent opioids: Morphine = hydrocodone <
    oxycodone < hydromorphone < fentanyl
  – Scheduled dosing PO q4-6h, plus lower dose q2h prn

Pharmacokinetics of Short-Acting Opioids By Route of Administration*

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Onset</th>
<th>Peak Effect</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV/IM/SC</td>
<td>2-15 min</td>
<td>10-30 min</td>
<td>1-3h</td>
</tr>
<tr>
<td></td>
<td>PO/PR</td>
<td>15-30 min</td>
<td>60-90 min</td>
</tr>
</tbody>
</table>

*Helps determine frequency of reassessment and follow-up dosing

Treatment By Pain Timing

• **Incident pain**
  – Brief, precipitated by a specific activity
  – Premedicate with short-acting opioid 30 min. prior to activity
    (or use ultra short-acting opioid)

• **Breakthrough pain**
  – Acute/intermittent but lasts longer; occurs despite underlying opioids
  – Use short-acting PRN opioids

• **Continuous pain**
  – Constant; recurs once pain med wears off
  – Use long-acting opioids
Achieving Rapid Pain Control in Acute Pain

- Dose titration to effect
  - Lower dose initially, increase as needed
  - Calculate total daily dose (TDD) of opioid
  - If pain uncontrolled, rapidly titrate dose upward (q1-2h)
    - Mild pain: 25% increase in TDD
    - Moderate pain: 50% increase in TDD
    - Severe pain: 75-100% increase in TDD
- No ceiling dose (except methadone) unless excessive sedation or respiratory depression

Case #1 – Cont’d

- Opioid adjustments made:
  - IV morphine infusion 1mg/h for 24h while other adjustments made:
    - IV morphine dose increased to 2mg q1h PRN
    - Morphine-ER added: 15mg PO BID
  - Pain control improved
    - PRN doses proportional to her home doses
    - Addition of long-acting opioid

Case 2

- 62yo man admitted to the hospital with ischemic leg with gangrene and required amputation
- He complained of such severe pain that the attending escalated his opioids rapidly
  - Hydromorphone 0.5, 1, 2mg doses given over a 6 hour period, with initial relief; prn doses given q2-4h
- On POD#2, he was sleepy but arousable, irritable, and complained of severe pain "all over" with minimal touching.
  - Further IV opioids do not seem to help relieve his pain

Opioid-Induced Hyperalgesia (OIH)

- Paradoxical hypersensitivity to painful stimuli
  - Escalating pain despite escalating opioid doses (in absence of progressive pathology); upregulated mu receptors
  - Symptoms: skin hypersensitivity, confusion, sleep disturbance, restlessness, irritability
  - Onset: within hours to days; may last for days
  - Risk factors: rapid dose increases; high doses
- Treatment:
  - Opioid rotation, dose reduction
  - Methadone, ketamine, DM, non-opioid interventions

Opioid Rotation

- Reasons to switch
  - IV to PO transition (preparation for discharge home)
  - Analgesic efficacy (tolerance; decreased absorption)
  - Limit adverse effects, cost
  - Individual (genetic) variation in response to opioids
  - Opioid-Induced Hyperalgesia
- How to switch: Equianalgesic dosing table
  - Calculate 24h morphine-equivalent dose
  - Reduce dose by >25-50% but provide adequate PRN short-acting meds (due to incomplete cross-tolerance)
### Equianalgesic Opioid Dosing (mg)

<table>
<thead>
<tr>
<th>PO/PR</th>
<th>Analgesic</th>
<th>IV/IM/SC</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>Codeine</td>
<td>60</td>
</tr>
<tr>
<td>15</td>
<td>Morphine</td>
<td>5</td>
</tr>
<tr>
<td>15</td>
<td>Hydrocodone</td>
<td>--</td>
</tr>
<tr>
<td>10</td>
<td>Oxycodone</td>
<td>--</td>
</tr>
<tr>
<td>4</td>
<td>Hydromorphone</td>
<td>1.5</td>
</tr>
<tr>
<td>5</td>
<td>Oxymorphone</td>
<td>--</td>
</tr>
<tr>
<td>--</td>
<td>Fentanyl</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**IR vs. ER/LA Opioids**

- **Immediate Release**
  - Opioid naïve; no tolerance
  - Intermittent or occasional pain
  - Incident or breakthrough pain despite ER/LA
  - Tramadol/Tapentadol, oxy/hydrocodone, morphine IR, oxy/hydromorphone, nasal sprays (fentanyl, butorphanol)

