Mehraneh Khalighi, MD
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Pain Management

Learning Objectives-

- ✓ Identify most common barriers to effective treatment of pain.
- ✓ Describe principles of effective pain management
- ✓ Define: addiction, physical dependence, hypersomnolence, and oversedation

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Case: 60 year-old woman with breast cancer and h/o bony metastases presents with severe mid-lumbar back pain with radiation into bilateral buttocks. She has no new neurologic deficits but pain has made her bed-bound over the last few days. Her pain medication regimen is: MS contin 120mg bid, MS IR 30mg q4h prn. She has taken her prn medications 6 times in the last 24 hours. Her exam is normal, she is fully alert. She weighs 50kg.

Overview-

- 1/3 of all cancer patients have either chronic or recurrent pain
- 60-90% of these patients have advanced cancer
- Eastern Cooperative Oncology Group (ECOG) conducted an "Outpatient Pain Needs Assessment Survey" to evaluate adequacy of pain relief:[1]
    - 1308 ambulatory patients with metastatic disease were surveyed: 871 (67%) had pain and took analgesics w/in one week and 475 (36%) had severe enough pain to impair function. 250/597 patients (42%) reported inadequate analgesic therapy
- Barriers to effective treatment of pain:
    - Patient factors leading to reluctance to report pain
        - Fear of disease progression
        - Cultural and religious preferences: suffering is good
        - If drugs are taken too soon, they might not work later when needed more
        - Pain medications are for the dying
        - Fear of addiction to pain medications
    - Physician factors leading to inadequate pain management
        - Inadequate pain assessment
        - Reluctance to prescribe narcotics
        - Inadequate knowledge regarding pain management

- Some of these barriers are easily addressed
    - In patients with no prior h/o addiction, cancer pain treatment with narcotic analgesics leads to <1% new addiction rate.
    - Addiction: psychological and behavioral syndrome characterized by loss of control over drug use and compulsive, continuous use despite harmful side effects.
    - Physical Dependence: pharmacologic property of drug that causes withdrawal when the drug is abruptly discontinued (e.g. rhinorrhea, lacrimation, diarrhea, anxiety, hyperventilation, hyperthermia, myalgias, vomiting, hostility, etc.)
- World Health Organization developed guidelines to improve cancer pain management in 1986.

World Health Organization Guidelines for Cancer Pain Management- "Pain Relief Ladder"[2]

Intensity of pain (subjective)	Treatment
Step 1 (Mild, 1-4)	Nonopiod agent (Around the clock coverage with Tylenol or NSAIDs ± adjuvant tx
Step 2 (Mild – Moderate, 5-6)	Weak opiod (e.g. codeine, oxycodone) + nonopioid agent ± adjuvant tx
Step 3 (Moderate – Severe, 7-10)	Strong opiod (e.g. morphine, hydromorphone, fentanyl) ± nonopiod or adjuvant tx

- Several studies, including prospective studies, have confirmed that when the WHO guidelines are followed, up to 70-90% of patients have effective pain management with a low rate of complications.[3]

The "Analgesic Elevator" Model-

- Challenges the clinical usefulness of "weak" opioids in mild to moderate pain
    - systematic reviews comparing the efficacy of NSAIDs vs. a weak opioid suggest that the transition from step I to step II drugs does not necessarily improve analgesia[4,5]
    - delays optimal pain control, especially in patients with rapidly progressive pain
- Proposes immediate response with strong opioids as first-line treatment of mild-moderate pain.
    - " transport of analgesics inside a lift would be quicker than stepping up a ladder"
    - Phase III study in 100 terminal cancer patients with mild-moderate pain showed[6]
        - Patients had significantly better pain relief and greater satisfaction with treatment
        - Patients required fewer changes in therapy and had greater reductions in pain when therapeutic changes were initiated

Principles of Pain Management-

- Adequate assessment of pain
    - Nature: elicit a good history
    - Cause: treat underlying pathophysiology if possible
    - Personal context: consider pain a serious and treatable symptom
        - Psychological
        - Social
        - Spiritual
        - Practical issues
- Use of appropriate interventions
    - Pharmacologic vs. Nonpharmacologic
    - Use opioids around the clock for frequent/continuous pain and add a breakthrough regimen as needed
    - Provide enough analgesia to permit normal functioning (e.g. sleep, social interactions)
    - Do not allow inappropriate concerns about addiction and dependence prevent the use of effective doses on a regular schedule
- Ongoing assessment of treatment outcomes and regular review of the plan of care
    - Obtain subjective measures of pain (0-10 scale, visual scale, etc)
    - Titrate analgesics to pain relief
    - Flexibility is essential—successful plans are tailored to the individual patient and family
    - Willingness to ask for help from colleagues with more expertise when the plan is not effective at controlling the patient's pain
- Use of other members of an interdisciplinary team
- Education of the patient, family, and all caregivers about the plan

