Palliative Care Emergencies

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VA Boston Healthcare System  
Instructor, Harvard Medical School

Outline

- Defining a palliative care emergency
- Principles of response
- Recognizing and treating specific emergencies  
  - Hemorrhage
  - Seizures
  - Spinal cord compression
  - Pain crisis
  - Hyperalgesia/opioid-induced neurotoxicity

What is a palliative care emergency?

- A sudden, urgent, usually unexpected situation or condition during which the life and/or the quality of life of a patient with an incurable disease are threatened
- Requires immediate action: “I cannot leave this patient/family until this is better.”
- “Can I prevent an emergency by anticipating a possible crisis?”
Palliative care emergencies can take many forms

- Bleeding
- Agitation
- Pain crisis
- Seizures
- Intractable cough
- Choking
- Stridor
- Breathlessness
- Spinal cord compression
- Hypercalcemia
- Obstructive nephropathy
- Fracture
- Superior vena cava syndrome
- Tamponade
- Hyperalgesia/opioid toxicity

Though specific clinical management will vary, response principles are the same

- Address the symptom
- Address the patient and family
- Remain present
- Remain calm
- Determine and address the underlying cause (if possible)
- Enlist the aid of others
- Anticipate and prepare for emergencies (if possible)

Clinical Case

- Mr. T is a 50yo M with extensive local HNC s/p multiple treatments who presented to the hospital with increasing cancer-related pain. His pain was managed by the inpatient palliative care team, and after multiple goals of care discussions, he elected to go home with hospice support. His neck looks like this:
Terminal bleeding is a dreaded palliative care emergency

- Distress can be great
- Traumatic for patients, family, caregivers
- Home management poses unique challenges and requires careful preparation

Bleeding is not uncommon in cancer, but massive bleeding is rare

- No consensus definition
  - Terminal hemorrhage ↔ catastrophic bleed ↔ major bleed ↔ hemorrhagic complication
- Incidence is likely overestimated
  - 6-10% of cancer patients have bleeding
  - 3-12% of cancer patients have terminal bleeding
- Incidence varies by cancer type & location
- Terminal hemorrhage = major, from an artery, and likely to result in death within a time period as short as minutes

Recognition of impending major bleed is not always straightforward

- “Sentinel” or “herald” warning bleed may precede a life-threatening bleed
- Ballooning or visible pulsatile arterial vasculature may be seen
- Some patients have no warning signs or symptoms, so consider risk factors
Many factors can increase the risk of bleeding

<table>
<thead>
<tr>
<th>Disease-related factors</th>
<th>Treatment-related factors</th>
<th>Systemic/other factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer type</td>
<td></td>
<td>Hematologic</td>
</tr>
<tr>
<td>• Head and neck</td>
<td>• Radical neck dissection</td>
<td>• Thromboeytopenia</td>
</tr>
<tr>
<td>• Hematologic</td>
<td>• Post-op hematoma</td>
<td>• Marrow failure</td>
</tr>
<tr>
<td>• Fungating tumors</td>
<td>• Radiation therapy</td>
<td>• DIC (from sepsis, etc.)</td>
</tr>
<tr>
<td>• GI (prior bleeding)</td>
<td></td>
<td>• Coagulopathy</td>
</tr>
<tr>
<td>Tumor size, location</td>
<td></td>
<td>Biochemical</td>
</tr>
<tr>
<td>Tumor location (close to</td>
<td></td>
<td>• Urema</td>
</tr>
<tr>
<td>major vessels)</td>
<td></td>
<td>• Hepatic dysfunction</td>
</tr>
<tr>
<td>Metastasis (liver, marrow)</td>
<td></td>
<td>Co-morbidities</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Diabetes, immunodef.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Age &gt;50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• cachexia/poor nutrition</td>
</tr>
<tr>
<td></td>
<td>Surgical interventions</td>
<td>Pharmacologic</td>
</tr>
<tr>
<td></td>
<td>• Radical neck dissection</td>
<td>• Anti-coagulants</td>
</tr>
<tr>
<td></td>
<td>• Post-op hematoma</td>
<td>• NSAIDs</td>
</tr>
<tr>
<td></td>
<td>Radiation therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chemotherapy (decreased platelet count)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wound complications</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Poor healing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>infections</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fistula (oropharyngeal, cutaneous, pelvic)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surgical interventions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hematologic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Thrombocytopenia</td>
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<td>• Marrow failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• DIC (from sepsis, etc.)</td>
<td></td>
</tr>
</tbody>
</table>
| Local or systemic treatments to control early bleeding depend on goals of care

