Comfort Measures: Be Not Afraid (The Last 72 hours/Beyond the Drip)

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Disclosure:

I have no conflicts of interest to report relative to the material to be presented.
Focused Learning Objectives:

A case scenario approach will be used to highlight the following concepts:

“Total Pain” Concept coined by: Dame Cicely Saunders, OM, DBE, FRCS, FRCP, FRCN founder of modern hospice movement

Pain Management

- Opioid
  - Pharmacodynamics
  - Equianalgesic dosing
  - Pain Crisis Management with IV opioid
- Non Opioid Options

Active Dying: “The last 72 hours”

- Physical Signs predicting mortality within three days
- Management of commonly encountered sources of distress
Our Patient
(Scenario is based on a combination of real patients.)

• 55 yo male. Initial presentation to urgent care 12/23/**, with two-week history of progressive itching not responding to Benadryl.

• Additional complaints of mild nausea, loss of appetite, moderate abdominal pain responsive to Tylenol. No fever or chills. Fatigued, but functioning at work as a construction superintendent. No weight loss. Initially denied any history of significant past medical problems.

• Wife noticed yellowing of skin and eyes.

• PE: General alert, no acute distress, not cachectic. Eyes: icteric. Skin: yellow with areas of linear excoriations. Abdomen soft, but with mild UQ tenderness and palpable edge of liver 2 fingers below costal margin.

• A scar was noted on his abdomen. When quizzed he noted that he had a kidney removed several years ago for renal cell cancer. He had not followed up with his urologist as he understood he had a surgical cure.
You knew him peripherally due to both having kids in high school as well as living in the same neighborhood. You had previously seen two of his children for acute issues in urgent care. They, in addition, had autism spectrum disorder. He, and importantly, his wife had appreciated your sensitivity to how you approached them.

He was able to appreciate your concern for him. He reluctantly accepted your recommendation to have CT imaging and labs on an expedited basis.

CT imaging was consistent with a large metastatic mass to liver with ductal dilatation.

LABS: demonstrated markedly elevated Alk Phos, Bili of 7 and moderately elevated transaminases.

In a follow up discussion later that day, as his symptom burden was minimal, you recommend he spend the holiday with his family. It was agreed that nothing likely could be accomplished diagnostically over the Christmas Holiday. He was to call if he developed fever, vomiting or increasing pain.

Interval symptom management for itching was Cholestyramine.

His urologist was contacted and arrangement was made for admission on 12/26.

Subsequent biopsy demonstrated metastatic renal cell carcinoma.
Fast-forward six months:

- He had undergone debulking procedure as well as stenting to relieve biliary stasis.
- Immune therapy was initiated with a positive initial response.
- During that interval both he and his family had established a relationship in your practice.
- You have had the opportunity to assist with elements of the big four: Psychological adjustment to illness/disability (as well as his family), existential distress of facing death, financial aspects of illness by assisting in application for disability and suggestions for questions to pursue with Oncologist.
- Cancer-related therapy including symptoms was primarily managed by his Oncologist.
- Patient requested urgent visit: **He is in severe pain.**
- His Oncologist had told him he should enroll in Hospice.
The (H)ospice Bomb

The Oncologist said, “There is nothing more I can do for you... You should enroll in Hospice.”

“My wife is not ready for me to enroll in Hospice. She does not think I am going to die in the next few days.”

The issue of recommending a solution before defining the goal
Hospice: Maximizing Life Quality

- Benefit not a place
  - Provides wide range of services, **but not room and board or custodial care**
  - Medication for symptoms
  - DME
  - AIDE, Spiritual Advisor, Social Worker, RN Nurse Manager
  - Physician oversight

- Qualification
  - Life limiting illness with prognosis of life expectancy < 6 months (50% probability)
  - Intent to pursue comfort focused care with no return to hospital for life extending interventions. DNR status not mandatory but logical

- Hospice conjures negative images for some about hastening death and reducing days to live
- People tend to enroll very late in the course of an illness. Therefore, perpetuates image of death in days
- Patient and family satisfaction rates are phenomenally high for those who enroll
- Truly a wonderful service but I am biased
Dame Cicely Saunders, OM, DBE, FRCS, FRCP, FRCN

Founder of Modern Hospice Movement,

Coined Phrase: “TOTAL PAIN”

“Pain demands the same analysis and consideration as an illness itself. It is the syndromes of pain rather than the syndromes of disease with which we are concerned.”
“Total Pain”

- **Physical Pain**

- **Spiritual Pain**
  - Arises from the impact on a person’s sense of control, identity, justice, and meaning
  - Some will have their faith threatened by pain while others will have their faith strengthened

- **Social Pain**
  - Social pain results from loss of position and role within family and society

