



Management of Cancer Pain in the Primary Care Setting

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Disclosures

- None

Learning Objectives

- Describe a multimodal approach to treating cancer pain that is based on where a patient is on his/her cancer trajectory
- Recognize the distinctions and differences between chronic non-malignant pain and chronic cancer-related pain
- Describe a Universal Precautions approach to prescribing opioids

Case 1- New Cancer-Related Pain

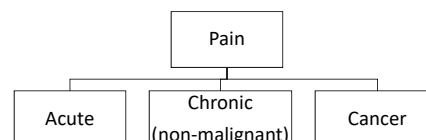
- 60 yo woman presented with a large, painful, cervical lymph node. She has been taking 800mg ibuprofen and 1000mg acetaminophen three times per day with minimal relief. She has 9/10 pain.
- Recent CT scan showed multiple nodules in her lungs, concerning for metastatic disease.
- Biopsy is pending for next week, after which an Oncology appointment will be made.
- She presents to your clinic with uncontrolled pain and distress

Case 2- Cancer-Related Pain in Long-term Cancer Survivor

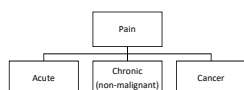
- 45 yo man with hx of Stage IV H/N Ca.
- Received surgery following by chemoradiation
- No evidence of recurrence for 14 months
- Persistent pain in neck and throat following cancer treatment
- Currently moved to your area. Receiving 5mg oxycodone 3 tabs per day and Morphine-ER 15mg every 12 hours. Pain is well controlled.
- You are able to confirm his cancer history and appropriate opioid use with his Oncologist

Classic Categories of Pain

Cancer pain is often separated from other types of pain



Blurred Distinctions between Chronic and Cancer Pain



- *Patient with chronic LBP well managed on naproxen for years. Now with cancer and unable to take NSAIDS*
- *Patient with an extended prognosis but pain from anticancer treatment*
- *Long term cancer survivor with persistent pain*

Pain in Patients with Cancer

- Pain is common symptom for patients with cancer
 - 55% during cancer treatment
 - 66% in advanced, metastatic or terminal cancer
 - 40% after curative treatment
- Prevalence varies by tumor type
 - Solid tumors: 71%
 - Hematologic malignancies: 41%
- Etiology of pain
 - Direct tumor involvement of bone, nerves, viscera, or soft tissue (70%)
 - Anticancer therapy (20%)
 - Causes unrelated to cancer or its therapy (10%)

Everdingen M, et al. JPSM 2016

Pain Assessment in Cancer

- Determine etiology of pain
- Determine severity and effect on function
- Recognize red flags
 - Neurologic deficits
 - Rapidly increasing pain
 - Pain without a clear etiology

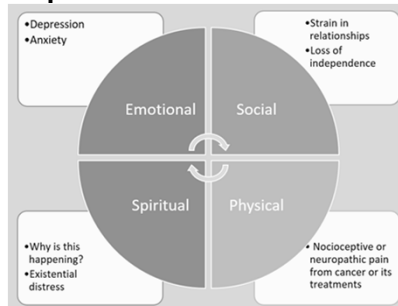
Types of Pain

- | Nocioceptive | Neuropathic |
|--|--|
| <ul style="list-style-type: none"> • Somatic <ul style="list-style-type: none"> • Tumor/Mass effect • Musculoskeletal • Often described as dull, throbbing, and localized • Ex: bone mets • Visceral <ul style="list-style-type: none"> • Infiltration, compression, extension, or stretching of the thoracic, abdominal, or pelvic viscera • Described as pressure, deep, squeezing <ul style="list-style-type: none"> • Not well-localized • Can be associated nausea, diaphoresis • Often referred • Ex: peritoneal carcinomatosis | <ul style="list-style-type: none"> • CA compressing or infiltrating nerves/nerve roots/blood supply to nerve <ul style="list-style-type: none"> • Focal disruption of afferent neural signaling pathways in peripheral and central nervous system • Shooting, sharp, burning, “pins & needles” • Can be due to: <ul style="list-style-type: none"> • Cranial neuropathies • Post-herpetic neuropathies • Brachial plexus neuropathies • Post-radiation • Post chemo |

Determining “Severity” of Pain

- Pain is a subjective experience
- Numeric scores are helpful in tracking a patient’s experience, but should not be used solely
- Functional status is equally important
 - Has pain interfered with activities of daily living?
 - PEG- Pain, Enjoyment of life, General activity Scale
 - Numeric pain score
 - How pain has interfered with enjoyment of life
 - How pain has interfered with general activity

