

# Update in Palliative Care

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## Case

- ▶ 64 yo female with metastatic ovarian cancer
  - ▶ Treated with paclitaxel carboplatin
  - ▶ Several surgeries
- ▶ Main complaint neuropathy in feet and legs
- ▶ Anxious about disease and progression
- ▶ Managing pain with medical marijuana

## Palliative care recs

- ▶ Oxycodone for pain
- ▶ Bowel regimen
- ▶ Counseling for anxiety

## Palliative care

- ▶ Approximately 2.6 million people die in the US
- ▶ Usually as a result of a chronic illness (cancer and heart disease)
- ▶ Palliative care
  - ▶ Symptom management
  - ▶ Patients goals
  - ▶ Care giver support
- ▶ When provided to patients with some types of cancer it can actually prolong life

Patient and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering

## Definitions

- ▶ World Health Organization Palliative care
  - ▶ Improves the quality of life of the patient through symptom control
    - ▶ Improves QOL for family
  - ▶ Also addresses spiritual and psychosocial aspects of patient care
  - ▶ Does not hasten or impede death
  - ▶ Team approach
    - ▶ Physicians, nurses, social workers, pharmacists, chaplain, music therapist
  - ▶ Can be utilized at any time during the course of a chronic illness

## Definition

- ▶ Hospice
  - ▶ A home providing care for the terminally ill
  - ▶ Hospice care is treating symptoms at the end of life so the patient can die with dignity.
    - ▶ Also provide emotional and spiritual support for the patient and family.
  - ▶ Treatments for the terminal illness are stopped when hospice care is initiated.
  - ▶ To be eligible for the hospice benefit treatment must focus on symptom control not disease treatment.

▶ <http://www.nhpco.org/about/hospice-care>

## Role of the Pharmacist

- ▶ Participate in team meetings
- ▶ Review medications for drug interactions
- ▶ Review medications for disease state interactions
- ▶ Recommendations for symptom management
- ▶ Educate patients and families



## Symptom management

- ▶ Pain
- ▶ Nausea/vomiting
- ▶ Constipation
- ▶ Dyspnea
- ▶ Liver disease



## Pain management

- ▶ Assessment
  - ▶ Scale, 1-10.
  - ▶ What is the patient's goal? What can they live with?
  - ▶ Location, quality, onset, type of pain
- ▶ Nociceptive vs neuropathic pain
  - ▶ Nociceptive is somatic or visceral pain
    - ▶ Somatic pain results from bone, joint, muscle or connective tissue
    - ▶ Localized, aching throbbing pain
    - ▶ Responsive to NSAIDs or steroids or radiation



## Visceral pain

- ▶ Originates in internal organs
  - ▶ Cramping, aching, pressure
  - ▶ Caused by bowel obstruction or cancer metastasis to liver
  - ▶ Opioids, antiemetics or anticholinergics might help



## Neuropathic pain

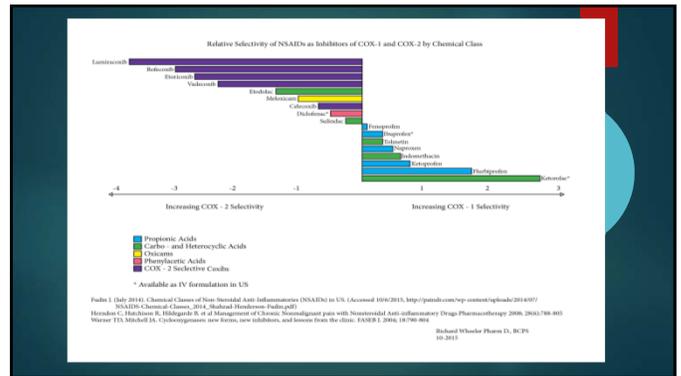
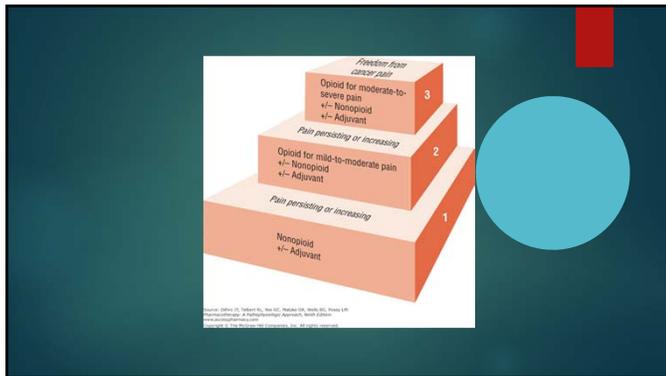
- ▶ Caused by dysfunction in the CNS
- ▶ Numbness, tingling, burning, or radiating pain
- ▶ Opioids may work, often need a medication with a different mechanism of action
  - ▶ TCAs, muscle relaxants, anti epileptics