Goals of Pain Management-

- Either eliminate pain or reduce it by at least 50% by subjective ratings
- Keep side effects minimal
    - Sedation and respiratory depression: tachyphylaxis develops within a few days (far before tolerance develops)
        - Hypersomnolence: patient is not confused and awakens easily, just catching up after extended periods of sleep deprivation
        - Oversedation: altered mental status, delirium, hard to arouse, may need to use naloxone reversal if severe
        - Avoid full opioid reversal with naloxone in patients who are tolerant: use 1/10 of usual dose of naloxone (0.04mg) IV q 3-5 minutes and titrate to desired arousal
        - Most patients will improve with simply stopping opioids until more alert, then restarting at 75% of the previous opioid dose
    - Nausea: resolves usually within 24 hours of initiation
    - Physical dependence: develops after 2 weeks of treatment
        - Decrease dose by 50% every 2-3 days to taper.
        - If taper is smaller than unit dose, then taper frequency until can omit.

- Constipation: most common adverse effect. Should be managed prophylactically and aggressively with stool softeners and stimulants (docusate and senna)
- Itching: histamine release mediated (not a true allergy).
  - Can use antihistamines or switch agents if necessary.
- Urinary retention: may need to decrease dose or add adjuvant medications

- Choose the most appropriate pain regimen for your patient
  - Always consider age and hepatorenal function of patient
    - Opioids and their metabolites can accumulate in renal insufficiency as well as the elderly and can lead to excessive side effects
    - Avoid drugs with long t ½ e.g. methadone (15-150 hrs).
    - **In these patients hydromorphone (dilaudid) is the best choice given short t ½ (2-3 hrs)**: has least adverse reactions but associated with increased psychological dependence.
  - Avoid Meperidine which has higher likelihood of neurotoxicity with repeated dosing
  - Nausea and CNS side effects: Oxycodone < Morphine.
  - Gastrointestinal side effects: Fentanyl Patch << oral pain medication
  - Rectal preparations bypass first pass hepatic metabolism and absorption is variable but similar bioavailability to oral preparations have been reported: can use similar doses to oral preparations but may need to lower doses as needed

Equivalent Analgesic Doses of Selected Narcotics-

Drug	**Dose (for equivalent analgesia)**	**Half-life (hr)**	**Peak (hr)**	**Duration (hr)**
Morphine	10 mg IM/IV 30-60 mg PO*	2-4 2-4	0.5-1 2	4-6 4-6
Morphine, slow release (Kadian, MS Contin, Oramorph SR)	30-60 mg PO*	3-4	4-6	8-12
Hydromorphone HCl (Dilaudid)	1.5 mg IM 7.5 mg PO	2-3 2-3	0.5-1 1-2	4-6 4-6
Levorphanol tartrate (Levo-Dromoran)	2.0 mg IM 4.0 mg PO	12-16 12-16	0.5-1 1	4-6 4-6
Methadone HCl (Dolophine HCl, Methadose)	Non-linear kinetics**	15-150+ 15-150+	0.5-1.5 0.5-1.5	4-6 4-6
Codeine phosphate, codeine sulfate	130 mg IM 200 mg PO	2-4 2-4	1 1-2	4-6 4-6
Oxycodone HCl	20 mg PO	2-3	1	3-6
Meperidine HCl (Demerol)	75 mg IM 300 mg PO	3-4 3-4	0.5-1 1-2	3-5 4-6
Fentanyl (Sublimaze)	0.1 mg IV	3-4	0.25	0.5-2
Fentanyl (Duragesic)	Variable			

*With long-term dosing, relative potency of IM:ORAL formulations changes from 1:6 to 1:3
** consult palliative care or pain service before prescribing methadone

Initiation of Oral/Outpatient Pain Management in opiod-naïve patient-

- Initial test dose (use short-acting agents):
  - 30-60mg codeine/5-10mg oxycodone/15-**30mg morphine IR q4h** **(Morphine 5mg IV = Morphine 15-30mg PO = Oxycodone 10mg PO = Codeine 100mg)**
- If pain not improved by ½ within 30-60 minutes of dose or pain control not lasting at least 3 hours, can double dose unless patient is excessively sedated
- Rescue dose of MS IR 15mg po q1h prn
- Assess pain relief and side effects over next 1-2 days.
  - Increase baseline dose to accommodate prn dose and continue q4h dosing until pain relief has been achieved (only 2-3 prn doses needed per day)
- Convert total daily dose to long-acting medication e.g. MS contin q12h or q8h
- **10-20% of total 24h dose used for breakthrough dose q1-2h**
- For mild to moderate pain, a dose escalation of 25-50% may be sufficient
- For severe pain, need to increase dose in at least 50% increments to double the drug effect:
  - e.g. MS Contin 100mg q12h → MS Contin 150mg q12h