Concept of Total Pain



Emily Jane Harrop et al. Arch Dis Child Educ Pract Ed 2017;102:230-243

Pain Treatment Options

- Pharmacologic
 - Non-opioid medications
 - Opioids
- Non-pharmacologic
 - Behavioral (CBT, etc)
 - Interventional (Epidural steroid injections, neuromodulation techniques, et)
 - Integrative (acupuncture, therapeutic massage, etc)

Very important, especially in long-term cancer survivors. May not be practical for some during cancer treatment

Non-Opioids

- NSAIDS
 - e.g. bone mets, soft tissue infiltration and inflammation
 - Often limited by side effects, not used long-term
- Acetaminophen
- Topicals
 - Lidocaine patch
- **Clinical Tips**
 - Use for mild/moderate pain
 - “ceiling effect”
 - Start at lowest effective dose
 - Beware of comorbid illnesses and organ dysfunction
 - NSAIDS and acetaminophen may be contraindicated in patients undergoing some anticancer treatments

Non-Opioid Adjuvants

- Antidepressants
 - TCAs for neuropathic pain, no sig difference in efficacy between different TCAs
 - SNRI
- Anticonvulsants
 - e.g. carbamazepine, gabapentin, pregabalin
- Corticosteroids
- Antispasmodics
- Muscle relaxants
- NMDA-blockers
- Systemic local anesthetics
- Bisphosphonates

Resource: OSUWMC Clinical Practice Guideline: Outpatient Non Opioid Management of Chronic Pain
<https://techlicenseexpress.com/>

Opioid Use in Cancer Pain

- Compared to chronic non-malignant pain, opioids are more often, but not always, required to treat cancer related pain, particularly in advanced cancer
 - Provides rapid analgesia for severe pain
 - Non-opioid alternatives are often limited in patients with advanced cancer and/or receiving anticancer treatment
 - Impaired ability to participate in non-pharmaceutical modalities

Universal Precautions Approach to Opioid Prescribing

All Patients

- Opioid Agreement
- Risk Assessment
- Access PDMP—OARRS in Ohio
- Beware of Federal, State, and institutional requirements

Resources:
 NCCN Adult Cancer Pain
 CDC Guideline for Prescribing Opioids for Chronic Pain
 State Medical Board of Ohio Regulations for Chronic and Subacute Opioid Prescriptions

Opioid Treatment Agreement

Benefits

- Opportunity for patient education and informed consent
- Outlines physician/provider responsibilities
- Sets expectations about appropriate use of opioids

Potential Drawbacks

- Need for effective analgesia adds element of coercion
- Violations of opioid contracts may occur for reasons other than misuse/diversion
- Only weak evidence of reduction of misuse

Starrels JL, et al. Annals of Int Med 2010

Risk Assessment

• *No tool has been validated in a cancer population that predicts future opioid misuse*

Opioid Risk Tool (ORT)	5 item questionnaire. Can be completed by patients. Asks about family history
Screener and Opioid Assessment for Patients with Pain (SOAPP)	5, 14, or 24 item questionnaire. Complete by patients.
Pain Assessment and Documentation Tool (PADT)	Assesses 4 domains. Completed by physicians
Scoring system to predict outcome (DIRE)	Assesses 4 domains (diagnosis, intractability, risk, efficacy). Complete by physicians
Current Opioid Misuse Measure	17-item questionnaire. Completed by patients.

Ballantyne JC. BMJ 2013

Risk Assessment

• **Minimum:**

- Assess for active substance abuse
 - CAGE questionnaire (cut down, annoyed, guilty, eyeopener)
 - 4 C's (impaired control, compulsive use, continued use despite consequences, craving)
- Assess for personal and family history of substance abuse and current living situation
- Assess for concurrent Psychiatric conditions
- Document in your note

Physician Drug Monitoring Program

- Ohio Automated Rx Reporting System
 - Available through IHIS
- PDMPs were made specifically to prevent “doctor shopping”
- They can also help verify last fill dates of opioids
 - Only as accurate as the pharmacy that reports the fills
 - Does not account for NH/SNF or VA fills

State Medical Board of Ohio Opioid Regulation—Acute Pain

- “Requirements do not apply to a patient who has cancer or another condition associated with the individuals cancer or history of cancer”

State Medical Board of Ohio Opioid Regulation—Subacute and Chronic Pain

- Subacute pain (6-12 weeks) and Chronic pain (>12 weeks)
 - Prior to treating or continuing to treat subacute or chronic pain with an opioid, the physician needs to first consider and document non-medication and non-opioid treatment.
 - If opioid medication is appropriate, the physician should prescribe it for the least amount of days and strength to adequately address the pain.
 - Prescribers should complete and document in the patient’s record: history and appropriate physical exam, diagnostic tests if substance misuse disorder is suspected or known, the patient’s history in OARRS, functional pain assessment and a treatment plan.