- **Emotional/Psychological Pain**
  - Fear, depression, anxiety and demoralization can intensify pain as well as making it more resistant to treatment
  - There is cognitive dissonance between what the patient is told and the reality of their situation that increases the sense of isolation
TOTAL PAIN

Hard work and resilience are required to redefine one’s sense of self to cope with the psychosocial and spiritual challenges

Dame Cicely Saunders, OM, DBE, FRCS, FRCP, FRCN
Goals of Pain Management

- Improve quality of life
- Efficient use of medication(s)
- Minimize adverse effects
- Use appropriate methods of administration
- Simplify medication dosage schedules
- Anticipate disease progression
- Educate patient and caregivers
Pain Assessment

- Characterize multiple dimensions of the pain
- Formulate an understanding of the nature of the pain
- Characterize the impact of pain on QOL domains
- Clarify extent of underlying disease, treatment, prognosis
- Elucidate medical comorbidities
- Elucidate psychiatric comorbidities
- Determine other needs for palliative care interventions
Our Patient’s Pain

- PAIN (PQRST: palliative/provocative, quality, region radiation, referral, severity, temporal factors)
  - Back and leg pain
    - 9/10
    - Deep aching hollow quality
    - Low back and thighs
    - Aggravated by standing
    - No relief hydrocodone/acetaminophen 10/325 mg (averaging 10 tablets daily)
    - Unable to function
  - Abdominal pain
    - 6/10
    - Generalized
    - Bloated feeling with nausea but non-vomiting
    - Food ingestion aggravates pain
Non-Pharmacologic Management

- Physical modalities
  - PT/OT
  - Cutaneous stimulation (heat/cold)
  - Exercise
  - TENS (transcutaneous nerve stimulation)
  - Massage; Healing touch

- Palliative Radiation
- Nerve Blocks

- Psychosocial/Spiritual
  - Relaxation and guided imagery
  - Distraction, hypnosis
  - Music, prayer
  - Reframing
  - Patient/family education
  - Meditation/Spiritual Reflection

- Other
  - Biofeedback
  - Aromatherapy
Rational Prescribing

- Minimize number of medications used
- Alternatives should be considered
- Start low and go slow
- Titrate to effect
- Educate patient/caregiver(s)
- Reassess regularly
Pharmacologic Management

- **Non-opioids**
  - Acetaminophen
  - NSAIDs
    - Systemic/Topical

- **Opioids**
  - Morphine
  - Oxycodone
  - Hydrocodone
  - Hydromorphone
  - Fentanyl
  - Methadone

- **Epidural/Intrathecal**
  - Opioids
  - Clonidine
  - Bupivacaine
  - Ziconotide

- **Adjuvant Agents**
  - Tricyclic Antidepressants
  - SNRIs, SSRIs
  - Gabapentin/Pregabalin
  - Steroids
  - Capsaicin
  - Muscle Relaxants
  - Ketamine
  - Bisphosphonates
Pharmacologic Treatment for Neuropathic Pain

- SNRI/SSRI
  - Duloxetine
  - Venlafaxine

- Topical Agents
  - Lidocaine
  - Capsaicin

- Methadone

- Anticonvulsants
  - Gabapentin
  - Pregabalin
  - Carbamazepine

- Tricyclic Antidepressants
  - Amitriptyline
  - Nortriptyline
Returning to our Patient
His Goals:

- You were able to explore his values and priorities as well as his fears and hopes. Misconceptions about hospice were addressed.

- There are no more viable **disease directed** treatment options:
  - None available
  - None desired
  - Risks / Harms ... Benefits

- Patient defines pain relief as his primary concern and to be able to function.

- Accepts hospital admission for further assessment and pain control.

- Hospice Eligibility: Not at this time
  - Due to advanced malignant disease meets basic eligibility of >50% probability of death within six months.
  - Current goals of care are **not exclusively** comfort focused.
At Admission:

ROS
- Nausea
- Poor appetite
- Difficulty standing
- Gait unsteady
- Generalized aching
- No bowel movement for 10 days
Physical Exam

- Bitemporal wasting
- Facial grimacing / restless
- Abdomen firm and diffusely tender
- Mucous membranes dry
- Lower extremities weak with atrophic musculature
- Hyperreflexia of both lower extremities
## LABS

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine</td>
<td>5.0</td>
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<tr>
<td>BUN</td>
<td>60</td>
</tr>
<tr>
<td>K+</td>
<td>6</td>
</tr>
<tr>
<td>Calcium</td>
<td>12</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.1</td>
</tr>
<tr>
<td>Hgb</td>
<td>10</td>
</tr>
<tr>
<td>PLT</td>
<td>80k</td>
</tr>
</tbody>
</table>

- Hct: 30
- Bili: 5
- Alk Phos: 1200
- SGOT: 100
- SGPT: 90
- INR: 2.4
Recent Imaging