Failure of Outpatient Pain Management/ Acute pain-

- Usually need to admit patient to the hospital for parenteral (PCA) administration of pain medications
- Consider loading dose of Morphine for immediate pain relief[7]
  - Loading dose of Morphine 0.1mg/kg IV
    - Similar analgesic response pattern to lower dose Morphine 0.05mg/kg IV
    - Patients more likely to experience pain relief 10 minutes after the injection
    - Improved patient satisfaction with pain relief
    - Trend towards 2x incidence of adverse effects overall (4x level of emesis) but statistically not significant
- Need to monitor patients closely within the first 6-8 hours of initiation of IV narcotics to avoid overdoses
  - Danger of overestimating IV dose requirements if poor pain control was related to decreased absorption of oral medications.

Institution of Patient-Controlled Analgesia (PCA) in Patients with Severe Cancer Pain[8]

	Continuous IV dose	**PCA dose**	**Oral dose**
Establish current 24 hour oral dose			"total dose" used as oral **morphine** in 24 hours
Initiate IV dosing	1/3 of "total oral dose" over 24 hours	1/2 hourly dose is available every 1 hour	None
Adjust IV dose	Add prior 24 hours of PCA doses to provide new 24-hour rate	If doses are requested more than hourly, double the PCA dose	None
Sufficient IV analgesia		Only 2-3 supplemental doses required per day	None
Convert to oral	Reduce IV basal rate by 50%	Continue IV PCA at previously established dose	3x50% of IV dose/24h, divided into 2-3 doses (q8-12h)
		If IV PCA requirements increase, increase oral dose	Increase oral doses by 50-100%
	D/C IV basal rate	Continue IV breakthrough but encourage po meds	Add oral short acting morphine for BT doses: 6x IV BT dose or ~20% of total dose q1-4 hours

Adjuvants to Opiods for Treating Cancer Pain-

Class	Drugs	Approximate daily adult dose (mg)	Effects
Anticonvulsants	Carbamazepine	200-1,600	Decrease neuropathic pain
	Phenytoin (Dilantin)	200-600	
	Gabapentin	300-900	
Antidepressants	Amitriptyline HCl (Elavil)	10-100	Decrease neuropathic pain, improve sleep and appetite
	Doxepin HCl (Sinequan)	10-100	
Antihistamines	Hydroxyzine (Atarax, Vistaril)	15-400	Relieve itching; coanalgesic with opioids
Anxiolytics	Diazepam (Valium)	10-40	Relieve anxiety; sedative; relieve skeletal muscle spasms
	Lorazepam (Ativan)	1-8	
Corticosteroids	Dexamethasone sodium phosphate	8-96	Reduce swelling (e.g., spinal cord compression); improve appetite and sense of well-being
	Prednisone	5-120	
Muscle relaxants	Cyclobenzaprine HCl (Flexeril)	10-30	Relieve skeletal muscle spasms
Neuroleptics	Haloperidol (Haldol)	1-8	Relieve anxiety and restlessness; sedative; coanalgesic with opioids
	Methotrimeprazine (Levoprome)	10-40	
Psychostimulants	Dextroamphetamine sulfate (Dexedrine, Dextrostat)	5-10	Reduce opioid-induced sedation; coanalgesic with opioids
	Methylphenidate HCl (Ritalin)	10-15	

Bisphosphonates provide some pain relief resulting from bone metastases or osteoarthropathy.[9]

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Pain Management Problem Set:

Case: 60 year-old woman with breast cancer and h/o bony metastases presents with severe mid-lumbar back pain with radiation into bilateral buttocks. She has no new neurologic deficits but pain has made her bed-bound over the last few days. Her pain medication regimen is: MS contin 120mg bid, MS IR 30mg q4h prn. She has taken her prn medications 6 times in the last 24 hours. Her exam is normal, she is fully alert. She weighs 50kg.

How do you address her pain?

Case continued: Patient continues to c/o 8/10 pain and pushes her morphine PCA every 10 minutes.

What do you do next?

Case continued: Patient uses her PCA only twice in the next hour and rates her pain as 2/10.

What do you do next?