State Medical Board MED “Check Points”

- > 50 Morphine equivalents daily (MED), required to:
 - Re-evaluate underlying condition, assess function, assess misuse
 - Obtain written informed consent
 - Consider consultation with specialist and naloxone script

Check Points

- > 80 MED
 - Look for signs of opioid prescription misuse
 - Consult with a specialist
 - *For example, spine clinic or PMR for back pain or Rheum for arthritis*
 - Obtain informed consent
 - Offer naloxone

Check Points

- > 120 MED
 - Obtain recommendation from board certified pain medicine physician or hospice/pall care physician that is based on face to face visit and examination

Exception to Check Points

- Those receiving medication for terminal conditions, in hospice, or hospitalized
- “Terminal condition”
 - Irreversible, incurable, and untreatable condition cause by disease, illness, or injury from which, to a reasonable degree of medical certainty...
 - There can be no recovery
 - Death is likely to occur within relatively short time if life-sustaining treatment is not administered

Routes of Administration for Opioids

- | | |
|--|--|
| <ul style="list-style-type: none"> • PO <ul style="list-style-type: none"> • Generally**, onset 45min-1hr • Generally, duration of action 3hr-4hr • Rectal <ul style="list-style-type: none"> • Similar to PO, used mainly in home hospice • IV <ul style="list-style-type: none"> • Generally, onset of action 10-15 min • Generally, duration of action 3-4hr • Subcutaneous <ul style="list-style-type: none"> • Similar to IV, with onset of action about 30 min • Used mainly in hospice | <ul style="list-style-type: none"> • Transdermal <ul style="list-style-type: none"> • Used only with opioid tolerant patients • Ex: Fentanyl patch • Sublingual/Transmucosal <ul style="list-style-type: none"> • Fast acting (similar to IV) • Ex: Fentora (transmucosal fentanyl) • IM <ul style="list-style-type: none"> • NEVER use IM • Painful, risk of hematoma |
|--|--|

**** Applies to oxycodone, morphine, hydromorphone. Fentanyl and Methadone have unique pharmacokinetics.**

Starting Doses for Common Immediate Release Oral Opioids

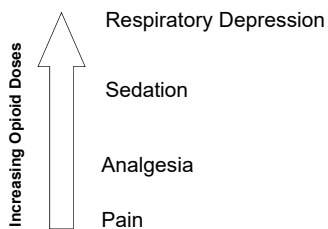
For opioid naïve patients:

- Morphine
 - 7.5-15mg
- Oxycodone
 - 5-10mg
- Hydromorphone/Dilaudid
 - 2-4mg
- Tramadol
 - 25-50mg
- Hydrocodone
 - 5-10mg
- Vicodin= hydrocodone+acetaminophen

Opioid Side Effects

- Common
 - Constipation
 - Dry mouth
 - Nausea/vomiting
 - Sedation
 - Sweats
- Uncommon
 - Nightmares/hallucinations
 - Dysphoria/delirium
 - Myoclonus/seizures
 - Pruritis
 - Respiratory depression
 - Urinary retention

Opioid Toxicity



Return to case 1

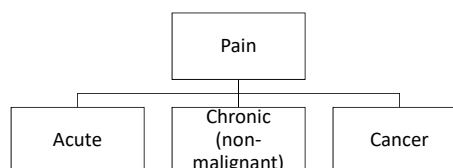
- Our patient very likely has cancer related pain
- Her pain remains severe despite acetaminophen and ibuprofen use
- No red flags
- Opioids can help relieve her pain. Although not required, you may consider:
 - Providing a treatment agreement
 - Asking about history of substance use disorder
 - A point of care urine test shows no illicit substances
 - Checking OARRS

Return to case 1

- Oxycodone 5mg is prescribed for severe pain, every 4 hours as needed up to 4 doses per day. Advise her to continue her acetaminophen.
- 1 week script is given (28 pills)
- Senna 17.2mg at night is prescribed, with instructions to increase to twice per day if needed
- Education about opioid use is provided

Case 2

- Patient with persistent pain related to cancer and cancer treatment
- Is this cancer-related pain?



