Complex Pain Management in Oncology

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Objectives

- Demonstrate a comprehensive pain assessment in a patient with cancer including physical assessment and differential diagnoses
- List pharmacologic strategies to manage pain according to the pain syndrome

Problem of Cancer Pain

Pain affects the majority of patients sometime during the disease
- ~53% of patients receiving treatment have pain
- ~59-64% of patients in advanced stages have pain
- ~33% of patients post curative treatment
Who reports the most pain?

- 70% with head and neck cancer
- 60% with gynecologic malignancies
- 59% with gastrointestinal cancer
- 55% with lung cancer
- 54% with breast cancer
- 52% with urogenital cancer
- Over 1/3 who have pain rated it as moderate to severe

Pain Assessment

Interview
Physical Examination
Radiographic Examination

Pain Interview

- Conversation
- Therapeutic Interview Skills
  - Verbal/Nonverbal
  - Focus on the patient
  - Explore fears, treatment expectations, goals
  - Clarify understanding
  - Encourage to talk
  - Communicate a therapeutic alliance

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Saturday
• Substance Use Disorder?
  – Withhold judgement
  – ACE
  – Family and social support
  – History of depression, anxiety, psychiatric disorders
  – SUD history
  – Screen for risk
  – Access PDMP
  – Urine drug screening

Location

Body Diagrams
• Point
• May involve more than one location of pain

Intensity

Choose a number between 0 to 10 that best describes your pain.
Quality

- Sharp
- Dull
- Cramping
- Radiating
- Constant
- Deep
- Pressure
- Pins and Needles
- Intermittent
- Stretching
- Episodic
- Sore
- Aching

Temporal Factors

- Constant versus episodic
- How pain changes over time
  - Increase with movement/activity
  - Increase at night
- What makes pain better?
- What makes pain worse?
- Breakthrough Pain
  - Incident
  - Idiopathic
  - End of dose failure
  - Nonbreakthrough

Brief Pain Inventory (BPI)

- Pain Severity
  - Average
  - Least
  - Worst
- Impact on Daily Functioning
- Percent relief
- Reliability: Cronbach alpha reliability ranges from 0.77 to 0.91s
Chronic Pain Goals – 4 A’s

- Analgesia - Decrease pain
  - Treat underlying cause where possible
  - Minimize medication use
- Activities of Daily Living - Restore function
  - Physical, emotional, social
  - Correct secondary consequences of pain
    - Postural deficits, weakness, overuse
    - Maladaptive behavior, poor coping
- Adverse Events – Minimize side effects
  - Manage untoward side effects
- Aberrant Behaviors – Prevent abuse and diversion
  - Monitor at each visit

Somatic Pain

- Pain Syndromes
  - Bone metastases
  - Arthritis
  - Muscular pain
- Post-operative arthroplasty

- Characteristics
  - Culturally sensitive
  - Sharp or dull, deep, aching
  - Well-localized
  - Triggered with movement or activity

Strategies
- NSAIDs
- Bisphosphonates
- Opioids

Visceral Pain

- Pain Syndromes
  - Pancreatic cancer
  - Liver cancer
  - Cirrhosis
  - Lymphedema
  - Post-operative pain

- Characteristics
  - Aching, gnawing, cramping
  - Poorly localized
  - Can be referred

Strategies
- NSAIDs
- Corticosteroids
- Anticholinergics – spasm
- Octreotide
- Opioids
Neuropathic Pain

- Pain Syndromes
  - Brachial plexopathy
  - Lumbosacral plexopathy
  - Radiculopathy
  - Chemotherapy-induced neuropathy (CIPN)
  - Diabetic neuropathy
  - Sciatic nerve pain

- Characteristics
  - Central: Shooting, burning, lancinating, electric-shock like, burning, aching
  - May radiate down an extremity

Strategies
- Antidepressants
- Anticonvulsants
- Antispastics
- Local Anesthetics
- Corticosteroids
- Opioids