- CT imaging
  - Multiple hepatic metastasis
  - Large amount of stool noted
  - Large lytic lesions in both femurs
  - Lytic lesion in lumbar region

- Lumbar spine MRI
  - Lytic lesions
  - Multiple areas of cord compression
Assessment

- Uncontrolled pain likely due to metastatic bone disease
  - Current oral Morphine equivalents of 100 mg hydrocodone (100 OME) daily
  - >3000 mg of Acetaminophen /day

- Risk of paralysis due to cord compression
- Risk of pathologic femur fractures
- Hypercalcemia
- Dehydration
- Acute kidney injury
- Severe constipation, probable source of abdominal pain
- Hepato Renal Syndrome?
Metastatic Bone Pain

- Opioid
- Palliative Radiation Therapy
- Chemotherapy
- Adjunctive Analgesics
  - NSAID or Steroid (e.g., Dexamethasone)
  - IV Bisphosphonate
  - Anticonvulsant (e.g., Gabapentin)
Malignancy-Induced Hypercalcemia

- **Symptoms**
  - Weakness
  - Constipation
  - Fatigue
  - Generalized pain
  - Poor appetite

- **Treatment**
  - Hydration is first step
  - Bisphosphonates
Principles of Opioid Prescribing

- Select appropriate opioid based on patient’s illness and renal and hepatic function
- “Start low and go slow”
- ALWAYS prescribe pro-motility agent (e.g. Senna) to prevent expected constipation
- Situational Awareness

- Regulatory Rules:
  - Check the Maps
  - Educate patient/caregiver (Consent)
  - Risk Assessment
Opioids

- Meperidine
  - Neurotoxicity
- Tramadol
  - Toxicity
- Codeine
  - Pro-drug converted to morphine
  - Variable metabolism
- Morphine
- Hydrocodone/Acetaminophen
  - Acetaminophen burden is limiting
- Oxycodone
- Hydromorphone
- Fentanyl
- Buprenorphine
- Methadone
Tramadol / Trama-don’t

- Compared to pure opioids:
  - Higher risk of delirium
  - Risk of serotonin syndrome
  - Risk of hypoglycemia
  - Risk of seizure activity
  - Higher hospitalization rate within the first 30 days of prescribing
Opioid Side Effects/Risks/Benefits

- Side effects that improve with time
  - Sedation always precedes
  - Respiratory depression: Assess with RASS
  - Nausea
  - Histamine Release
    - Hypotension
    - Itching
- Constipation does not improve with time
  - Scheduled Senna stimulant is MANADATORY

- Benefit
  - Pain control
  - Dyspnea control
    - Usually much lower dose required for pain

- RISK
  - Tolerance is a two-sided coin
    - Lower risk of respiratory depression with time
    - Higher dose requirement usually means disease progression
  - Addiction generally is a non issue in the setting of limited life expectancy, absent previous history of substance abuse.
Opioid-Induced Neurotoxicity

- Caused by metabolite byproduct of opioid
- Associated with:
  - Myoclonus/seizures
  - Acute delirium
  - Hallucinations
  - Hyperalgesia
- Opioid-induced delirium is different from sedation side effect of opioid
- Can occur with any opioid agonist
Myths About Opioids

- Opioid use typically leads to addiction
- Opioids always cause heavy sedation
- Older adults should not use opioids
- Opioids have a high risk of depressing respirations
# Opioid Equivalents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Oral/Rectal (mg)</th>
<th>IV/SC (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30</td>
<td>10</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20</td>
<td>N/A</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>7.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Codeine</td>
<td>200</td>
<td>120 (IM only)</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>30</td>
<td>N/A</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>N/A</td>
<td>100 mcg</td>
</tr>
</tbody>
</table>
Teaching Points

- Opioid conversion tables are an approximation only.
- Individuals experience incomplete cross tolerance to opioids of another type.
  - As rule of thumb, if changing from one opioid to another, the starting dose should be 25-50% less than the calculated equivalent dose.
  - to provide a safety margin.
Teaching Points

- Opioid tolerant is defined as >60 mg of Oral Morphine Equivalents (OME)/day for 7 days.
- In not opioid “tolerant” you’re opioid “naïve”.
- If opioids are interrupted for as little as 72 hours, tolerance is lost. (This is felt to be a significant contributor to accidental overdose deaths as users tend to return immediately to their usual dose after an interruption.)
Opioids in Renal Failure

• **Avoid**
  - Codeine
  - Morphine
  - Tramadol

• **Consider with caution**
  - Oxycodone
  - Hydromorphone

• **Preferred**
  - Fentanyl
  - Methadone
Opioids in Liver Disease

- **Caution**: Delayed Clearance
- Limit dose and frequency
- Preferred opioids generally include morphine and hydromorphone
- Caution with Methadone given its metabolism by cytochrome systems
- Avoid hydrocodone-Acetaminophen combinations
Teaching Points