Chronic Pain in Long Term Cancer Survivors

- This is a situation that blurs the distinction between “cancer pain” and “chronic pain”
- Number of survivors in 2016 was 15.5 million
- 2016-2017 National Health Interview Survey of adult cancer survivors
 - 16.1% had HICP
 - High impact chronic pain- chronic pain + major activity restriction
 - 34.6% chronic pain

Jiang C, et al. JAMA Oncol 2019

Pain Management in Long Term Survivors

- Transition to long term survivorship affects several aspects of pain management:
 - Goals of therapy
 - Assessment
 - Therapeutic/treatment options

Goals of therapy

- In addition to pain relief, there is added emphasis on:
 - Improved functionality
 - Limiting adverse events/side effects

Pain Assessment

- New or acute pain
 - Ddx should include disease recurrence, secondary malignancy, and late onset treatment effects
- Chronic pain
 - Specific cancer pain syndrome should be identified if possible
 - Emphasis on non-opioid and non-pharmacologic options

Syndrome Based Treatment Approach

Syndrome	Example treatments
Post-radical neck dissection syndrome	Mirror therapy, cognitive therapy, neuropathic adjuvants
Post mastectomy Post thoracotomy	Intercostal nerve block, TENS unit, neuropathic adjuvants
Lymphedema	Manual lymphatic drainage, compression garments
Myofascial pain	Trigger point injections, acupuncture, NSAIDS
Vertebral compression	Vertebroplasty, weight bearing therapy, muscle relaxants, bisphosphonates, NSAIDS
Neuropathic pain	Pharmacologic non opioid treatments to address neuropathy, physical therapy

2019 NCCN Practice Guidelines: Survivorship

Interdisciplinary Approach

Specialty	Example Interventions
PM&R	PT/OT, ultrasound, exercise program
Psychological	Cognitive behavioral therapy, guided imagery
Interventional	Nerve blocks, vertebroplasty
Integrative	Massage, acupuncture
Neurostimulatory	TENS, spinal cord stimulation

Paice, J.A. Management of Chronic Pain in Survivors of Adult Cancers: ASCO Clinical Practice Guideline. Jour Clin Onc, 2016

Chronic Pain and Opioids

CDC Recommendations

- **If not currently on opioids**
 - Avoid opioid therapy
- **If currently receiving opioid therapy**
 - Develop individualized treatment plan
 - Do not abruptly taper or discontinue current opioid treatment
 - Consider suboxone (buprenorphine/naloxone) if evidence of opioid use disorder

Wood, et al. JAMA 2019

CDC Guidance for Tapering CDC 2016

- Empathetically review risks associated with continuing high dose opioids
- Collaborate with patients who agree to taper their dose
- If tapering, taper slowly enough to minimize withdrawal symptoms
- Individualize the pace of tapering

Tapering Opioids

- Tapering and opioid reduction should be considered for both cancer related and non cancer related pain
- Set expectations early
- Benefits:
 - Improvement in: constipation, mental clouding, neuro-endocrine effects, sleep disordered breathing, and more
- Rate of taper depends on
 - Concern for abuse, misuse, or diversion?
 - Desire to reduce risks
- Tapering should be done in context of psychological support and pain management with non opioid treatments

Tapering Guidelines

- Reevaluate necessity of opioid regularly.
- Consider 10-20% reduction at a time to avoid opioid withdrawal
- For patients with no signs of inappropriate opioid use, a slow taper (months to years) may be most appropriate
- Consider specialist referral to help patient get down to lowest tolerated opioid dose

Goodlev, E., et al. J of Pall Med, 2019

Return to Case 2

- Universal precautions approach taken
 - Opioid treatment agreement
 - Opioid Risk Assessment
 - Check PDMP (OARRS)
- Discussion about opioid use
 - Agreement to try to taper opioids to improve overall safety and wellbeing
 - Referrals to specialists where appropriate
 - Introduction of non-opioid medications and non-pharmacologic treatments
- An initial first taper may be reduction in oxycodone to 10mg max 3 tabs per day, and continuation of long acting Morphine

Take Home Points

- The approach to treating cancer related pain depends on the patient's cancer trajectory
- Use a Universal Precautions Approach to opioid prescribing
- Opioid tapering in long term cancer survivors involves a multimodal approach and is individualized