Opioids and adjuvant analgesics in palliative care

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Objectives

- Identify the challenges and barriers to adequate pain control in cancer patients in the setting of the opioid epidemic
- Recognize 4 risk factors for opioid misuse and ways to screen for this and monitor opioid use with universal precautions
- Practice calculating equaianalgesic opioid conversions
- Describe 3 non-opioid adjuvant analgesic treatments for pain

- No financial disclosures

Pain: An Epidemic

- Pain is the most common reason patients seek medical attention
  - 100 million Americans suffer with chronic pain
  - 25 million suffer acute pain from surgery or accident
- Globally
  - 120 million adults (1 in 5) have chronic pain
  - 60 million (1 in 10) newly diagnosed with chronic pain each year
  - 1 in 3 elderly adults have trouble living independently due to chronic pain

American Academy of Pain Management 2013
Goldberg DS, McGee SJ. Pain as a global public health priority. BMC Public Health 2011

Pain: An Epidemic

- 67% of cancer patients report pain
- Burden of pain on society
  - $100 billion per year
    - Expenses, lost income, and lost productivity

Physician attitudes and practice in cancer pain management

- Survey of 354 medical oncologists on their practice of pain
  - Rated questions on scale of 1 to 10
- Stated that they felt oncologists can treat pain well (7) as compared to their peers who are more conservative (3)
- Quality of pain training was rated as a 3 for medical school and 5 for residency

Breuer B, Fleishman SB, Cruciani RA and RK Portenoy. Medical Oncologists' Attitudes and Practice in Cancer Pain Management: A National Survey. J Clin Oncol 2011.

Physician attitudes and practice in cancer pain management

- Barriers to pain management
  - Poor assessment, 6
  - Patient reluctance to take opioids (5) or to report pain (6)
  - Physician reluctance to prescribe opioids (5) and perceived excessive regulation (4)
- In response to two challenging clinical vignettes
  - 60% and 87% endorsed treatment decisions that would be considered unacceptable by pain specialists.
  - Referrals to pain or palliative care specialists were reported by only 14% and 16%

Breuer B, Fleishman SB, Cruciani RA, and RK Portenoy. Medical Oncologists' Attitudes and Practice in Cancer Pain Management: A National Survey. J Clin Oncol 2011.

Line Up

- How many of you would take opioids for chronic pain?
- If not, why?

Practical use of opioids

- Opioids are essential therapy for acute and chronic pain in patients with advanced illnesses
- Use non-pharmacologic and non-opioid therapies for chronic non-malignant pain
- Clinicians must acquire skills
- With increasing rates of misuse and abuse of prescription opioids, there has to be high level of assessment including etiology and type of pain, screening and monitoring, documentation

Risk factors for opioid misuse

- Gender
  - Males>Females
- Age
  - Higher risk for younger people
- Family history
- Unemployment and failure to meet educational goals
- Marital status
  - Higher risk for those who cohabitate but have not been married, or those in unstable marriages
  - Increased risk if partner exhibits problematic behavior

Fudin J et al. Chronic pain management with opioids in patients with past or current substance abuse problems. *Journal of Pharmacy Practice* 2003;16.4:291-308.

Opioid Risk Tool

FACTOR	MALE PATIENTS	FEMALE PATIENTS
Family history of substance abuse		
• Alcohol	❑ 3 points	❑ 1 point
• Illegal drugs	❑ 3 points	❑ 2 points
• Prescription drugs	❑ 4 points	❑ 4 points
Personal history of substance abuse		
• Alcohol	❑ 3 points	❑ 3 points
• Illegal drugs	❑ 4 points	❑ 4 points
• Prescription drugs	❑ 5 points	❑ 5 points
Age between 16 and 45	❑ 1 point	❑ 1 point
History of preadolescent sexual abuse	❑ 0 points	❑ 3 points
Psychiatric disease		
• Attention deficit disorder, obsessive-compulsive disorder, bipolar disorder, schizophrenia	❑ 2 points	❑ 2 points
• Depression	❑ 1 point	❑ 1 point

- Low risk 0-3, Moderate risk 4-7, High risk ≥ 8

Aberrant drug-related behavior: Behavioral predictors of opioid misuse

Behaviors More Predictive	Behaviors Less Predictive
Using prescription medication inappropriately (cutting time release tabs, "borrowing" others' meds)	Aggressive complaining
Obtaining medication from nonmedical source	Drug hoarding when symptoms are milder
Illicit behavior (selling, forgery, multiple prescription "losses")	Requesting specific drugs
Continual resistance to change in therapy despite clear adverse effects	Unsanctioned dose escalation once or twice in frequency
Concurrent alcohol or illicit drug abuse/positive urine or blood screens	Unapproved use of the drug to treat another symptom
Objective evidence of substance-related deterioration in ability to function (work, family, social)	Occasional impairment in personal functioning
Meeting DSM-IV criteria for substance abuse or dependence	Reporting psychic effects not intended by the clinician

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Universal Precautions for opioid prescribing