## WHO pain management ladder

- ▶ Step wise approach
- ▶ Acetaminophen.... No need to discuss
- ▶ NSAIDs-
  - ▶ COX 2s
- ▶ Opioids
  - ▶ <http://paindr.com/home/>
- ▶ Anti epileptics
  - ▶ Gabapentin and pregabalin
- ▶ steroids





- ### Neuropathic pain
- ▶ Meta analysis published in Feb 2015
    - ▶ Included trials that lasted at least 3 weeks
  - ▶ First line recommendations:
    - ▶ gabapentin or extended release gabapentin or enacarbil 1200mg to 3600mg/day
    - ▶ Pregabalin 300 mg to 600 mg/day
    - ▶ Duloxetine 60 mg to 120 mg/day
    - ▶ Venlafaxine ER 150-225 mg/day
    - ▶ Tricyclic antidepressants (one not recommended over others)

- ### Neuropathic pain
- ▶ Second line use- weak evidence
    - ▶ Capsaicin 8% patches- one to 4 patches applied for up to 60 mins every 3 months
    - ▶ Lidocaine patches one to 3 patches once a day for up to 12 hours
    - ▶ Tramadol 200-400 mg/day
    - ▶ Tapentadol

- ### Neuropathic pain
- ▶ Third line
    - ▶ Botulinum toxin A sub Q 50-200 units every 3 months
    - ▶ Opioids
      - ▶ Methadone for neuropathic pain
      - ▶ Blocks the NMDA receptors
        - ▶ Titrate slowly
        - ▶ Opioid adverse effects
        - ▶ QTc prolongation at higher doses has been seen at 200 mg doses
          - ▶ Get baseline EKG

- ### Neuropathic pain
- ▶ Combination regimens
    - ▶ Pegabalin or gabapentin and duloxetine or TCAs
      - ▶ Good regimen to combine instead of trying to push the doses of the individual medications

## Opioids

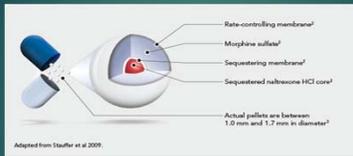
- ▶ FDA opioid action plan
  - ▶ Abuse deterrent formulations
  - ▶ Warnings and safety information on short acting formulations
  - ▶ Increase provider training
  - ▶ Reviewing the pain management recommendations

## Abuse deterrent formulations

- ▶ Physical chemical barriers
  - ▶ Use tablet formulation to prevent extracting the opioid through solvents
- ▶ Agonist/Antagonist combinations
  - ▶ Antagonist can be sequestered and released upon manipulation

## Morphine/naltrexone (Embeda)

- ▶ Novel agent- contains pellets of morphine and sequestered naltrexone



## Morphine/naltrexone (Embeda)

- ▶ Initial doses start at 20mg/0.8mg once a day
  - ▶ Titrate every 1 to 2 days
- ▶ Conversion from oral morphine
- ▶ Give half of the total daily morphine dose as Embeda q 12 hours OR all of the patient's total daily dose as Embeda once a day
- ▶ Conversion from other opioids to Embeda
  - ▶ Dc all opioids, initiate Embeda at 30mg/1.2mg once a day
  - ▶ No established conversion ratios to Embeda
- ▶ Oral dose 3x the IV

