PAIN MANAGEMENT AT THE END OF LIFE

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"Thoughtful Approaches to Pain Management"

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DISCLOSURE

- I have no financial conflicts of interest related to today's learning. I am an employee of Allina Health.
- All treatment recommendations are based on specialty guidelines, community standard of practice, and personal experience.
- The medications used in hospice and palliative care are mostly off label, and NOT FDA approved.

OBJECTIVES

- Understand pain as a common physical disorder at end of life with distinct physiologic causes.
- Understand total pain as an experience influenced by social, psychological and spiritual well being.
- Be able to order effective treatment for pain relief.
- Review case studies and our own experience for new learning on hospice care.

Principles of Pain Treatment in Hospice

- Pain assessment.
- Goals of care.
- Opioid options and pharmacokinetics
- Adjuvant pain treatment

Pain Assessment is NOT…

- Relying on changes in vital signs
- Deciding a patient does not "look in pain"
- Knowing how much a procedure or disease "should hurt"
- Assuming a sleeping patient does not have pain
- Assuming a patient will tell you they are in pain

Total Pain

- Pain is subjective
- Pain occurs in the context of a person's life:
  - fears and hopes for the future
  - spiritual beliefs
  - pressure and support from family
  - social and economic realities
- Thus—a patient's report of pain will be filtered and modified by these factors

Pain Assessment

- 5 components for a thorough pain assessment
  - Basic History of Pain
  - Analgesic History (Pharmacologic)
  - Analgesic History (Non-pharmacologic)
  - Impact and Meaning of Pain
  - Pain Causality and Basic Goals

Analgesics for moderate to severe pain

- OPIOIDS
  - All opioid analgesics produce pain relief via interaction with opioid receptors in the brain/spinal cord and perhaps via peripheral opioid receptors.
  - The *mu* receptor is the dominant analgesic receptor, but other receptors play a role in analgesia for certain opioids.
  - There is no pharmacologic dose ceiling for opioids, only for acetaminophen in combination products.

Oral Short Acting Opioids

- Parenteral or Oral
  - morphine
  - hydromorphone
  - oxymorphone
  - codeine
- Oral only
  - oxycodone
  - hydrocodone (combination meds with acetaminophen)

Oral Short Acting Opioids

- Oral dosing:
  - onset in 20-30 min
  - peak effect in 60-90 minutes
  - duration of effect 2-4 hours (6-8 hours for oxymorphone)
  - Can be dose escalated or re-administered every 2-4 hours for poorly controlled pain (as long as the daily acetaminophen dose stays < 4 grams for combination products).

Equianalgesia

- 10 mg IV MS = 30 mg po MS
- 10 mg IV MS = 1.5 mg IV Hydromorphone
- 30 mg po MS = 7.5 mg po Hydromorphone
- 30 mg po MS = 20-30 mg po Oxycodone

Note: Conversion factors are only a rough guide to approximate the correct dose.

Sedation / Respiratory Depression

- With increasing dose, all opioids lead to a predictable sequence of CNS events:

Sedation with or without delirium then …

Further decrease in consciousness then …

Coma and respiratory depression

Respiratory Depression

- Risk Factors
  - Renal insufficiency
  - Liver failure
  - Parenteral opioids; especially rapid dose escalation in opioid naïve patients
  - Severe pulmonary disease (CO_2 retainers)
  - Sleep apnea
  - Rapid dose escalation of transdermal fentanyl or methadone

Mindy J.

- 65 yo enrolled in hospice January 2017
  - CHF, lvef=20-25%, CAD, DM, MRSA wound
  - Weakness, dyspnea, falls, PPS=50%
  - Chronic pain
  - 43 listed drug allergies, including morphine, gabapentin
- Pain = 0/10, 4/10, often 10/10
- Meds: duloxetine, diphenhydramine, glucosamine, lorazepam, pramipexole, **benzonatate, acetaminophen, cyclobenzaprine, melatonin, polyethylene glycol, sennosides-docusate**

MJ: Pain treatment on hospice

- Pt reported experiencing pain "all over" which she jokingly rated at 25/10 on pain scale. She reported she always has pain but prefers not to take pain medication, she reports managing pain mentally instead.
- Cardiac care: frequent cardiology appts, f/u echo, labs, full code changed to DNR, O2 dependent at 5 LPM, weight loss, glucose=53 → 600
- Massage therapy
- No opioids

Jane R.

- 90 yo admitted to hospice October 2017 with CLL, CHF, weight loss
- Chronic pelvic pain, followed by palliative care, multiple hospitalizations (4 more after hospice admission)
- Meds: escitalopram, methadone 40 mg tid, mirtazapine, pregabalin, polyethylene glycol
- Pain = 7/10, ER trips for 10/10 pain
- PMH: fibromyalgia, severe scoliosis, osteoarthritis, degenerative disk disease, and severe chronic pelvic pain

Pain treatment on hospice

- Minimal relief from previous trials of extended-release morphine, fentanyl patch, and virtually ALL immediate release opioids
- **continue Methadone 40mg twice daily and at bedtime.**
- **-continue IR morphine, increase to 20-40mg every two hours PRN breakthrough pain**
- **-increase** pregabalin **to 200mg twice daily and at bedtime**
- **-start trial of oral ketamine, 10-20mg every hour PRN for pain uncontrolled by opioids alone**

Treatment results

- Ketamine titrated to 20 mg tid with good pain relief and no side effects.
- Jane R lived at home for 5 months following hospice admission
- After another brief hospital episode Jane R moved to a hospice residence.
- She experienced progressive weakness and dyspnea due to heart failure, with a peaceful death 10 days later.