**Local interventions**
- Compressive dressings
- Hemostatic agents
- Vasoconstrictive agents
- Radiation
- Surgery
- Endoscopy
- Endovascular techniques

**Systemic interventions**
- Volume resuscitation, transfusion
- Vitamin K
- Vasopressin/desmopressin
- Antifibrinolytic agents (aminocaproic acid, tranexamic acid)
- Octreotide
- Sucralfate (PO, NG, PR)

In major/terminal bleed, goal is to initiate supportive measures and give crisis meds

<table>
<thead>
<tr>
<th>PREPARATION for the event</th>
</tr>
</thead>
</table>
1) Identify patients at risk
2) Identify and reduce risk factors
   • Medication review
3) Engage in sensitive discussions
   • Patient and families
   • Other professionals
4) Prepare crisis plan
   • Teach family/caregivers positioning and pressure
   • Have dark towels, other equipment ready
   • Prepare medication plan
   • Establish DNR orders

**THE EVENT**

**Assurance**
• Reassure the patient you are with them right now!

**Be there!**
• Above all, stay with the patient

**Comfort and Calm**
• Dark towels, basins
• Sedatives/anxiolytics
• Opioids if pain or dyspnea

Adapted from Ubogagu & Harris, 2012.
Medications may be used, but should not interfere with presence and support

- Goal is to alleviate distress and provide comfort, NOT hasten death
- Benzodiazepines are the mainstay for anxiolysis/sedation
  - Midazolam most frequently recommended
  - Dosing and route varies
- Opioids are more controversial; use if pain or dyspnea
- Ketamine may be an alternative

Harris, 2009

Goals of management are to initiate supportive measures and give crisis meds

<table>
<thead>
<tr>
<th>PREPARATION for the event</th>
<th>AFTER the event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Identify patients at risk</td>
<td>1) Supportive measures</td>
</tr>
<tr>
<td>2) Identify and reduce risk factors</td>
<td>2) Disposal of waste</td>
</tr>
<tr>
<td>3) Engage in sensitive discussions</td>
<td>3) Psychological support</td>
</tr>
<tr>
<td>4) Prepare crisis plan</td>
<td>- Offer ongoing psychological support, bereavement counseling, +/- debrief session with all involved</td>
</tr>
<tr>
<td>- Medication review</td>
<td></td>
</tr>
<tr>
<td>- Patients and families</td>
<td></td>
</tr>
<tr>
<td>- Other professionals</td>
<td></td>
</tr>
<tr>
<td>- Teach family/caregivers positioning and pressure</td>
<td></td>
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<tr>
<td>- Have dark towels, other equipment ready</td>
<td></td>
</tr>
<tr>
<td>- Prepare medication plan</td>
<td></td>
</tr>
<tr>
<td>- Establish DNR orders</td>
<td></td>
</tr>
<tr>
<td>- Reassure the patient you are with them right now!</td>
<td></td>
</tr>
<tr>
<td>- Above all, stay with the patient</td>
<td></td>
</tr>
<tr>
<td>- Use dark towels, basins</td>
<td></td>
</tr>
<tr>
<td>- Pressure, suction</td>
<td></td>
</tr>
<tr>
<td>- Sedatives/anxiolytics</td>
<td></td>
</tr>
<tr>
<td>- Opioids if pain or dyspnea</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Ubogagu & Harris, 2012.

Clinical case

- Mr. M is a 65yo M with stage IV NSCLC with recently diagnosed brain metastases. A month ago, he was treated with whole-brain radiation therapy. He takes a low-dose of dexamethasone daily (4mg), from which he is being weaned. He is brought in by EMS with a generalized tonic-clonic seizure.
Anguish over recurrent seizures remains common in modern day medicine

- Distressing for patients, families
- Fear of recurrence can be great
- Home management poses unique challenges

Seizures are common in primary and metastatic brain tumors

- Presenting symptom in 25-40% of primary brain tumors; another 15-30% of pts develop
- Presenting symptom in 10-20% of brain mets and 15% of leptomeningeal carcinomatosis; another 10% of pts will develop
- Tumor location is the most important predictor