- Pain control for this individual is primary.
- Patients who choose to focus on comfort as a primary goal still deserve thorough assessment to guide therapy.
- Maximizing functionality/quality of life is accomplished by managing specific problems.
- There are many factors to be considered in the selection of an opioid. (Renal and Hepatic function)
- In addition there are non-opioid medications and interventions that can be employed to reduce need for high dose opioid.
- There are compounding problems to be addressed which interplay to aggravate known opioid side effects. These should be addressed directly.
Pain Crisis Management: The best way to manage a pain crisis is with IV Opioid

- Morphine and Hydromorphone are the two most commonly employed IV agents
  - Morphine IV, cheap and effective
    - IV 3x as potent as oral (first pass metabolism)
    - Morphine is contraindicated in setting of renal failure (accumulation of toxic metabolite → myoclonus → seizures)
    - IV use can trigger hypotension due to sometime intense histamine release with initial doses
  - Hydromorphone IV
    - 20 x as potent as oral Morphine
    - 6.5 x as potent as IV Morphine (1.5 mg of IV Hydromorphone = 10 mg IV Morphine)
  - Fentanyl IV
    - 100 x as potent as IV Morphine, dose usually expressed as micrograms (100 mcg IV Fentanyl = 10 mg IV Morphine)
    - Use generally restricted to patients in ICU or inpatient Hospice
    - Minimal cardiovascular side effects
    - Cheap and easy to synthesize and available, leading agent in accidental overdose
Achieving Rapid Pain Control: How do we Safely fill the barrel?

Evaluate

- Pain Level Assessment
  Goal: Acceptable (3-5/10)

- Sedation Assessment (RASS)
  RASS Score 0 to -1
Opioid Pharmacokinetics 101

- Short-acting opioids and acute pain relief
RICHMOND AGITATION-SEDATION SCALE (RASS)

**STEP 1**

Sedation Assessment

<table>
<thead>
<tr>
<th>Scale</th>
<th>Label</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+4</td>
<td>COMBATIVE</td>
<td>Combative, violent, immediate danger to staff</td>
</tr>
<tr>
<td>+3</td>
<td>VERY AGITATED</td>
<td>Pulls to remove tubes or catheters; aggressive</td>
</tr>
<tr>
<td>+2</td>
<td>AGITATED</td>
<td>Frequent non-purposeful movement, fights ventilator</td>
</tr>
<tr>
<td>+1</td>
<td>RESTLESS</td>
<td>Anxious, apprehensive, movements not aggressive</td>
</tr>
<tr>
<td>0</td>
<td>ALERT &amp; CALM</td>
<td>Spontaneously pays attention to caregiver</td>
</tr>
<tr>
<td>-1</td>
<td>DROWSY</td>
<td>Not fully alert, but has sustained awakening to voice (eye opening &amp; contact &gt;10 sec)</td>
</tr>
<tr>
<td>-2</td>
<td>LIGHT SEDATION</td>
<td>Briefly awakens to voice (eyes open &amp; contact &lt;10 sec)</td>
</tr>
<tr>
<td>-3</td>
<td>MODERATE SEDATION</td>
<td>Movement or eye opening to voice (no eye contact)</td>
</tr>
</tbody>
</table>

If RASS is ≥ -3 proceed to CAM-ICU (Is patient CAM-ICU positive or negative?)

-4 DEEP SEDATION No response to voice, but movement or eye opening to physical stimulation

-5 UNAROUSABLE No response to voice or physical stimulation

If RASS is -4 or -5 → STOP (patient unconscious), RECHECK later

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Sessler, et al., Am J Respir Crit Care Med 2002, 166: 1336-1344
Ely, et al., JAMA 2003; 286: 2983-2991
Strategy one:
Start an infusion and escalate hourly at the nurse’s discretion for persistent pain

Recall it takes 5 half-lives to reach steady state (15-20 hours).

In the presence of uncontrolled pain the nurse is authorized to increase the basal rate, and generally feel compelled to do so.

Almost inevitably this leads to shooting through the therapeutic window at steady state.

Commonly 12 hours later when heavy sedation occurs, in a bit of panic a narcan bolus is given → Pain Crisis
Naltrexone

- Use of Naltrexone should be considered more thoughtfully in patients with pain in the setting of life-limiting illness compared to other populations due to risk of pain crisis and withdrawal syndromes

- NARCAN
  - If patient is hyper somnolent but breathing >10 rpm and saturating well, then simply HOLD OPIOIDS and closely monitor
  - If patient is hyper somnolent and < 10 rpm, then give 0.1 mg Narcan (rather than standard 0.4 -2 mg mg dose), and repeat Q3-5min to desired effect, (Alternative: 2 mg amp diluted to volume of 10 ml with saline in syringe, administer 0.5 – 1 ml at similar intervals [0.1-0.2 mg])
Strategy 2: Fill the barrel with Bolus

Dosing: May administer bolus at 10-minute intervals; “Dose Stacking”

Evaluate prior to each dose pain/sedation
Recall sedation will occur prior to respiratory depression.