## Other abuse deterrent formulations

- ▶ Zohydro ER (hydrocodone)
- ▶ Opana ER (oxycodone)
- ▶ Exalgo ER 24hr (hydromorphone)

## Dyspnea

- ▶ No strict definitions
  - ▶ Patient perception of awareness of breathing and uncomfortableness
  - ▶ Causes panic worry, confusion, frustration and anger
- ▶ Treat the underlying cause if possible
  - ▶ COPD, CHF, pneumonia, PE, lymphoma
- ▶ Reposition the patient more upward position
- ▶ Oxygen may not be effective, patients who report breathlessness may not be hypoxemic

## Dyspnea

- ▶ Opioids can reduce the sensation of breathlessness by decreasing the ventilator drive
- ▶ Opioids naive – start 5 to 15 mg and titrate to response
- ▶ All routes effective
  - ▶ Data on nebulized morphine is limited
  - ▶ Cochrane review of data for palliation of breathlessness
    - ▶ Most studies low quality, small n and not a control arm
    - ▶ No evidence that inhaled morphine is effective
- ▶ Anxiolytics are helpful, but not as effective as opioids
  - ▶ Additional sedation and potential to cause confusion

## Dyspnea

- ▶ Corticosteroids may treat underlying disease COPD, asthma
  - ▶ Make patients feel good
  - ▶ Reduce edema or tumor growth
  - ▶ Adverse effects, insomnia
    - ▶ Administer early in the day
  - ▶ Bronchodilators can be useful for bronchospasm
    - ▶ Not much data in dyspnea

## Nausea and vomiting

- ▶ Common symptom in patients with cancer
  - ▶ Females
  - ▶ Younger than 65
  - ▶ Stomach or pancreatic cancer
  - ▶ Recent chemotherapy
- ▶ Important to try and figure out the etiology for selection of treatment
  - ▶ Dietary measures are important
    - ▶ Avoid, sweet, salty, fatty or spicy foods
    - ▶ Small frequent meals

## Nausea and Vomiting

- ▶ Dopamine antagonists, antihistamines, anticholinergics, serotonin antagonists and prokinetic medications are mainstay of treatment
  - ▶ Prochlorperazine, promethazine and chlorpromazine
    - ▶ Can cause sedation, anticholinergic adverse effects because they affect more than just the dopamine receptors
  - ▶ Butyrophenones- specific for dopamine
    - ▶ Parkinsons like symptoms as adverse effects

## Nausea and Vomiting

- No randomized trials for droperidol, haloperidol and nabilone
- ▶ Cohort study favors haloperidol
  - ▶ Metoclopramide as first line agent
  - ▶ Haloperidol as second line
    - ▶ Adding dexamethasone does not improve nausea control

## Olanzapine for Nausea/Vomiting

- ▶ In a study in patients who had refractory chemotherapy nausea and vomiting olanzapine was added on to the antiemetic regimen.
  - ▶ CINV is driven by serotonin receptors and dopamine receptor activation
  - ▶ Olanzapine antagonizes multiple serotonin and dopamine receptors
  - ▶ Dose 5 to 10 mg/day
  - ▶ Approximately 70% of patients responded to olanzapine

## Olanzapine in palliative care

- ▶ Not as much data as there is in CINV
- ▶ Case series of 14 patients with difficult to control nausea given olanzapine 5 mg at bedtime
  - ▶ No symptom relief with more than one agent
  - ▶ Adverse effects to treatment
- ▶ Nausea controlled by patient report
  - ▶ One patient had no relief
  - ▶ One patient complained of excessive sedation after 2 week, but nausea was controlled
- ▶ All other patients nausea controlled with minimal adverse events