Seizures can be caused by structural damage to the brain or a systemic insult

<table>
<thead>
<tr>
<th>CNS</th>
<th>Toxic-Metabolic</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary or metastatic tumor</td>
<td>Medication toxicity or withdrawal</td>
<td>Chemotherapy (cisplatin, MTX, ifos, vinca alkaloids, many others)</td>
</tr>
<tr>
<td>Leptomeningeal metastasis</td>
<td>Renal or liver disease</td>
<td>Meperidine, other opioids</td>
</tr>
<tr>
<td>Brain irradiation</td>
<td>Electrolyte abnormalities (Na+, Ca2+, Mg2+)</td>
<td>High-potency neuroleptics</td>
</tr>
<tr>
<td>RPLS</td>
<td>Hypoglycemia</td>
<td>Bisphosphonates</td>
</tr>
<tr>
<td>Paraneoplastic limbic encephalitis</td>
<td>Hypoxia</td>
<td>Ondansetron</td>
</tr>
<tr>
<td>Meningoencephalitis, abscess</td>
<td>Non-CNS infection</td>
<td>Imipenem, penicillins, other antibiotics</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>Tumor lysis syndrome</td>
<td>Amphotericin</td>
</tr>
</tbody>
</table>
Workup of seizures depends on goals of care

- A prompt history and physical can help determine the cause
- Further workup may be warranted:
  - Labs (CBC, BMP, Ca, Mg, LFTs, glucose)
  - MRI brain
  - LP with CSF cytology, infectious workup
  - EEG

Status epilepticus has high morbidity and mortality

- Status epilepticus is a true medical emergency, with a mortality risk of 11-34%
- Complications include acidosis, rhabdomyolysis and cerebral damage
- Prolonged convulsions lead to neuronal injury and pharmacoresistance
  - 30-50% are refractory
- Treatment should be instituted when a convulsion lasts 5 minutes or more

The DOs and DON’Ts of non-pharmacologic acute seizure management

<table>
<thead>
<tr>
<th>DO</th>
<th>DO NOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Place patient in a prone or lateral position</td>
<td>1) Put anything in the mouth</td>
</tr>
<tr>
<td>2) Protect from hazards</td>
<td>2) Try to hold the tongue</td>
</tr>
<tr>
<td>3) Remove eyeglasses</td>
<td>3) Restrain or grab hold of the patient</td>
</tr>
<tr>
<td>4) Loosen tight clothing around the neck</td>
<td>4) Give liquids or oral meds (during or immediately after)</td>
</tr>
<tr>
<td>5) Observe pt until fully awake and aware of environment</td>
<td>5) Perform CPR</td>
</tr>
<tr>
<td>6) Reassure family (and pt after)</td>
<td>6) Shout or expect verbal commands to be obeyed</td>
</tr>
<tr>
<td>7) Give meds if &gt;5min</td>
<td></td>
</tr>
</tbody>
</table>
There are many IV medication options to acutely treat seizures

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>10mg over 2-5min, repeat after 15min</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>0.5-1mg/kg (4mg), repeat in 20 min</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>1mg bolus, 2-10mg over 24 hrs</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.1-0.3mg/kg bolus, 0.05-0.4mg/kg/h</td>
</tr>
<tr>
<td>Phenytoint</td>
<td>15-20mg/kg infusion</td>
</tr>
<tr>
<td>Fosphenytoin</td>
<td>15-20mg PE*/kg, then 4-5 mg/kg/day</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>10-15 mg/kg/d, over 1h, then 15-60 mg/kg/d (BID-QID)</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>10-20mg/kg, then 1-4 mg/kg/day</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>10-20mg/kg, then 0.5-3mg/kg/hr</td>
</tr>
<tr>
<td>Propofol</td>
<td>1mg/kg, then 1-15mg/kg/hr</td>
</tr>
</tbody>
</table>


Options when IV is not available

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diazepam</td>
<td>PR</td>
<td>10-20mg, repeat in 15min</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>IM, IN, SC PR SL</td>
<td>Similar to IV, Slow absorption</td>
</tr>
<tr>
<td>Midazolam</td>
<td>SC</td>
<td>Similar to IV</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>SC</td>
<td>Similar to IV</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>PR</td>
<td>200-1200mg q6h (adults) or 15-20 mg/kg (peds) via suppositories or retention enemas</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>SC</td>
<td>100-200mg bolus, then 600-2400mg/d</td>
</tr>
<tr>
<td>Fosphenytoint</td>
<td>IM</td>
<td>Similar to IV, SC (fos only)</td>
</tr>
<tr>
<td>Pentobarbital</td>
<td>PR</td>
<td>60-200mg, re-dose q 4h</td>
</tr>
</tbody>
</table>


Anticonvulsant prophylaxis for brain mets is not recommended if no prior seizure

- Evidence does not support pharmacologic prophylaxis in patients who have not had a prior seizure except:
  - 1 week after neurosurgery
  - Possibly brain mets from melanoma, choriocarcinoma, renal cell carcinoma, thyroid papillary cancer, and testicular cancer
- Patients should take corticosteroids before, during and immediately after cerebral radiotherapy
Clinical case

Ms. L is a 57 yo woman with a history of breast cancer with prior thoracic vertebral metastases treated with radiation. She presents now with thoracic back pain and slowly progressive difficulty in walking. She is found to have a thoracic vertebral lesion on MRI which is impinging on the cord.