Initial nominal bolus dose:
Morphine, 2-4 mg range if opioid naive (0.2-0.5 mg hydromorphone).

If opioid tolerant 10% of previous 24-hour OME converted to IV form. Example 150 OME = 50 mg IV morphine x10 % = 5 mg.

If initial dose is ineffective may increase by dose by 50-100%

Goal is acceptable pain control.
Nurse controlled analgesia is preferred over PCA pump.
Calculating an initial basal rate: Goal is to achieve steady state (basal infusion rate = rate of metabolism)

Opioid naïve: No basal rate in first 24 hours

Opioid tolerant: Previous 24-hour OME converted to IV /24. Our Patient was taking 100 mg of hydrocodone/day =100 OME. Converting to Hydromorphone IV = 5 mg/24 = rate of 0.2 mg/hour.

In setting of pain crisis not necessary to consider adjust for incomplete cross tolerance.
Adjusting the Basal Rate

- Opioid tolerant:
  - After pain control is established.
  - Total the amount of bolus medication required to maintain control over a four-hour period (not including the time nor the bolus amounts required to establish initial control). Divide by four, this amount should roughly correspond to what has been metabolized on an hourly basis. Therefore, it should be safe to increase the basal rate by that quantity.
  - If there has been only one or two bolus doses required over 4 hours, there is no need to adjust the basal rate.
  - Adjust bolus dose to equal the hourly basal rate.
  - RASS assessments should be done on an hourly basis. Target RASS score of 0 to -1 (alert to mildly sedated).
  - Note: if pain has been protracted and patient is sleep deprived from pain, expect catch up sleep.
  - Orders should include “hold opioid for RASS scores below -2” unless specifically targeting, with patient’s permission, higher levels of sedation.
Adjusting the Basal Rate:

- **Opioid Naïve: No basal rate in first 24 hours**
  - Calculate average: the total amount of bolus medication required to establish control in 24 hours (Assumes no excessive sedation)
  - Adjust bolus dose to equal the hourly basal rate
  - RASS assessments should be done on an hourly basis. Target RASS score of 0 to -1 (alert to mildly sedated)
  - Note: if pain has been protracted and patient is sleep deprived from pain, expect catch up sleep
  - Orders should include “hold opioid for RASS scores below -2” unless specifically targeting higher levels of sedation (Requires discussion: Is sedation acceptable?)
Opioids as a Bridge

- Pain is a potent neural stimulator and of respiratory drive. Mitigation of pain stimulus may result in relative sedation. In the setting of anticipated improvement, more reliance on short acting agents may be appropriate.

- By example:
  - Steroids: may take 12 or more hours
  - Bisphosphonates: 3-7 days
  - Radiation: 7-14 days
  - Adjuncts such as SNRI or Gabapentin (peak benefits): weeks to months
  - Nerve blocks generally have near immediate benefit
  - Surgical stabilization will be complicated by post operative pain
Teaching Points

- Continuous infusion of IV opioids, long acting oral or topical opioids should only be considered for use in individuals who are opioid tolerant.

- Initial IV hourly basal rate should not exceed the calculated 24-hour equal analgesic amount divided by 24.

- Know the pharmacological dynamics

- Consider the totality of the circumstance

- Risk is relative to need

- Reasonable Caution is always prudent but Don’t be Afraid
Returning to Our Patient Scenario

Assessment:

- Uncontrolled pain likely due to metastatic bone disease
  - Current oral Morphine equivalents of 100 mg (100 OME) daily
  - Risk of paralysis due to cord compression
  - Risk of pathologic femur fracture
- Hypercalcemia
- Dehydration
- Acute kidney injury: Creatinine 5
- Constipation
- Hepato-Renal Syndrome?
Our Patient’s Pain

- PAIN (PQRST: palliative/provocative, quality, region radiation, referral, severity, temporal factors)
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    - 6/10
    - Generalized
    - Bloated feeling with nausea but non-vomiting
    - Food ingestion aggravates pain
Our patient
Pain control Interventions

Options?
- IV Opioid (which one?)
  - Hydromorphone chosen over Morphine due to renal impairment
    - Time 0: Pain 10/10, RASS +2 (mild agitation), primarily bone pain
    - Bolus dose of 0.2 mg: at T + 10 minutes: pain 9/10, RASS +1 (restless)
    - Increase bolus to 0.3 mg: at T + 20 minutes: pain 6/10, RASS 0 (calm)
    - Over the next two hours he received 3 x 0.3 mg bolus. Pain fluctuating between 4-7/10. He noted the nurse was very busy and that it sometimes took 45 minutes for the nurse to deliver the next dose, but by that time the pain had reached level of 7.
  - PCA started with dose of 0.3 mg/10-minute lockout: Pain level varied 4-5, RASS: 0 to -1
    - Total of 6 mg of hydromorphone (x20 = 120 OME) over next 12 hours
Additional Interventions