## Malignant bowel obstruction

- ▶ Antisecretory medications like octreotide are effective for nausea associated with malignant bowel obstruction
  - ▶ Adding antiemetics improves efficacy
  - ▶ Octreotide 300 to 600 mcg/day + prochlorperazine or haloperidol
- ▶ Combination of antiemetics granisetron + dexamethasone + haloperidol also effective
- ▶ Olanzapine effective in patients refractory to other treatments
  - ▶ Average dose 5 mg /day average treatment duration 23 days
  - ▶ Decrease the average nausea score by 90% and decreased vomiting

## Opioid induced nausea and vomiting

- ▶ Incidence of moderate to severe nausea and vomiting 19% with a 40% incidence of vomiting
- ▶ No evidence for using prophylactic antiemetics
- ▶ Patients do develop tolerance to this adverse effect
- ▶ No good evidence for using any antiemetics for treatment of nausea due to opioids metoclopramide, ondansetron were not superior to placebo in one small study
- ▶ Best to try to determine mechanism of nausea, vestibular or constipation and let that guide treatment options

## Constipation

- ▶ Opioid induced most common
  - ▶ No data to support one laxative over another
  - ▶ Try to keep the bowel regimen as simple as possible
- ▶ Methylnaltrexone
  - ▶ Effective where traditional laxatives have failed

## Methylnaltrexone

- ▶ Selective antagonist of peripheral mu receptors
- ▶ Doesn't affect analgesia
  - ▶ Pilot study in long term methadone patients did not put patients in withdrawal
- ▶ In a randomized placebo controlled trial
  - ▶ Methylnaltrexone subQ every other day or matched placebo
  - ▶ Continue on laxatives
  - ▶ Significantly more patients had a bowel movement 4 hours after the methylnaltrexone dose and did not need rescue laxatives
  - ▶ Adverse events: abdominal pain, flatulence, nausea, increase body temp

## Palliative care in end stage liver disease

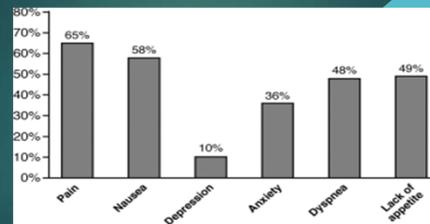
- ▶ Liver failure, advanced disease or cirrhosis
- ▶ Only cure is transplantation
- ▶ Estimated that 2% of the US population are affected by ESLD
  - ▶ Main causes hepatitis C and alcohol
- ▶ Prognosis predictor MELD score
  - ▶ Model for End-Stage Liver Disease
  - ▶ INR, bilirubin, and creatinine to predict survival
  - ▶ Higher the score the worse the disease

## MELD score and survival

MELD Score	6 month	12 months	24 months
10-19	92%	86%	80%
20-29	78%	71%	66%
30-36	40%	37%	33%

## Liver disease

Symptom burden in patients with ESLD



Clinical Liver Disease  
Volume 16, Number 1, page 19-21, 28-34, 2015. DOI: 10.1002/cld.478  
<http://onlinelibrary.wiley.com/doi/10.1002/cld.478>

## Liver disease

- ▶ Barriers to palliative care for patients with liver disease
  - ▶ Disease can decompensate then become stable
  - ▶ Patients may have a poor understanding of their disease
  - ▶ Over estimate of life expectancy
  - ▶ Is patient capable of making decisions

## Indications for palliative care in liver disease

- ▶ Pain, cramping, nausea anorexia
- ▶ Fear of dying, guilt
- ▶ Family distress or conflict
- ▶ Accelerated needs for symptom control (more frequent paracentesis)
- ▶ Patient denied transplant
- ▶ Lack of curative options

## Liver disease

- ▶ Increased risk of adverse effects, most drug metabolized in the liver
- ▶ Morphine, oxycodone and hydromorphone clearance is delayed, constipation may exacerbate encephalopathy
  - ▶ Fentanyl may be the best choice, although little data
- ▶ Ascites the most common reason for admission
- ▶ Hepatic encephalopathy

## Liver disease

- ▶ Palliative care while on transplant list
  - ▶ Can be difficult situation
  - ▶ Symptom management
  - ▶ Caregiver support

## Questions?

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