- **Extended/Long-Acting**
  - Opioid tolerant patients
  - Constant, significant pain
  - To stabilize pain relief when patient using multiple doses of IR
  - Morphine SR, oxycodone ER, fentanyl patch, methadone, hydrocodone, hydromorphone, buprenorphine patch

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**Fentanyl Patch**

- Transdermal absorption into SC adipose reservoir within 24h
  - Educate patients: Initial effect after 6-8h, full effect by 48h
- Patch size (mcg) = (24h OME* dose) ÷ 3
  - Round to nearest 12mcg increment, dose q72h
- 25mcg fentanyl = 45-135mg oral morphine/24h = 1mg/hr IV morphine drip
- Do not increase patch dose more often than every 48-72h
- Other forms available: IV, PO, buccal, intranasal
  - Fentanyl 100mcg PO = 1mg IV morphine

*OME = Oral Morphine Equivalent

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**Options for Treating Refractory Pain**

- Increase dose or switch to more potent opioid
- Adjuvant medications
  - TCAs, gabapentin, SSRI/SNRIs, steroids
- IV opioid infusion (inpatients)
- Nerve blocks, epidural/intrathecal pumps, neurosurgical procedures
- NMDA blockers
  - Methadone, ketamine, memantine, dextromethorphan

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**IV Opioid Infusions for Severe Uncontrolled Pain/Dyspnea**

- **Indications:**
  - Ongoing, severe symptoms despite frequent IV bolus doses
- **Benefits:**
  - Faster pain control (following initial bolus dose)
  - Easily titrated to effect
  - Safer; fewer side effects of nausea, sedation, or hypotension
  - More uniform pain control
  - Less breakthrough pain; lower 24h total dose
  - Greater patient satisfaction
- Morphine, fentanyl, or hydromorphone

Case #1 – Revisited

• Pain control improved on ER and IR opioids
• However, she has not had a BM in 5 days
  – Now with low appetite/oral intake, nausea, abdominal discomfort and cramping

Pitfall: No OIC Prophylaxis

• Inadequate prophylaxis of opioid-induced constipation (OIC)
• Possible Adverse Effects:
  – Nausea +/- vomiting (and aspiration risk)
  – Reflux
  – Bowel obstruction
  – Abdominal perforation and sepsis

Opioid-Induced Constipation

• Most feared side effect (per patients)
• Prevalence: 40-80% of pts on opioids
• No tolerance develops
• Mechanism:
  – Mu-opioid receptors on intestinal cells and enteric neurons
  • Suppression of forward peristalsis
  • Increase fluid reabsorption
  • Reduce intestinal secretions
  • Increase sphincter tone

Managing Constipation

• Encourage adequate hydration and activity
• Avoid fiber unless adequate PO fluids also given
• Maintenance laxative regimen (target 1BM q1-2d)
  – Prophylaxis with bowel stimulant (senna, bisacodyl)
  – Escalate laxatives q1-2 days as needed
  – Add osmotic laxatives (MOM, lactulose, polyethylene glycol), softeners/detergents (docusate) bisacodyl, enemas
  – R/O fecal impaction or bowel obstruction

Other Agents for Constipation

FDA approved for OIC:
  – Naltrexone
  – Methylnaltrexone
  – Alvimopan
    • for post-op ileus
  – Naloxegol
    • in non-cancer pain
  – Lubiprostone
  – Naloxone/opioid combinations

Agents that improve colonic transit time:
  – Probiotics
  – Metoclopramide
  – Linaclotide
  – Citalopram*

*Non-FDA approved indication

Case #3

- 65 man with stage 4 esophageal cancer, who has a PEG tube, debility and 20# weight loss/cachexia, and worsening pain control despite escalating fentanyl patch (now 200mcg) gradually over the past 3 months
- Admitted with intractable pain and dyspnea
- Albumin is 2.0 and BMI is 17

Pitfall: Medication Ineffectiveness

- Fentanyl patches poorly absorbed
  - Weight loss, cachexia
  - Decreased adipose tissue
  - Hypoalbuminemia, low BMI
- Results:
  - Gradual loss of efficacy in relieving pain

Pearl: Consider Methadone For Chronic Refractory Pain

- Mu-agonist with NMDA receptor antagonism
- Advantages
  - Very potent, least costly, and well-tolerated; IV, PO, PR, SL
  - The only LA opioid that can be crushed or given as a liquid and still remains long-acting!
  - Useful for neuropathic pain and hyperalgesia
- Pharmacokinetics
  - Onset within 1 hour; duration 6-12h; hepatically metabolized
  - Long acting; Dose $t_{1/2}$=24h; elimination $t_{1/2}$ <190 hrs
- Dosing
  - Starting dose 2.5mg PO q8-12h (or daily in elderly)
  - Methadone 10mg/d PO = Fentanyl 25mcg patch/72h = 40-90mg PO morphine/24h