- Day 1
  - Hydration with IV fluids: Dehydration, AKI, Hypercalcemia
  - Dexamethasone 4 mg, initial dose IV, followed by BID regiment: Pain and risk of cord compromise
  - Bisacodyl suppository, Senna: Constipation
  - Radiation Oncology consult: Recommend 10 fractions to spine, (Patient will consider)
  - Neuro surgical consult: bracing but no operative intervention
  - Ortho consult: consider prophylactic femoral rods to reduce risk of pathological fracture: (Patient declined)
Day 2

- Pain 2-3/10, RASS 0, 10 (0.3) mg bolus via PCA over 24 hours (3 mg hydromorphone = 60 OME), episodic severe sharp radiating pain in legs with standing, refused to wear clam shell brace as it was very uncomfortable
- Patient noted he would sleep for an hour after PCA dose and suggested maybe it is now too high of a dose
  - Would like to think about going home. Decided against Radiation if pain is able to be controlled.
  - Jokingly, ‘Love you guys and all, but I don’t want to die here’
  - PCA stopped, started on Oxycodone 5-10 mg Q3 PRN for breakthrough and Fentanyl Patch 25mcg=50 OME
- Methyl Naltrexone ordered as still having abdominal pain and no bowel movement
- Mucous membranes now well hydrated: BUN 20, Creatinine 6.5, K+ 5, Calcium 11, INR 3.5, Bili 8
  - Renal Consult requested, ‘consider dialysis’. Patient declines, “It won’t fix my cancer”
- New complaint of severe hiccups
  - Not an uncommon side effect of Dexamethasone: Dexamethasone reduce to 2 mg BID oral route
  - Started Gabapentin 100 mg at HS as adjunct for neuropathic pain and can also reduce hiccups, low dose as renal cleared
Converting to Oral Regiment

- Generally the goal is to establish control of the pain crisis and use the 24-hour IV Opioid need as a guide to convert to an oral regiment that can be duplicated on an out patient basis.
- It is important to set and maintain appropriate expectations.
- Keep in mind, the goal is acceptable functional status, not zero pain.
- Generally, a combination of long acting medication for basic control and short acting for breakthrough will be required (target 80:20 ratio).
- Long-acting agents should be paired with short-acting agents of the same type:
  - Morphine IR with Morphine SR (MSContin)
  - Oxycodone IR with Oxycodone SR (OxyContin)
- Simple better than complex (BID better than TID).
- Cheaper better than expensive.
- Control better than crisis.
- Fentanyl Patch:
  - Desirable agent in setting of renal failure.
  - If ability to continue oral intake is suspect.
Hospital Course

Day 3

- Pain well controlled 3/10 in back and legs
  - Two doses of Oxycodone for break through pain 4-5/10
  - 25 mcg Fentanyl patch well tolerated, not feeling at all sedated
- Large bowel movement abdominal discomfort minimal
  - Scheduled Senna and MiraLAX
- Increased Ascites and edema noted on exam
- Requiring assistance to transfer due to weakness in legs
- Considering Hospice: ‘Sensing calm before the storm’
- Hiccups resolved
- Priority is to get home
Day 4: A Turn for the Worse

- Signs of deterioration
  - Poor oral intake
  - More somnolent
  - Urine output dropping
  - Unable to get out of bed

- LABS
  - Creatinine: 7
  - K+: 6.5
Goals of Care Revisited

- Family Meeting (Roadmap)
  - REMAP
    - Reframe: Warning shot: “Your condition has changed.” Followed by the Headline: “Your kidneys and liver have failed.”
    - Expect emotion: “NURSE”
    - Map out the patients Goals: “This is what I hear is important to you.”
    - Align with Goal: “I will try to help you achieve XYZ.”
    - Propose a plan: “This is what I suggest to accomplish your goals.”
  - NURSE dealing with emotion (Name, understand, respect, support, explore)
I recognize that my time is short, but I don’t really want to know how short.

I would like to die at home.

Wife crying, “I can see how sad you are.”

“That’s not the issue. I am afraid. I don’t know what to tell the younger kids.”

“I can only imagine how difficult this has been for all of you.”

Son, “This sucks.”

“You have all shown remarkable courage over the last few months. It has truly been my privilege to help care for you. I will continue to support you as best I can.”

“May I make a recommendation?”

“I believe that with the support of Hospice we can achieve your goal of being at home and with additional skill of the Hospice social worker and chaplain, offer additional support to your children.”

