Effective Pain Management: Part II

Steve Wiesner, MD
May 17, 2013
Acknowledgments

• Dr. Kate Christensen
  ▪ TPMG, Hospice Program, Martinez, California

Overview of Today’s Presentation

• Participants will understand
  ▪ The concepts of palliative care and hospice
  ▪ The WHO Analgesic Ladder
  ▪ The impact of cancer-related pain and reasons for inadequate pain control
  ▪ General approaches to cancer related pain
Today’s Presentation

• Don’t worry that there are so many slides!
  ▪ Most are there for your reference
  ▪ Various appendices for more information
    ▪ Appendix I
      ▪ Definitions
    ▪ Appendix II
      ▪ Assessment Tools
    ▪ Appendix III
      ▪ Pain Management Fast Facts
    ▪ Appendix IV
      ▪ Inflammatory Management
Today’s Presentation

- Various appendices for more information
  - Appendix V
    - Opioid Equivalent Dosing
  - Appendix VI
    - Breakthrough Pain
  - Appendix VII
    - Morphine
  - Appendix VIII
    - PCA Use
  - Appendix IX
    - Advanced Procedures
“Palliative care is an **approach** that improves the quality of life of patients and their families facing the problems associated with life threatening illnesses, through the **prevention and relief of suffering** by means of early identification and impeccable assessment and **treatment of pain** and other problems, physical, psychological, and spiritual.”
“Hospice is a philosophy, not a specific place of care, geared towards providing humane and compassionate care for people at the last phases of terminal illness. The goal is to enable patients to live fully and comfortably, and obtain the best quality of life possible surrounded by their loved ones up to the last days of life.”
Cancer-related Pain

• An estimated 60% of patients with cancer experience pain
  ▪ 25% to 30% have severe pain

• Presence of pain, fatigue and insomnia can all lead to decreased functional status
Reasons for Inadequate Pain Management

• **Health care provider’s lack of**
  - Knowledge and skill
  - Time to appropriately prescribe and adjust analgesics
  - Lack of communication between patients and clinicians
  - Limitations in assessment tools

• **Health care provider’s misperceptions about**
  - Use of drugs to treat cancer pain
  - Use of morphine
  - Opiate addiction
  - Fear of respiratory depression
  - About opiate administration options
Reasons for Inadequate Pain Management

- Patient-related factors also contribute to inadequate pain control
  - Low expectations for pain control
  - Beliefs that prevent them from taking analgesics as prescribed and/or requesting a change in medications that are not working.
  - Fear of addiction and side-effects
  - Need to save the strong medication until they really need it
  - Lack of communication with providers because
    - They don’t want to “bother” the physician
    - They are not a good patient if they raise concerns about their pain
    - That increasing pain is assumed to be due to disease progression
Reasons for Inadequate Pain Management

• Lai and colleagues identified that the stronger a patient’s belief they could control their pain, themselves, the less likely they were to adhere to treatment

• Oldenmenger found that the stronger the patient believed that medication was necessary to control their pain, the more adherent the patient was to treatment
General Approaches to Cancer-related Pain

• **Initial and ongoing assessments:** See Appendix II
  - Detailed history
  - Physical examination
  - Psychosocial evaluation
  - Diagnostic work-up
  - Medical record review

• **WHO analgesic ladder:** See Appendix III
General Approaches to Cancer-related Pain

- Pain severity and pharmacotherapy
- Opioid-naïve versus opioid-tolerant patients
- Opioid dosing: See Appendix V
- Treatment of breakthrough pain: See Appendix VI
- Treatment of side effects
- Comments on methadone: See Appendix VII
- Routes of administration
- Opioid rotation/switching
- Pain syndromes: See Appendix III and IV
- Non-pharmacological approaches
World Health Organization Analgesic Ladder

See Appendix III

• Cornerstone of cancer pain management
• Matches treatment to the pain intensity
• Non-opioid analgesics: WHO Step 1 ladder
  ▪ Aspirin
  ▪ Acetaminophen
  ▪ NSAID’s
• Opioid Medication (weak): WHO Step 2 ladder
  ▪ Codeine and hydrocodone
  ▪ Mild-to-moderate pain
  ▪ Dose may be limited by acetaminophen
World Health Organization Analgesic Ladder