Methadone Conversion Ratios

<table>
<thead>
<tr>
<th>TDD* morphine (PO)</th>
<th>Ratio (MS:Methadone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;60mg</td>
<td>5:1</td>
</tr>
<tr>
<td>60-200mg</td>
<td>10:1</td>
</tr>
<tr>
<td>&gt;200mg</td>
<td>20:1</td>
</tr>
</tbody>
</table>

*TDD=Total Daily Dose

(Note: These are more conservative estimates for starting doses, based on new CPG from Am. Pain Soc. 2014)

Methadone Pitfalls

- Rapid dose escalations or use in elderly can lead to respiratory depression, sedation, torsades, and death
  - Titrate dose $t_r$ 5-7 days (due to long half-life)
- Use with caution in the presence of benzodiazepines, alcohol, grapefruit juice, or meds that ↑ QTc (see list)
- Avoid or stop if EKG shows prolonged QTc>500ms
- Reduce dose in hepatic failure or ESRD

Drugs To Avoid With Methadone (Increase QTc)*

- Antibiotics
  - Fluoroquinolones, Macrolides
- Antipsychotics
  - Haloperidol, ziprasidone, thorazine, quetiapine
- Antiarrhythmics & Cardiac meds
  - Amiodarone, dronedarone, ibutilide, dofetilide, quinidine, sotalol, ranolazine
- Others
  - Cisapride, Coartem, Conavaptan, Posaconazole, Saquinavir, Selegiline, Thioridazine, Vemurafenib, Vandetanib, Vardenafil

*Not an all-inclusive list
Opioid Side Effects

Case #4 A & B

- Scenarios:
  - 69 yo obese man with COPD and chronic pain (on MS-ER 15mg TID) becomes somnolent after being outside all day in July heat. RR 6, sats 87%.
  - 15 min. after giving 4mg IV morphine to a patient with chronic cancer pain, she becomes somnolent (but arousable), RR 8/min., SpO2 91%.

- What should you do?
  A. Immediately give naloxone 0.4mg IV
  B. Give naloxone 0.04mg IV
  C. Provide O2, monitor pt, and wait for opioid effects to wear off

Pitfall and Pearl: Respiratory Depression

- Most feared adverse effect
  - Rare (<1%) with short-acting opioids
  - Rapid tolerance
- Treatment
  - Assess if life-threatening
    - Pt not arousable; RR<6/min or hypoxic
  - Naloxone 0.04 mg IV (max. 0.1mg)
  - Note: This is 1/10 the usual dose (to avoid complete blocking of analgesic effects which would result in severe, untreatable pain and immediate withdrawal)

Who Is At Risk for Respiratory Depression?

- Underlying cardiopulmonary disease
  - Chronic resp. failure (CHF, OSA, COPD/asthma w/ CO2 retention)
- Upper respiratory infections*
- New or worsening kidney/liver disease*
- Concurrent sedative use (BZD, alcohol)
- Advanced age or prior hypoxic response
- Opioid naïve patients requiring frequent, large or escalating doses (e.g. post-op/trauma)
  - Also with too rapid dose increases of long-acting opioids


Opioid Dosing Precautions Near or At End of Life

- Dehydration, renal or hepatic failure
  - Use use lower doses less frequently
  - If oliguric or anuric, use mainly prn IR dosing
    - Avoid ER/SR forms of morphine
  - Alternatives to morphine: fentanyl > buprenorphine > hydrocodone or hydromorphone
- Weight loss, cachexia, hypoalbuminemia
  - PO > TD route; reduce dose
- Fever
  - Reduce fentanyl patch dose (enhanced absorption)

Opioid Dosing in Renal Failure

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Morphine</th>
<th>Hydrocodone</th>
<th>Hydromorphone</th>
<th>Methadone</th>
<th>Fentanyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50</td>
<td>100% of original dosing</td>
<td>50%–100% of original dosing</td>
<td>100% of original dosing</td>
<td>100% of original dosing</td>
<td>100% of original dosing</td>
</tr>
<tr>
<td>10-50</td>
<td>50%–75% of original dosing</td>
<td>50% of original dosing</td>
<td>50% of original dosing</td>
<td>100% of original dosing</td>
<td>75%–100% of original dosing</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Not recommended</td>
<td>25% of original dosing</td>
<td>Not recommended</td>
<td>50%–75% of original dosing</td>
<td>50% of original dosing</td>
</tr>
</tbody>
</table>

GFR: glomerular filtration rate. Source: Reference 16.