Patient, “I would welcome that. Before I forget, I would like to thank you for the two days I spent at home last Christmas... By the way, don’t play poker. I knew this day was coming after our first conversation.”
Afternoon of day 4
- Getting home remains priority
- Home with Hospice

Continuing pattern of decline over the next week
- Minimal oral intake/Difficulty swallowing
- Palliative Performance Scale → decline to 20%
- Oxycodone Tablet: switched to oral concentrate form Oxycodone 20 mg/ml
- Gradual Increasing need for breakthrough pain management >100 OME/day
- Fentanyl Patch increased to 50 mcg strength
### Palliative Performance Scale (PPSv2)

<table>
<thead>
<tr>
<th>PPS Level</th>
<th>Ambulation</th>
<th>Activity Level &amp; Evidence of Disease</th>
<th>Self-care</th>
<th>Intake</th>
<th>Conscious level</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPS 100%</td>
<td>Full</td>
<td>Normal activity &amp; work No evidence of disease</td>
<td>Full</td>
<td>Normal</td>
<td>Full</td>
</tr>
<tr>
<td>PPS 90%</td>
<td>Full</td>
<td>Normal activity &amp; work Some evidence of disease</td>
<td>Full</td>
<td>Normal</td>
<td>Full</td>
</tr>
<tr>
<td>PPS 80%</td>
<td>Full</td>
<td>Normal activity &amp; work with effort Some evidence of disease</td>
<td>Full</td>
<td>Normal or reduced</td>
<td>Full</td>
</tr>
<tr>
<td>PPS 70%</td>
<td>Reduced</td>
<td>Unable normal activity &amp; work Significant disease</td>
<td>Full</td>
<td>Normal or reduced</td>
<td>Full</td>
</tr>
<tr>
<td>PPS 60%</td>
<td>Reduced</td>
<td>Unable hobby/house work Significant disease</td>
<td>Occasional assistance</td>
<td>Normal or reduced</td>
<td>Full or confusion</td>
</tr>
<tr>
<td>PPS 50%</td>
<td>Mainly sit/lie</td>
<td>Unable to do any work Extensive disease</td>
<td>Considerable assistance</td>
<td>Normal or reduced</td>
<td>Full or drowsy or confusion</td>
</tr>
<tr>
<td>PPS 40%</td>
<td>Mainly in bed</td>
<td>Unable to do most activity Extensive disease</td>
<td>Mainly assistance</td>
<td>Normal or reduced</td>
<td>Full or drowsy +/- confusion</td>
</tr>
<tr>
<td>PPS 30%</td>
<td>Totally bed bound</td>
<td>Unable to do any activity Extensive disease</td>
<td>Total care</td>
<td>Reduced</td>
<td>Full or drowsy +/- confusion</td>
</tr>
<tr>
<td>PPS 20%</td>
<td>Totally bed bound</td>
<td>Unable to do any activity Extensive disease</td>
<td>Total care</td>
<td>Minimal sips</td>
<td>Full or drowsy +/- confusion</td>
</tr>
<tr>
<td>PPS 10%</td>
<td>Totally bed bound</td>
<td>Unable to do any activity Extensive disease</td>
<td>Total care</td>
<td>Mouth care only</td>
<td>Drowsy or coma</td>
</tr>
<tr>
<td>PPS 0%</td>
<td>Dead</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Instructions: PPS level is determined by reading left to right to find a ‘best horizontal fit.’ Begin at left column reading downwards until current ambulation is determined, then, read across to next and downwards until each column is determined. Thus, ‘leftward’ columns take precedence over ‘rightward’ columns. Also, see ‘definitions of terms’ below.

### Definition of Terms for PPS

- **Full**: No significant difficulty
- **Reduced**: Significant difficulty
- **Mainly**: Usually able to do
- **Totally**: Unable to do
- **Dead**: Unresponsive
The Last 72 Hours

- 7 Physical Signs:
  - Peripheral Cyanosis
  - Cheyne-Stokes breathing
  - Decreased urine output (<100 ml over the last 12 hours)
  - Apnea periods
  - Respiration with mandibular movement
  - Death rattle
  - Pulselessness of radial artery

- High likelihood of death within 3 days

- With implications for important decisions such as hospital discharges and enrollment into care pathway at the end of life.
Figure 1. Frequency and onset of clinical signs among 203 patients who died in acute palliative care units. (A): The median time of onset (95% confidence interval) is shown. The median onset was three days before death for seven of these signs.
Management of Pain
In the Actively Dying