• Opioid Medication (strong): WHO Step 3 ladder
  ▪ Morphine
  ▪ Hydromorphone
  ▪ Oxycodone
  ▪ Meperidine
  ▪ Fentanyl
  ▪ Methadone
  ▪ Levorphanol
  ▪ Oxymorphone
  ▪ Fentanyl
Pain Severity

• Used to determine use of low-potency versus high-potency drug
  ▪ Most low-potency opioids are less suitable for severe pain due to
    ▪ Dose limitations
    ▪ Presence of ceiling effects

• Most cancer pain will require high-potency opioids
Pharmacotherapy

- Usually treat side-effects, first, before switching opioids
  - Sequential opioid trials may need to be performed
- Be familiar with equianalgesic dosing
  - Know the pharmacokinetics of opioids
  - See Appendix V
• Opioid-naïve Patients
  ▪ Initial evaluation
    ▪ Identify that pain is actually related to cancer and/or associated treatment
    ▪ Identify severity
    ▪ Location of pain
    ▪ Baseline renal function
      ▪ Consider hydration, if necessary
Opioid-naïve Patients: Step 3 of Ladder

- **Morphine 10mg orally or 5mg iv/sc every 4 hours**
  - Morphine 5 mg orally every 2 hours for breakthrough pain

- **Hydromorphone 2mg orally (1 mg iv/sc) every 4 hours**
  - Hydrocodone 1 mg orally (0.5 mg iv/sc) every 2 hours as needed for breakthrough pain

- **Oxycodone 5mg orally every 4 hours**
  - Oxycodone 5 mg orally every 2 hours for breakthrough pain
Opioid-naïve Patients: Titration and Maintenance

• Continue to titrate over the subsequent 3-4 days to achieve optimal pain relief

• Follow up with maintenance regimen
  - Continue as long as effective and necessary
  - Add adjuvant medications, as needed
  - Monitor for side-effects, including nausea and constipation

• Once stable on initial opioid program, can consider switch to sustained release opioid
Opioid Tolerant (non-naïve) Treatment

- Avoid previous opioids that were ineffective and/or led to side effects
- Determine total daily opioid dose
  - Increase by 30%
  - Give in divided doses every 4 hours or every 12 hours
    - Provide every 2 hour dosing for breakthrough pain
Opioid Tolerant Patient

- **Long-acting opioid (q12 hr)**
  - Morphine
  - Oxymorphone
  - Oxycodone

- **Long-acting opioid should NOT be given q8 or q6**
  - Leads to poor pain control with marked opioid side effects
    - “Stack up”: Drug goes in faster than goes out
Opioid Responsive Patient

• Can be dosed q 16 or q 24 hrs in patients with
  ▪ Liver failure
  ▪ Renal failure
Opioid Tolerant Patient

- **Upward titration d/t increased pain**
  - When tolerance occurs
  - When disease progression occurs

- **Downward titration when**
  - Pain improves d/t other treatment modalities
    - Radiation/chemo
    - Nerve block
  - Adequate pain control but excessive sedation
  - Toxicity
Transitioning to Sustained Release (SR) Opioid

• **Determine the 24-hour opioid dose in mg**
  - Includes around-the-clock and breakthrough doses
  - Use an opioid conversion table to convert to a morphine equivalent daily dose (MEDD)
    - See Appendix V
  - Begin sustained release opioid every
    - 12, 24 or 72 hours, based on SR opioid
Breakthrough Pain (BTP)

See Appendix VI

• Described as a transient exacerbation of pain that occurs either
  ▪ Spontaneously or
  ▪ In relation to a specific event, despite relatively stable and adequately controlled background pain

• BTP is characterized by a typical temporal pattern which includes
  ▪ Short onset: generally a few minutes and
  ▪ Short duration (30–90 minutes)
Breakthrough Pain

• Approximately 55–60 % of breakthrough pain is related to a precipitating event, most commonly movement or activity

• About 65% of cancer patients experience episodes of BTP

• Higher incidences of breakthrough pain are seen in patients who are younger, and have bone metastasis and/or neuropathic pain
Breakthrough Pain