Malignant Spinal Cord Compression (MSCC) is a dreaded complication

- If untreated can lead to progressive pain, paralysis, sensory loss, and debility
- Delay in diagnosis or treatment leads to loss of mobility and decreased survival
- Early recognition and treatment is well tolerated and can provide symptomatic relief

Malignant Spinal Cord Compression is most often extradural (epidural)

Definition: compression of the dural sac and/or contents by a tumor mass
- Majority extradural
- Minority are intra-dural or intramedullary
Malignant spinal cord compression is not rare

Incidence
- 20% of cancers present with MSCC
- 2.5% of terminal cancer patients had an admission for MSCC
- 5% of terminal patients have MSCC in last 2 years of life
- Incidence ranges from 0.2% in pancreatic cancer to 7.9% in myeloma

Tumor type
- Lung 23%
- Breast 21%
- Prostate 20%
- Renal Cell Carcinoma
- Non-Hodgkin’s lymphoma
- Multiple Myeloma

Back pain is the most common presenting symptom

- 83-95% of patients will have back pain
- Pain can be local, referred or radicular

Patterns of Referred Pain

<table>
<thead>
<tr>
<th>Lesion Site</th>
<th>Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>Mid-scapular</td>
</tr>
<tr>
<td>Thoracic</td>
<td>Hip/Lumbosacral</td>
</tr>
<tr>
<td>Lumbosacral</td>
<td>Thoracic</td>
</tr>
</tbody>
</table>

- 50% can have bowel or bladder dysfunction
- 60-85% have focal weakness
- 60% are non-ambulatory

Talcott model identifies six predictive factors

<table>
<thead>
<tr>
<th>Talcott Model</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inability to walk</td>
<td>1</td>
</tr>
<tr>
<td>Increased deep tendon reflexes</td>
<td>1</td>
</tr>
<tr>
<td>Compression fractures</td>
<td>1</td>
</tr>
<tr>
<td>Bone metastases</td>
<td>1</td>
</tr>
<tr>
<td>Bone mets diagnosed &gt; 1 yr ago</td>
<td>1</td>
</tr>
<tr>
<td>Age &lt; 60</td>
<td>1</td>
</tr>
</tbody>
</table>

6 Risk Factors 87% risk MSCC
0 Risk Factors 4% risk MSCC
MRI is mandatory in patient with cancer and risk factors for MSCC

- MRI is 93% sensitive and 97% specific
- Up to 1/3 of patients have more than one spinal lesion
- In 45% of patients, MRI findings altered the radiation field

- MRI of the entire spine is therefore indicated

Management includes medications, procedures and communication

**Pain Control- Pharmacologic**
- Opioids
- Steroids
- Bisphosphonates

**Pain Control– Interventional**
- Radiotherapy
- Surgery
- Radiosurgery

**Anticipate**
- Constipation
- Depression
- Anxiety

**Goals**
- Pain control
- Improve/maintain function
- Bladder control
- Prolong life

Dexamethasone prior and during XRT increases ambulation

<table>
<thead>
<tr>
<th>Findings</th>
<th>Dosing</th>
<th>Efficacy</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back pain and epidural disease without MSCC</td>
<td>Moderate dose: 10 mg IV x one, then 4 mg q6h for two weeks</td>
<td>No trials</td>
<td>Tremulousness, insomnia, delirium, hyperglycemia</td>
</tr>
<tr>
<td>MSCC with pain but no neurologic symptoms</td>
<td>Moderate dose: 10 mg IV x one, then 4 mg q6h for two weeks</td>
<td>No trials</td>
<td>Tremulousness, anxiety, insomnia, delirium, hyperglycemia, GI bleed, infection, myopathy, edema, insomnia</td>
</tr>
<tr>
<td>MSCC with pain and neurologic changes</td>
<td>High dose: 100 mg IV x one, 24 mg q6h for three days, then taper</td>
<td>81% v. 63% ambulatory after Rx</td>
<td>59% v. 33% ambulatory at 6 mos.</td>
</tr>
</tbody>
</table>
**Prognosis depends on functional status at time of diagnosis and disease type**