- Make a diagnosis with appropriate differential, etiology and type of pain
- Psychological assessment including risk of addictive disorders
  - Tools include: CAGE, SOAPP, ORT, STAR
- Informed consent
- Treatment agreements, random urine tox screens, random pill counts

Universal Precautions for opioid prescribing

- Pre and post intervention assessment of pain level and function
- Appropriate trial of opioid +/- adjunctive medication
- Reassessment of pain score and level of function
- Regularly assess the Four As'
  - Analgesia, Activity, Adverse effects, Aberrant behavior
- Periodically review pain diagnosis and comorbid conditions including addictive disorders
- Documentation

Random Urine Drug Testing

- Can be used to assess adherence to treatment plan

- Tests are qualitative, not quantitative
  - If level is below "cutoff" will be negative
    - Possible that if a patient taking low dose prn, may not appear

- Most immunoassay screens for opioids typically do not assess for methadone, fentanyl or oxycodone
  - These drugs need to be specifically requested

- Cocaine only tests positive for 2-3 days post last use

Case 1

- 64 year old Caucasian female with extensive stage small cell lung cancer has worsening pain over the last week in her mid-back which is aching, 8/10 which radiates around her torso bilaterally superior to her umbilicus and feels like a tight cord pulling her there.
- She is taking norco 7.5/325mg four times per day which brings the pain down to 5/10
- On exam she has worsened pain to light touch which a numb feeling over her torso bilaterally.
- What other questions do you want to ask?
- She denies any bowel incontinence, urinary retention, arm or leg weakness, or perineal sensory changes.
- What work up would you like to order? What else is important to know about her?
- MRI reveals a bone metastasis with nerve root impingement at T8
- What type of pain does she have?
  - Acute nociceptive somatic pain with neuropathic component, thoracic radiculopathy
- What treatments would you consider?

Case 1

- What is her OME?
- Norco 7.5mg X 4 times per day = 30mg OME
- She has normal renal and liver function tests
- Convert to morphine SA, oxycodone ER, fentanyl patch, methadone
- How do you calculate prn dosing of opioids?
- The hand that writes the opioid is the hand that writes the _______________?

Equianalgesic Table

Opioid	PO	Parenteral	Ratio
Morphine	30	10	3:1
Codeine	200	130	1.5:1
Oxycodone	20	10	2:1
Hydromorphone	7.5	1.5	5:1
Meperidine	300	100	-

24 Hour dose of oral morphine	Conversion ratio—morphine:methadone
<90mg	4:1 (25%)
90-300mg	8:1 (12.5%)
>300mg	12:1 (8%)

daily morphine dose range	methadone conversion ratio
0-30mg	2/1
30-99mg	4/1
100-299mg	8/1
300-499mg	12/1
500-999mg	15/1
>1000mg	20/1

Conversion Short Cuts

- **PO** morphine -> **IV/SQ** Dilaudid
  - Divide 24 hour total PO morphine dose by 20
- **IV/SQ** Dilaudid -> **PO** morphine
  - Multiply 24 hour total IV/SQ dilaudid dose by 20
- 25mcg fentanyl patch= approx 75mg PO morphine
- 1:3 ratio fentanyl:PO morphine

Case 1 continues

- Morphine SA 15mg BID
- Oxycodone ER 10mg BID
- Fentanyl patch 12mcg every 72 hours
- Methadone 2.5mg PO TID
- What other treatments could help her with her bone pain?
  - Palliative Radiation
  - Steroid versus NSAID?
- What might you consider for an adjuvant analgesic for her neuropathic pain?
- What dose of gabapentin would you order and how would you titrate?

Case 1

- Would adjuvant for neuropathic pain may you consider if she has insomnia, poor appetite or depression?
  - Nortriptyline 25mg PO at bedtime
  - Side effects?
  - What to check?
- What adjuvant for neuropathic pain may you consider if she has peripheral neuropathy from her chemotherapy, fatigue, depression or anxiety?
  - Duloxetine 30mg PO daily
- What if they are already on Zoloft?
  - Are SSRIs helpful for pain?
  - Can we add a second antidepressant?

Case 2

- 56 year old Hispanic male with colon cancer has intraperitoneal mets and a partial MBO with nausea and vomiting, no bowel movement in 2 days and severe, cramping abdominal pain. He also has several large metastasis in his liver with a dull, aching pain in his RUQ radiating to his lower back.
- He is prescribed hydromorphone 1mg IV q3h prn and is receiving this around the clock with inadequate pain control, it brings the pain from a 10 to a 7.
- What type of pain does he have?
  - Nociceptive visceral abdominal pain due to bowel obstruction and liver capsular dilitation
- Convert him to a PCA of hydromorphone (basal rate and PCA button dosing)
  - Hydromorphone 0.3mg/hr, 0.1mg lock out every 10 min

Case 2

- What would you consider for an adjuvant analgesic for the cramping abdominal pain? The dull RUQ pain?
  - Glycopyrrolate 0.2mg IV TID
  - Dexamethasone 4mg IV am and mid-day