- Treat breakthrough pain with short acting opioid given
  - Every 1-2 hours
  - At 10-15% of MEDD
    - If patient on SR morphine 100 mg every 12 hours, consider 15 mg every 2 hours as needed OR
  - Can consist of the equivalent of 25% to 50% of patient's 4 hours dosing needs
Opioid Maintenance

• Assess for
  ▪ Effectiveness of opioid
  ▪ Side effects/toxicities
    ▪ Opioid switching may be required when dose-limiting side-effects occur
  ▪ Disease progression
Opioid Side-effects

- Nausea/vomiting
- Constipation
- Somnolence
- Respiratory depression
- Delirium
- Myoclonus
- Fatigue and asthenia
- Urinary retention
Managing Side-effects: General Treatment Options

- Hydration
- Opioid rotation
- Decreasing dose
Managing Side-effects: Nausea

- Antiemetic use
  - Metoclopramide 10 mg every 4 hours for the first 48 hours
    - 10 mg every 2 hours, prn for breakthrough nausea
    - Followed by 10 mg every 4 hours prn
  - Metoclopramide also for decreased gut function
  - Haloperidol 1-2 mg/day
  - Scopolamine patch
Managing Side-effects: Constipation

- When not managed can lead to obstipation and severe pain
  - Assess for obstruction and decreased bowel sounds
- Laxative use: Senna and Docusate
  - Sennoside 8.6 mg, 1-2 tablets bid
    - May require more, based on response
  - Docusate qd or bid can be added
  - Avoid combination medications as they limit ability to titrate separately
  - If senna ineffective (must be activated in the gut) consider bisacodyl
Managing Side-effects: Constipation

• Other options
  • Milk of Magnesia Concentrate
    • 2400mg/10 ml equals 30 ml’s of regular MOM
    • MOM both softens and stimulates so may not require anything else
  • Lactulose for liver encephalopathy
    • 30 ml 2-to-4 times per day
    • Titrate to 1-to-2 loose stools per day
    • Can serve as liquid laxative but causes gas and cramping
  • Refractory constipation: oral naloxone
Managing Side-effects: Constipation

• Don’t use bulk forming agents with opioids
  ▪ Peristalsis is diminished
  ▪ Spasms of smooth muscle, including sphincters, replace peristalsis

• Avoid mineral oils on routine basis
Managing Side-effects: Sedation

- Sedation is often transient, but if persisting greater than 1 week consider
  - Caffeine
  - Use of a stimulant such as methylphenidate.
Managing Side-effects: Respiratory Depression

- Respiratory depression is associated with a reduced level of consciousness
  - Most serious and toxic effect of opioids
  - Fortunately it is rare
    - Tolerance to the respiratory effects of opioids develops rapidly
    - Rarely develops when the doses of opioids are carefully adjusted to pain relief
Respiratory Depression

• Treatment
  - Naloxone guidelines must be closely followed due to potential to precipitate withdrawal in opioid tolerant patients
  - Naloxone must be diluted (one 0.4-mg vial in 10 mL saline)
  - The dose must be adjusted slowly to bring respiratory frequency to 8–12 breaths/minute
  - If respiratory depression occurs with slow-release opioids or with methadone, close monitoring for at least 24 hours is advised
Transdermal Fentanyl

- Consider in patients who can’t use oral route
- Slow-onset
- Long-lasting
- Convenient and best used for stable pain
- Lengthy times required for titration
- No worry about “stack up” with Fentanyl
- Dosing equivalent
  - 25mcg/hr equivalent to 10 mg of morphine q 4 hours or
  - 30 mg every 12 hours
- Takes 12 hours to start working
- Change q 3 days
Fentanyl Warning

- Patient must be opioid tolerant and require total daily dose at least equivalent to fentanyl 25 mcg/hr
- Use in patients who are not opioid tolerant may lead to fatal respiratory depression
  - Over-estimating dose when converting from another opioid can lead to fatal overdose with initial fentanyl dose
Opioid Tolerant

- Taking of the opioid for a week or longer
- > 60 mg of morphine per day
- > 30 mg of oral oxycodone per day
- > 8 mg of oral hydromorphone per day
- Or equianalgesic dose of another opioid
Methadone