<table>
<thead>
<tr>
<th>Functional status before treatment</th>
<th>Percent ambulatory after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulatory</td>
<td>60-100%</td>
</tr>
<tr>
<td>Para-paretic</td>
<td>36-40%</td>
</tr>
<tr>
<td>Paralyzed</td>
<td>13-15%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Percent paralyzed after treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>50%</td>
</tr>
<tr>
<td>Prostate</td>
<td>40%</td>
</tr>
<tr>
<td>Breast</td>
<td>10%</td>
</tr>
</tbody>
</table>

**Radiotherapy is very effective**

- 60-90% pain relief with XRT and steroids
- Regimens:
  - 3 Gy x 10 fractions
  - May decrease late recurrence
  - Hypofractionated: 4 Gy x 7 days OR 8 Gy x one
  - No difference in outcome of ambulation
  - Survival shorter with short course
  - May be easier for patient

**Surgery provides longer survival in the appropriate patient**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Surgery and XRT</th>
<th>XRT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulatory</td>
<td>84%</td>
<td>57%</td>
</tr>
<tr>
<td>Duration of walking</td>
<td>122 days</td>
<td>13 days</td>
</tr>
<tr>
<td>Regained ambulation</td>
<td>62%</td>
<td>22%</td>
</tr>
</tbody>
</table>

**Who is the appropriate patient?**

- Solitary site
- Absence of visceral or brain mets
- Radio-resistant tumor
- Age < 65
- Spinal instability
- KPS > 70
- Low co-morbidities
- Maintained ambulation
- Acute neurologic findings: myelopathy or impending paralysis
- Slow progression of neuro symptoms
- Prognosis > 3 months
- Non ambulatory for < 48 hrs
Prognosis

- Median prognosis of < 6 months
- Poor prognostic indicators:
  - Tumor other than breast, prostate, myeloma or lymphoma
  - Other bone or visceral metastases
  - Non ambulatory status before therapy
  - Interval from tumor diagnosis of < 15 mnths
  - Motor deficits developing < 14 days prior to therapy
  - 10% develop recurrence at median 4.5 months
  - 50% recur at 2 yrs

Clinical case

Mr H 75 yo W with stage IV NSCLC with mets to ribs, vertebral spine and left hip. Was relatively comfortable at home until last night when he developed acute pain in right hip. Now moaning, crying, and unable to get comfortable. Tender to touch; worse with movement.

MEDS:
- OxyContin 80 mg bid
- Oxycodone 15-20mg po q 2hrs
(taking 3-5 doses/day; took 2 doses in last 5 hrs – no relief)

Managing a pain crisis involves more than medication

- Address the symptom
- Address the family (and patient)
- Remain present
- Determine and address the underlying cause – as appropriate
- Enlist aid of others
A fair bit of math is involved

- Elicit level of pain: “15/10”
- Calculate total daily opioid requirement
  - OxyContin 80mg bid = 160mg oxycodone
  - oxycodone pm: 20 x 3 = 60mg po oxycodone
  - 220mg po oxycodone = 330mg po morphine
- Calculate PRN medication dose
  - 10% total opioid use
  - 330mg/10 = 33mg PO morphine = 11mg IV morphine
- Administer the drug
- Re-assess in 15 minutes

Dose changes are based on clinical response

- Give X mg IV opioid
- Re-assess in 15 minutes
  - Pain = 15/10 (no change; no side effects)
  - Pain = 9/10 (reduction <50%)
  - Pain = 4/10 (reduction >50%)
- Double opioid dose
- Repeat same dose
- Consider this the new prn dose
- Re-assess in 15 minutes
- Re-assess in 2-3 h

Pain crisis management is time and labor intensive

<table>
<thead>
<tr>
<th>Time</th>
<th>Pain Score</th>
<th>Medication</th>
<th>Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 min</td>
<td>15/10</td>
<td>Oxycodeone 30mg</td>
<td>Distressed, RR 28</td>
</tr>
<tr>
<td>45 min</td>
<td>12/10</td>
<td>1 mg IV dilaudid = 7 mg IV morphine</td>
<td>Uncomfortable, RR 24</td>
</tr>
<tr>
<td>60 min</td>
<td>7/10</td>
<td>Declines dose</td>
<td>More comfortable</td>
</tr>
<tr>
<td>75 min</td>
<td>6-7/10</td>
<td>Resting</td>
<td>RR 18</td>
</tr>
<tr>
<td>90 min</td>
<td></td>
<td>PCA started morphine 4 mg IV bolus q 15 min</td>
<td></td>
</tr>
<tr>
<td>3.5 hrs</td>
<td>5-6/10</td>
<td>Dosing, easily aroused</td>
<td>RR 14</td>
</tr>
<tr>
<td>24 hrs</td>
<td>5-6/10</td>
<td>MRI to evaluate cause of pain</td>
<td></td>
</tr>
</tbody>
</table>
There are 3 accepted methods to calculate PRN dose