- If Pain has been a significant burden, pain medication should be continued even after loss of consciousness
- Dosing guided by non-verbal pain assessment
- Commonly half-lives are prolonged due to hepatic and renal failure
- Not all individuals experience pain near death for some air hunger/dyspnea dominates
- Dyspnea/air hunger is not uncommon and highly responsive to opioid
- Sub Q morphine and hydromorphone are options, peak effect in 30 minutes
- Oral concentrated forms of Morphine and Oxycodone 20 mg/ml are available and useful in those who are unable to swallow pills and tend to be effective even in those struggling with liquids, as volumes are very small
- Contrary to popular myth, only about 10% of sublingual opioids are absorbed through oral mucosa, if held in the mouth for 5 minutes. They trickle down to be absorbed through GI tract. Exception is Fentanyl as it is lipophilic
- Onset of action of oral opioids occurs at 30 minutes with peak effects in about an hour. Duration of action 3-4 hours
  - If consistently insufficient relief in an hour, dose needs to be increased
  - If relief not lasting until next dose is due, increase frequency of dosing
Patients with Cognitive Impairment

- Behavioral observations & Caregiver Proxy reports
- Verbal cues
- Facial expressions
- Body movements
- Clenching of fists, Restlessness, Guarding
- Social Interactions (being withdrawn)
Management of Delirium in the Actively Dying

- Terminal delirium is not uncommon and is best managed with Benzodiazepines with short to intermediate half lives.
  - Lorazepam is our agent of choice. It is available as tablets, oral concentrate and injectable forms, preferably IV, as subQ administration results in erratic absorption.

- Particularly in individuals with Dementia, Benzodiazepines can aggravate delirium.
  - Alternatives are atypical antipsychotic, typically Haloperidol or Olanzapine
Palliative Sedation:

“The lowering of patient consciousness using medications for the express purpose of limiting patient awareness of suffering that is intractable and intolerable.” – NHPCO definition

- Palliative sedation (Terminal Sedation) is ethically acceptable and legal in Michigan as the intent is to relieve suffering not hasten death.
  - In practice it is rarely needed to achieve pain control.
  - In our busy practice of full-time hospital based Palliative Care and Hospice, two full time physicians and four advanced practice providers, we have employed the technique only once in two years.
  - It should be only undertaken with explicit consent of the patient or their surrogate.
  - The technique relies on use of a short acting Benzodiazepine or Barbiturate to produce sedation in combination with an opioid targeting pain relief. We do not use opioids to intentionally cause sedation.
  - Opioids do have the side effect of sedation, however tolerance to sedative side effects rapidly develop.
  - It is our practice to specifically inquire if mild sedation is acceptable, if required to achieve adequate pain control.
Management of Other Symptoms Encountered in the last 72 Hours

- “Death Rattle”: This sound derives from air passing through pooled secretions as a result of ineffective cough.
  - It is generally best managed by repositioning. Suctioning is ineffective and should be avoided.
  - First step is education of family that this is far more distressing to us than it is to the patient.
  - That being said, it still sounds like they are drowning.
  - Common agents used are all anticholinergics: Hyoscyamine, Atropine eye drop solution administered orally, Scopolamine patch, and Glycopyrrolate. All cross the blood brain barrier except Glycopyrrolate, as such, they can aggravate delirium.
Closure

- Home visit 24 hours to passing (Primary Care Physician can manage Hospice patients)
  - Minimally responsive
  - Pain controlled
  - Family grieving
    - Wife tearful but in command
    - Children coping (hospice social worker had identified additional community resources)
- Death
  - Risk of complicated grief identified
  - Hospice grief support extends a year and a day
  - To this day family remains immensely grateful for Hospice.
Acknowledgements

With gratitude to Romàn Barraza, MD, Medical Director, Hospice and Palliative Medicine, colleague and friend, who graciously gave permission to use material from his library of resource material and PowerPoint presentations.
The Morphine Drip opioid infusions in comfort care, Alex Sable-Smith MD, MPH

- https://youtu.be/pXJHx7AnzYE
Thank You for your attention.
Resources and Suggested Readings

References:
* Suggested reading/review prior to conference
** Priority read
> Excellent resource for opioid conversions

Davis, Mellar et. al. Essential Practices in Hospice and Palliative Medicine (5th ed.) Unipac 3 Pain Assessment and Management. Chicago, IL; American Academy of Hospice and Palliative Medicine, 2017. **
Resources and Suggested Readings

References

Hui, David et. al. “Clinical Signs of Impending Death in Cancer Patients”. The Oncologist, June 19(6), 2014 681-687


Resources and Suggested Readings

References

McPherson, Mary. Demystifying Opioid Conversion Calculations (2nd ed.) Bethesda, MD; American Society of Health-System Pharmacists, 2018.


Sable-Smith, Alex. “The Morphine Drip. Opioid Infusions in Comfort Care”.

www.youtube.com/watch?v=XJHx7AnzYE.*
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Skarf, Lara et. al. Essential Practices in Hospice and Palliative Medicine (5th ed.) Unipac 5 Communication And Teamwork. Chicago, IL; American Academy of Hospice and Palliative Medicine, 2017