See Appendix VII

- Methadone is 10-15 times more potent than morphine
- Dosing can be every 6, 8 or 12 hours
- Analgesia usually lasts 8 hours
  - Some patients may need every 6 hour dosing
- Once on methadone, keep patient on it
  - Rectally
  - Sublingually
  - Transdermally
  - IV
- Never constant infusion
Methadone

- Five days to reach steady state after EACH dosage change
- May be good choice in patients with renal insufficiency
  - No active metabolites and metabolized by liver
- Low doses are usually effective
- When switching from morphine to methadone, ratio changes as the daily morphine dose increases
Routes of Opioid Administration

- Oral preferred
- Other routes to be considered if the following are present:
  - Dysphagia
  - Delirium
  - Obtundation
  - Bowel obstruction
Patient-controlled Anesthesia (PCA)

See Appendix VIII

• May provide psychological advantages by providing patient with sense of
  - Self-management of pain and of the general medical situation

• In other patients the opposite is true
  - Responsibility for controlling one’s own pain and fear of drug abuse can lead to anxiety and insecurity
Opioid Rotation/Switching

• Consider when pain
  ▪ Uncontrolled despite high dose opioid and/or
  ▪ When tolerance or side effects develop
  ▪ Leads to difficulty with high dose opioid administration

• Reduced cross tolerance between different agents makes rotation of opioid drugs an effective option for managing tolerance
  ▪ Avoids escalating dosage requirements and the resulting side effects
Opioid Rotation Process

- Calculate total daily dose
- Calculate dose of new opioid using equianalgesic dose conversion
- Reduce the new opioid dose by 30-50% to account for incomplete cross-tolerance between opioids
- Establish regular daily dose of the new opioid via
  - Scheduled short-acting at frequent dosing or
  - SR opioid
- Breakthrough pain management
- Ongoing assessments
Pain Syndromes
See Appendix III and IV

• Type of pain:
  - Visceral
  - Muscle
  - Bone
  - Neuropathic
  - Pleuritic
  - Colic
Pain Syndromes

- Multidisciplinary medication approach is often required
  - Non-opioids
    - NSAD’s
    - Antidepressants
    - Anticonvulsants
    - Corticosteroids
    - Phenothiazines
    - Anesthetics
    - Bisphophonates
    - NMDA-Receptor antagonists
Pain Syndromes and Adjuvant Medication

- Depends on pain syndromes and associated treatment options
- Onset of benefit can take up to 4-6 weeks
  - Variable patient response
  - Titration often required
Intractable Pain

• **Possible confounding possibilities**
  - Disease progression
  - Somatization and pain
    - Educate on difference between pain caused by noxious stimuli and pain of chronic suffering

• **Identify and treat**
  - Anxiety
  - Depression
  - Adjustment disorder
  - Consider psychiatric consultation
Intractable Pain: Chemical Dependency

- Previous or ongoing problems with chemical dependency
  - Educate patient on difference between suffering and nociception
  - Educate patient of dangers with opioid escalation
  - Only one physician to prescribe
  - Consider restricting treatment to long-acting opioids
    - Limiting extra doses
  - Consider addiction specialist consultation
Other Pain Management Options: Physical Modalities

• May include
  ▪ Cryotherapy
  ▪ Biofeedback
  ▪ Iontophoresis
  ▪ Transcutaneous electrical nerve stimulation
  ▪ Massage
  ▪ TENS and massage are not performed directly over areas with known tumor
Other Pain Management Options: Physical Modalities

- **Deep heat:** Avoid directly over an area of tumor
  - Limited data, but one study in mice showed increase in tumor size
    - But no increase in rate of metastasis with application of ultrasound
Other Pain Management Options

• Psychological techniques including
  ▪ Positive imagery
  ▪ Distraction training
  ▪ Relaxation techniques

• Coping strategies
  ▪ Cognitive-behavioral Therapy

• Complementary and alternative medicine strategies
  ▪ Acupuncture
Other Pain Management Options: Procedures

- Trigger point injections
- Nerve blocks
- Vertebroplasty: Injection of cement into vertebral body
  - Metastatic spine pain involving one or more vertebrae
- Neuroablative Procedures
  - See Appendix IX
• Pain is a multidimensional experience requiring multidimensional assessments