1) Use the last effective dose
   - 1 mg IV hydromorphone q 1 hr prn

2) Use 50-100% of the hourly effective dose
   - 30 mg po oxycodone = 17 mg IV morphine +
   - 1 mg IV hydromorphone = 7 mg IV morphine
   - 24 mg IV morphine in 90 min
   - 16 mg IV morphine in 1 hour
   → 8-16 mg IV morphine q 1 hr prn

3) PCA: Calculate bolus to allow 50-100% of hourly effective dose in one hour
   - 16 mg/hr → 4 mg IV q 15 min

Other routes exist when IV medication is not an option

- Subcutaneous: serum levels equivalent to IV; slower onset
  - Reassess in 30-45 min
- Sublingual: best for lipophilic medications
- Buccal: similar to sublingual
- Rectal: Well absorbed
- Orally: re-assess in 45-60 minutes

Consider the addition of non-opioid treatments

- Steroids
- Ketorolac
- Ketamine
- Lidocaine
- Interventional approaches (blocks, pumps)
- Ice/Heat
- Hypnosis
- Breathing exercises
Communication is critical

- Address the meaning of the pain
- Address any fears of pain
- Educate patient and family on coping techniques
- Re-assurance that you will stay until the crisis is resolved
- Power of presence

Diagnostic studies to determine the underlying cause depend on goals of care

- Proportionate to:
  - Severity of distress
  - Refractoriness of distress
- Inversely proportionate to:
  - Proximity to death

Clinical case

Ms M is a 47 yo woman with melanoma metastatic to bone and brain who is admitted for pain control. Pain is in the right shoulder at the site of a metastases. She is in considerable pain and focus is on comfort.

<table>
<thead>
<tr>
<th>Day</th>
<th>Medication</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Morphine PCA no basal, 5mg iv q 15 min</td>
<td>Severe pain</td>
</tr>
<tr>
<td>10</td>
<td>Morphine at 20mg/hr</td>
<td>Severe pain</td>
</tr>
<tr>
<td>11</td>
<td>Morphine 40mg/hr</td>
<td>Confusion, agitation, pain</td>
</tr>
<tr>
<td>13</td>
<td>Ativan started; morphine 70 mg/hr</td>
<td></td>
</tr>
</tbody>
</table>
There is a differential diagnosis for opioid dose escalation with worsening pain

- New source of pain
  - Fracture
  - Cord compression
  - Disease progression
- Tolerance to medications
- Opioid induced neurotoxicity: hyperalgesia
- Opioid non-responsive pain

Opioid induced neurotoxicity has been described in both humans and animals

- Definition: syndrome of increasing pain and signs of nervous system excitability in patients treated with opioids
- Nervous system excitability:
  - Myoclonus
  - Allosthenia
  - Delirium
  - Seizures
- Derangement of neural pathways that mediate pain, such that opioids escalate or stimulate pain, rather than reduce it.
- Hyperalgesia: increasing sensitivity to noxious stimuli

Opioid neurotoxicity is more common in situations of:

- Rapid escalation of opioids
- Pain despite increasing doses of opioids
- Very high doses of opioids
- Diffuse pain
- Non tolerant patient
- Dehydration
- Renal insufficiency
- Phenanthrene opioids (morphine, hydromorphone, oxycodone, codeine, hydrocodone)
Management of opioid neurotoxicity involves skillful communication

- Patient is in pain
- Differential includes: increased source of pain, tolerance to pain medications.
- You are suggesting decreasing pain medication

There are several methods for treating opioid neurotoxicity

- Subdue the CNS
  - Discontinue neurotoxic medications
  - Start benzodiazepines
- Rotate opioids
  - Find the last effective opioid dose
  - Stop current opioid
  - Start another opioid at 25% MEDD, often methadone or fentanyl
- Add an adjuvant medication - ketamine
- Trial of hydration

Questions
References