Ketamine

- 10-20% of cancer patients experience refractory pain
- Used in anesthesia
- Pharmacology
  - NMDA receptor antagonist
  - Opioid receptor agonist
  - Half-life 2-3 hours
  - Not available as oral product (we use IV med, given orally)
  - Low oral bioavailability but active metabolite, norketamine
- Indicated for neuropathic pain, opioid resistance, hyperalgesia
- Oral solution for oral pain
- Evidence base: inconsistent

Ketamine

- Adverse effects
  - Arrhythmia, salivation, nausea, involuntary movements, bladder dysfunction
  - Dissociative reaction (12%, can be co-treated with lorazepam or haloperidol.)
  - Doses over 2 mg/kg
  - Potential for abuse
- Dosing ("subanesthetic")
  - 10-20 mg tid oral, or 20-60 mg daily, or 1-2x/week (for mood treatment)

Juan G.

- 52 yo man admitted to hospice December 2016
- COPD, depression, weight loss, O2 5 LPM + BiPap, PPS=60%
- Chronic pain, schizophrenia, chest pain, smoking
- Chronic pain, chronic back pain
- Meds: clonazepam, diphenhydramine, gabapentin, morphine ER, ondansetron, polyethylene glycol, sennosides-docusate, sertraline

Juan G pain treatment on hospice

- Pain = 7/10 to 10/10
- Frequent requests to increase doses
- Lost meds, requesting early refills
- Observed use of illicit drugs
- Extra pain meds hidden throughout house
- Lock box, pain medication agreement, home visits by hospice pharmacist

Juan G pain treatment on hospice

- Methadone added, titrated gradually 10 tid → 30 mg tid
- Oxycodone 20-30 mg q 4 hours prn, max 3 doses daily
- Morphine ER 30 mg qid
- Frequent antibiotic and steroid bursts for COPD exacerbation
- Progressive weakness and dyspnea, now housebound, on BiPap constantly (remove for eating and smoking)

Strategy for treating chronic pain and addiction on hospice

- Trusting relationship with hospice team.
- Reliable access to pain medications, with close supervision.
- Pain treatment agreement, pharmacist consultation.
- Dose increase to be avoided based on patient request, episodes of incident pain.
- Dose increase based on expected tolerance, loss of function, observed pain complications.
- Team care: social, spiritual, integrative care.

Chronic pain and addiction

- Medication dosage and tolerance
- Short acting or long acting medications
- Therapeutic trust and patient safety concerns
- Methadone treatment
- Special issues: Suboxone, Buprenorphine, cannabis

Neuropathic pain

- Caused by nerve injury
- Pain in a distinct somatosensory pattern
- Occurs in up to 40% of cancer patients
- Symptoms
  - Paresthesia (numbness and tingling)
  - Allodynia (pain with light touch)
  - Hyperalgesia (exaggerated pain with painful stimulus)

Neuropathic pain

- Gabapentin
- Tri-cyclic antidepressants
  - Amitriptyline, nortriptyline
- Other antidepressants
  - Venlafaxine, duloxetine, pregabalin
- Methadone
- Ketamine
- Amitriptyline/ketamine/baclofen gel
- "older" anticonvulsants: carbamazepine
- IV lidocaine?
- Cannabis?

Opioid induced neurotoxicity

Risk factors
- Increasing doses of opioids
- Renal failure

Symptoms
- Hyperalgesia, allodynia
- Worsening pain despite increasing doses
- Myoclonus, delirium, seizure

Proposed mechanisms
- Toxic effect of opioid metabolites (e.g. morphine-3-glucuronide or hydromorphone-3-glucronide).
- Central sensitization as a result of opioid-related activation of N-methyl-D-asparate (NMDA) receptors in the central nervous system.

Opioid induced neurotoxicity: treatment

- Reduce current opioid
- Consider IV fluids
- Change to new opioid: fentanyl, hydromorphone
- Add methadone (and ketamine?)
- Add adjuvant pain treatment: gabapentin, acetaminophen, baclofen
- Consider interventional pain consult (epidural, intrathecal)

Refusing pain treatment

- Case study: Your recent patient/family example.

- "That threw me for a loop. I will never take that again."
- "Family request we avoid pain medications and sedatives to allow patient to remain as alert as possible."
- "Son adamantly refuses any use of morphine. States, 'That's what killed my father when he was on hospice.'"

Refusing pain treatment

- By the patient
- By the family decision maker
- Ethics and moral distress
- Team support and strategies

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