Table 5. Recommendations for Opioids in Renal Impairment

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Recommended Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Not recommended due to accumulation</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Appears safe, but renal dosage adjustment may be necessary</td>
</tr>
<tr>
<td>Hydrocodone/acetaminophen</td>
<td>Use cautiously, adjust dosage</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Use cautiously, adjust dosage</td>
</tr>
<tr>
<td>Methadone</td>
<td>Appears safe, however, renal dosage adjustment may be necessary</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Not recommended due to metabolites</td>
</tr>
<tr>
<td>Morphine</td>
<td>Not recommended due to metabolites</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

Source: References 8, 16.


Table 3. Recommendations for Opioids in Hepatic Impairment

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>Not recommended, in severe hepatic dysfunction codeine is not converted to morphine, leading to poor outcomes</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>98% metabolized in liver; studies have not demonstrated PK alterations; careful monitoring is warranted</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>Use with caution, need for co-sedation due to parent compound not being converted to metabolites</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>Undergoes phase II reactions, however, use with caution due to its intermediate extraction phase</td>
</tr>
<tr>
<td>Methadone</td>
<td>Use with caution; use of co-sedation because of increased free drug</td>
</tr>
<tr>
<td>Meperidine</td>
<td>Not recommended, toxic metabolite, inappropriate, may accumulate</td>
</tr>
<tr>
<td>Morphine</td>
<td>Use with caution, need for co-sedation due to increased extraction ratio</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Use with caution, need for co-sedation recommend 1/2 to 1/3 of usual dose</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>Contraindicated in moderate-to-severe hepatic impairment</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Not recommended, significant PK changes in moderate-to-severe hepatic impairment</td>
</tr>
</tbody>
</table>

NC pharmacokinetics. Source: References 8, 16.


Other Opioid Side Effects

- **GI**: Constipation, nausea
- **Skin**: Itching
- **Neuro**: Sedation, confusion, myoclonus
- **Endocrinopathies**: Suppression of HPA axis; hypogonadism
- **GU**: Urinary retention
- **Reduced immune function**
- **Addiction**
- **Respiratory depression**
- **Overdose**
- **Death**

Managing Common Opioid Side Effects

- **Nausea**
  - Not an allergy
  - Tolerance develops within 1-3 days
  - Treatment options:
    - Metoclopramide
    - Other antiemetics (compazine, prochlorperazine, ondansetron)
    - If refractory symptoms, try dexamethasone, haloperidol or olanzapine (avoid if QT prolonged)

Managing Opioid Side Effects

- **Pruritis (Itching)**
  - 10% incidence
  - Not a true allergy
  - Not a contraindication to opioid use
  - More common with morphine
  - H1/H2-blockers mildly helpful
  - Switch to opioid of another class
Managing Opioid Side Effects

- Sedation and confusion
  - May also occur as patient nears death
  - Usually resolves after a few doses/days
  - Reduce opioid dose or switch to different opioid
  - Psychostimulants may help
- Neurotoxicity
  - Myoclonus, delirium, seizures
  - More common with high doses or in renal failure (morphine > hydromorphone) due to metabolite buildup
  - Change to different opioid (e.g. fentanyl, hydrocodone, oxycodone)

Case #5

- 88yo frail woman with severe aortic stenosis and CAD was brought to the ED after 1 week of progressive shortness of breath, weakness, fatigue, chest discomfort, nausea, low appetite and anxiety over 1 week
- She was hypotensive and hypoxic, fought O2 mask, and eventually became lethargic/obtunded
- Based on exam and data, she was diagnosed with STEMI, CHF with cardiogenic shock
- Family stated they “just want her to be comfortable” and declined cardiac cath or ICU admission

Common Symptoms at End of Life

- Pain
- Dyspnea
- Anxiety
- Secretions
- Fatigue, lethargy
- Restlessness
- Agitation

Comfort Care: You Only Have One Chance to Do It Well

What Is “Comfort Care?”