Pain Pathway

Opioid Analgesics

- Mu (µ) Agonists
  - Codeine
  - Fentanyl
  - Hydrocodone
  - Hydromorphone
  - Methadone
  - Morphine
  - Oxycodone
  - Oxymorphone
  - Tramadol
  - Tapentadol

- Partial agonist
  - Buprenorphine

- Mixed agonist-antagonists
  - Kappa (κ) opioids
  - Butorphanol
  - Nalbuphine
  - Pentazocine
Morphine

- Standard for comparison
  - Oral CR and IR available, liquid
  - SC, IV, PR, epidural, intrathecal
- Metabolites
  - Morphine-3-glucuronide (M3G)
    - antagonizes analgesic effect of morphine and M6G
    - paradoxical neuroexcitatory effects
  - Morphine-6-glucuronide (M6G)
    - more potent analgesic activity than morphine
    - contributes to overall analgesic effect

Oxycodone

- Availability: CR, IR, solution, combination with acetaminophen
- Caution when combined with acetaminophen
  - Should not exceed > 4 gms/day
- Active metabolite: oxymorphone but active drug primarily responsible for pain relief
  - No cumulative effects known
  - Mediated by CYP450 but implications unclear
- Recommendations
  - Consider if untoward side effects with other opioid
  - Consider in patients with renal compromise over morphine
- Greater potential for addiction?

Fentanyl

- Lipophilic – global tissue distribution
- Metabolized by CYP450 3A4 but implications unclear
- Transdermal patch
  - Onset 12 hours, peak 24-48 hours, duration 72 hours
  - Adhesive reaction: Triamcinolone inhaler, spray to skin before applying patch
  - Do not apply heat to patch
- Transmucosal/Intranasal (sucker, buccal tablet, sublingual, film, nasal)
  - Fast onset (5-10 minutes)
  - Duration of action up to 60 minutes
- Intravenous
  - Onset within minutes
  - Duration 15-30 minutes
- Intrathecal/Epidural
Fentanyl

- Variability Considerations
  - Consider delayed onset and delayed elimination (accumulation)
  - Differences in body weight
    - Obese – delayed onset
    - <BMI – may not achieve full benefit or decreased duration of action
    - Cachexia – Do Not Use!

Hydromorphone

- Availability: CR, IR, SC, IV, epidural, intrathecal
  - High solubility eases use in SC/IV administration
  - New extended release available
    - Available in 8 mg, 12 mg, 16 mg tablets
    - Dosage is every 24 hours
  - Active metabolites
    - Hydromorphone-3-glucuronide (H3G), hydromorphone-6-glucuronide (H6G)
    - Little data on the impact of these metabolites
  - Recommendations
    - Safe drug to use in hepatic and renal compromise although NCCN guidelines state to use with caution in renal compromise

Nonpharmacologic

- Interventions that affect perception
  - Distraction
  - Relaxation
  - Hypnosis
  - Anything that diverts the mind from the pain
- Psychological intervention
- Spiritual intervention
Antidepressants: Tricyclics

- Options: amitriptyline, nortriptylline
- Start at 10 mg hs and titrate upward
- Side effects:
  - Anticholinergic—increased sensitivity in elderly
  - Orthostatic hypotension
  - AV heart block
  - CNS effects
- Amitriptyline not recommended in the elderly
- Side effects of all TCAs may outweigh benefits

Antidepressants: Serotonin Norepinephrine Reuptake Inhibitors

- Duloxetine—first antidepressant approved for neuropathic pain
- Dosing: 60 mg/day usual effective dose
- Side effects
  - Anticholinergic
  - Decrease seizure threshold
  - Somnolence
  - Glaucoma
  - Hepatotoxicity – lower dose or avoid with liver compromise
  - Venlafaxine another SNRI (150-225 mg/day)