Case 3

- 51 year old Caucasian female with right sided ER/PR + breast cancer s/p mastectomy and right lymph nodes removed, chemo/RT and in remission.
- She has chronic low back pain due to DJD and prior back injury and was given oxycodone 10mg PO q6h prn by her PMD for this pain which she feels brings this from a 10 to a 6. No red flags on history or neuro exam. Imaging reveals bulging disc and spondylosis at area of L4/L5.
- She also complains of burning pain under her R axilla and anterior lateral chest wall
- What types of pain does she have?
  - Chronic non-malignant nociceptive somatic low back pain due to lumbar disc disease
  - Post mastectomy pain syndrome, neuropathic pain
- Prescribed medications are Lipitor, ASA, lisinopril, and oxycodone
- She is going through a divorce and lives with her 26 year old son who she wishes would get back to work and help out more around the house

Case 3

- She has a history of date rape as a teen. She smokes a half pack of cigarettes per day. She drinks 3-4 vodka drinks per day and smokes marijuana 4 times per week as it helps “chill her out”.
- When you speak about non-opioid options for her pain, she starts to cry saying, “I have tried all of those things, they don’t work and make me like a zombie”.
- What is your next steps/recommendations?
- Urine toxicology is + for oxycodone, oxymorphone, alprazolam and THC
- Now what?

Patients at risk for opioid misuse

- In patients who are at risk for opioid misuse, avoid giving short-acting opioid pills, large quantities
- Especially those with non-malignant pain, maximize non-opioid adjuvant analgesics
- Consider using BuTrans or fentanyl patch and have them return to the clinic for patch changes or place the used patches on a notebook to be returned to you.

In cases of suspected abuse or diversion

- If a patient consistently demonstrates behavior of addiction with the use of alcohol, opioids, benzodiazepines or other substances:
  - Opioids should be appropriately tapered and discontinued
  - Offer a non-opioid therapy
    - Both pharmacological and non-pharmacological
  - Refer to a substance abuse treatment program
  - Consider referral for behavioral health
  - Document that the patient had 4 successive negative urine toxicology screens for a period of ≥ 3-6 months
- Above should be documented before considering re-initiation of opioids
- Recommendations should be made on case-by-case basis and tailored for each individual patient

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Chemical coping

- When patients use medications, often opioids, in a non-prescribed way, to cope with the various stressful events associated with the diagnosis and treatments of cancer
- Ranges from mild (self dose escalation, increased pain expression, inability to discontinue after resolution of the painful condition; to severe opioid misuse which is continued use despite harm.
- In one study, 18% of cancer patients were diagnosed as chemical copers
- Associated with CAGE +, alcoholism, young age, many other non-pain symptoms, higher functional status
- Interdisciplinary team, including psychological support is needed, structure and setting limits, referral to substance abuse counseling, if necessary

Kwon JH, Tanco K, Park JC, Wong A, Seo L, Liu D, Chisholm G, Williams J, Hui D, Bruera E. Frequency, predictors, and medical record documentation of chemical coping among advanced cancer patients. The Oncologist. 2015, 20:692-697.

Existential suffering

- Opioids are often used in higher doses when the patient has related emotional pain, with associated complaints of severe, uncontrolled pain, often in many body areas, despite escalation of opioids and onset of adverse effects
- Physical/social pain overlap, social pain activate same areas of pain as physical pain
  - Those with genetic correlate of physical pain sensitivity, variability of Mu-opioid receptor gene, OPRM1, experience more physical pain and require more opioid to relieve pain as well as report sensitivity to social pain and rejection
  - Tylenol improves self reported hurt feelings over time when compared to placebo

Walter M, **Case AA.** Opioids in Oncology Care. Onc Times. 2017; 39(11):8-21.

Pain management in the elderly

- Opioids
  - Use for moderate to severe pain refractory to non-pharmacological treatments, Tylenol or NSAIDS
  - Start low go slow
  - For the first two weeks after initiating opioid therapy, but not thereafter, short-acting opioids are associated with a higher risk of fracture than are long-acting opioids. Higher doses (>or=50 mg/day) of opioids for chronic non-cancer pain were associated with a 2.00 increase in risk of fracture.

J Am Geriatr Soc 2011, J Gen Int Med 2010

Pain management in the elderly

- Opioids increase the risk of injury in older adults, particularly codeine combinations J Am Geriatr Soc 2010
- Use of opioid analgesics is associated with risk of falls and fractures in elderly adults with OA J Am Geriatr Soc 2013
- 2015 BEERS criteria update
  - Avoid opioids in elderly with history of falls
  - Avoid pentazocine, meperidine
  - Avoid indomethacin, ketorolac (includes parenteral)
  - Avoid muscle relaxants

Summary

- Believe the patient and assess type of pain
- Assess risk for opioid misuse before prescribing opioids
- Use adjuvants
- Treat side effects, specifically constipation
- Start low and go slow in the elderly
- No patient should live or die in pain, consult a specialist if needed!