- General/Nursing Care
  - Limit VS to q shift; RR q4h to assess comfort
  - Mouth care q 2-4h and prn; Lip balm
  - Eye care: eyedrops (or ointment) prn
  - Skin care: Turn q2-4h as tolerated; air overlay mattress
  - Foley catheter
- Discontinue certain non-comfort measures:
  - Medications, testing (lab, xray), and monitoring
  - ICD deactivation; artificial life support withdrawal
- Add medications to prevent or treat symptoms

Key Categories of Comfort Care Medications

- Opioids*
- Benzodiazepines*
- Anticholinergics*
- Antipsychotics*
- Antiemetics
- Antipyretics

*Core comfort medications (J Pall Med 2013; 16:38-43.)
Patient Death After Opioids: Ethics In Dying Patients

- Do these medications hasten death?
  - No; initiation of treatment (or dose increases) with opioids or sedatives is NOT associated with precipitation of death, when appropriate doses are used for symptom control.

- Ethical principle of **Double Effect**:
  - Treatment purpose is relief of symptoms/suffering
  - Death after opioid administration is due to the underlying disease and not due to the medication.

- Ethical duty to provide comfort and relieve suffering.

Opioids for Pain or Shortness of Breath

- Treat underlying cause
- May also use opioids as first-line treatment
- Preferred routes: IV (if severe), PO/SL, SC

- **Dosing:**
  - Initial: IV dose q15-30 min.
  - Increase dose by 25-50% q 4-12h until comfortable
  - Maintenance dosing PO or IV q4-6h + PRN dosing

- Adjunctive measures
  - Fans and anxiolytic medications

Anxiety

- Vicious cycle between dyspnea and anxiety
- Provide reassurance
  - Identify triggers; teach relaxation; identify isolation and spiritual concerns; provide companionship
- Anxiolytics useful if opioids insufficient
  - Short-acting agents initially
    - Lorazepam 0.5-1mg PO/SL/IV q4h, or 1-2mg IV q1h (if severe) until symptoms controlled
    - Midazolam 1-5mg IV q30 min. prn
  - Long-acting agents preferred if longer prognosis
    - Clonazepam 0.25-0.5mg PO BID

Oropharyngeal Secretions

- Suctioning not routinely recommended
- Postural drainage and repositioning may help
- Anticholinergics:
  - Scopolamine 1.5-3mg topically q72h
  - Hyoscyamine (Levsin) 0.125mg PO/SL q4h prn
  - Atropine 1% ophthalmic soln. 1-2 gtt q 30 min. prn
  - Fast acting, but potential for CNS/cardiac excitatory side effects
  - Glycopyrrolate (Robinul) 0.5-1mg PO BID-TID prn, or 0.2-0.4mg IV q4h prn

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  - Doesn't cross blood-brain barrier; less sedating

Delirium and Terminal Restlessness

- Treat underlying causes if appropriate
- Antipsychotics (Neuroleptics)
  - First-line drugs d/t rapid onset of action
    - Avoid if: seizures, Parkinsons, prolonged QTc interval
  - First-generation medications:
    - Haloperidol 0.5-2mg PO/IV/SC q2h prn
      - Dose range: nightly to q6h
      - Most rapidly acting; higher risk of extrapyramidal side effects (EPS); use lowest effective dose and taper as tol.
    - Chlorpromazine 12.5-50mg PO/PR/IV/IM q8h prn
      - Sedating; mainly outpatient use for terminal delirium

Atypical Antipsychotics

- Newer; similar efficacy but lower risk of EPS
- Examples
  - Risperdone 0.25-1mg PO/SL BID; max dose 4-6mg/d
    - Risk of EPS; avoid in Parkinsons
  - Olanzapine 5-10mg PO daily (or rapidly dissolving tablet 2.5-5mg SL q6h prn); max 20-40mg/d
    - Weight gain and hyperglycemia common; lower risk of EPS
  - Quetiapine 25-200mg PO BID (max. 400mg/d)
    - Fewer EPS; most sedating; safest in Parkinsons
- FDA warning in elderly (increased mortality)
  - Usually benefits > risks near/at EOL
Comfort Care: Case Conclusion

- Medications
  - Morphine IV drip begun at 2mg/hr, with prn IV boluses (q15min if needed) to get RR <20/min.
  - Glycopyrrolate 0.2mg IV x1; Scopolamine patch 1.5mg for secretions
  - Lorazepam 0.5mg IV q4h and q1h prn
  - Fan
- Admitted to Palliative Care service
- Died comfortably about 4 hours later

Summary

- Understand and apply principles of pain assessment and safe, effective treatment in the setting of chronic and/or terminal illness:
  - Acute and chronic pain management with opioids
  - Manage selected common opioid side effects
  - Comfort care medication types and dosing

Questions?