Opioid Dosing and Titration

- Perform titration after reaching steady state
  - Average 4-5 half-lives for IR opioids
  - Average 2-3 days for CR opioids (or >)
- Titrate 24 hour dose by 25-33%
- Keep breakthrough dose at approximately 10-20% higher with severe incident pain
- Consider dose reduction for incomplete cross tolerance
  - 50-75% with good pain control
  - 0-25% with poor pain control
Opioid Rotation

- When to rotate
  - Titration without analgesic improvement
  - Intolerable side effects
  - Pain crisis
- Use an equianalgesic conversion chart as a guide
- Consider dose reduction for incomplete cross tolerance
  - 50-75% with good pain control
  - 0-25% with poor pain control

Anticonvulsant: Gabapentin

- First line treatment for neuropathic pain of all types
- Dosing
  - Starting at 100-300 mg daily to effective dose 900-3,600 daily in 2-3 divided doses
  - Renal insufficiency
    - GFR 30-59 mL/min, 400 mg twice daily
    - GFR 15-29 mL/min, 300 mg twice daily
    - GFR < 15 mL/min, 300 mg daily
- Titration
  - Multiple steps of 50-100% every 3 days
  - Slower with elderly and renal insufficiency
- Side Effects
  - Somnolence dose limiting toxicity
  - Dizziness, ataxia, edema, wt. gain, dyspepsia, leukopenia

Anticonvulsant: Pregabalin

- Advantages
  - More efficiently absorbed through the GI tract
  - More rapid onset of analgesia
  - Simpler titration
- Dosing
  - Starting 150 mg daily
  - Usual effective dose 150-300 mg bid
- Titration simple with 2-3 steps
- Side Effects
  - Somnolence, dizziness, edema, ataxia, HA, confusion, diarrhea
Methadone

- Lipophilic
  - Significant tissue distribution
- Protein bound - alpha-1-acid glycoprotein (AGP)
- Metabolized by cytochrome p450
  - Drug-drug interactions
- No known active metabolites
- NMDA activity—may decrease tolerance and inhibit neuropathic pain
- High oral bioavailability—parenteral form may not be an advantage
- Cost effective

- Long half-life may lead to drug accumulation
  - 15-60 hours average; up to 120 hours
- Recommendations for administration
  - Should only be used by experienced clinicians
  - Should be used with caution in all patients
  - Start low and go slow
  - Consider delayed onset and delayed elimination (accumulation)
  - May want to avoid with polypharmacy issues
  - New guidelines recommend that everyone get a pretreatment EKG before starting methadone due to potential QT prolongation and cardiac arrhythmias; follow EKG up one at 30 days and then annually, and if the dose exceeds 100 mg/day

Converting to Methadone

- If morphine equivalents:
  - <90 mg ~ 1 mg methadone: 4 mg morphine
  - 90-300 mg ~ 1:8
  - >300 mg ~ 1:12
CYP450 Considerations

- **Inhibitors**
  - Antibiotics
  - Antidepressants
  - Diazepam
  - Antivirals
- Leads to decreased clearance
- May prolong elimination and increase plasma concentration of opioids

- **Inducers**
  - Anticonvulsants
  - Rifampin
  - Corticosteroids
- Leads to increased clearance
- May have a surge in opioid levels followed by a decrease in plasma levels

Miscellaneous Adjuvants

- Corticosteroids
- NMDA Antagonists
  - Ketamine, Dextromethorphan, Methadone
- Local Anesthetics
  - Lidocaine
- Alpha-2 Adrenergic Agonists
  - Clonidine
- Muscle Relaxants
- Antispasmodics
- Ziconotide

Summary

- Nurses can encounter tough pain cases while caring for patients with cancer
- Opioids and adjuvants are usually effective in managing pain
- Occasionally, out of the box strategies are necessary for comprehensive management, e.g. ketamine, lidocaine, intraspinal routes, etc.
- A team approach is essential to discuss management options