• Regular and frequent assessments are necessary
  ▪ Pain and other symptoms change rapidly in the patient with advanced cancer
Pain-related Palliative Summary Comments

• Reassure patient and their family
  ▪ That pain, for the most part, can be relieved
  ▪ About concerns and fears regarding opioid use

• Educate patient about differences of
  ▪ Physical dependence/withdrawal symptoms
  ▪ Tolerance
  ▪ Addiction
    ▪ Minimize concerns regarding addiction and dependence
Pain-related Palliative Summary Comments

- Encourage normal activity to fullest extent possible
- Treat pain promptly and aggressively
- Tailor plan to type and intensity of pain
- Schedule around-the-clock opioid along with breakthrough dosing
- Diagnose and treat opioid side-effects
Pain-related Palliative Summary Comments

- Use/add adjuvants as needed
- Prescribe anti-emetics and laxatives prophylactically
Additional References and Resources

- Textbook of Palliative Medicine, Part 8 Pain, edited by Bruera, Higginson, Ripamonti and van Gunten
- MD Anderson Cancer Center “Cancer Pain Algorithm”, 2011
- Campbell V. The challenges of cancer pain assessment and management. The Ulster Medical Society, 2011
- Davis MP, Lasheen W, Gamier P. Practical guide to opioids and their complications in managing cancer pain. Oncology. 2007;21(10):1229-1238; reviews 1238-1249
Additional References and Resources


**Additional References and Resources**

- Pharmacotherapy for Breakthrough Cancer Pain, Sebastiano Mercadante, Drugs 2012;72 (2): 181-190
Additional References and Resources

Additional References and Resources

Additional References and Resources

• [www.chcr.brown.edu/pain/FastFactsonPainManagement](http://www.chcr.brown.edu/pain/FastFactsonPainManagement)
• Robert Brindley, KP, Martinez Medical Center, Hospice Program
Appendix I: Definitions

• Addiction
  - A primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations
  - Behavioral characteristics include one or more of the following
    - Impaired control over drug use
    - Compulsive use
    - Continued use despite harm
    - Craving
Addiction

• Compulsive and persistent use despite
  ▪ Physical harm
  ▪ Psychological harm
  ▪ Social harm

• Cancer patients, when taking opioids correctly, are at minimal risk for addiction
  ▪ Don’t forget to address patient’s concerns about this potential fear
Pseudoaddiction

- Syndrome of abnormal behavior resulting from under-treatment of pain that is misidentified by the clinician as inappropriate drug-seeking behavior
  - Frequent pain assessments to minimize potential
  - Behavior ceases when adequate pain relief is provided
  - Not a diagnosis
    - Rather, a description of the clinical intention
Tolerance

• Loss of a drug’s effects over time or the need to increase the dose to maintain the effect
  ▪ Need to increase the dose to maintain effectiveness

• Normal physiological process
  ▪ Alterations in opioid receptors
  ▪ Changes in opioid metabolism

• Must assess for disease progression
Tolerance

• Fear of tolerance should NOT prevent the prescribing of opioids earlier in the disease
  ▪ Do NOT withhold opioids until end-of-life situations
Dependence

• Physical Dependence
  ▪ Normal physiological effect arising from chronic opioid use

• Syndrome that occurs due to
  ▪ Cessation of opioid
  ▪ Reduction in prolonged use of opioid
  ▪ Use of opioid antagonist
Withdrawal

- A syndrome that occurs due to the cessation or reduction of prolonged use of a drug
  - Dysphoria
  - Nausea or vomiting
  - Muscle aches
  - Lacrimation
  - Rhinorrhea
  - Pupillary dilation
  - Diarrhea
  - Yawning
  - Fever,
  - Insomnia
Minimizing Withdrawal Potential

- When opioid reduction or cessation is indicated
  - Opioid dose should be tapered down to the rate of
    - 10-20% each day
Appendix II: Assessment Tools


- Assessment tools
  - Does one tool exist that accurately captures the multidimensional nature of cancer pain?
  - De Wit showed that when using different assessment tools in the same patient population
    - The percentage of uncontrolled cancer pain ranged from 16-96%, depending on method used
Assessment Tool: Edmonton Staging System (ESS) for Cancer Pain

• Seven basic characteristics are rated
  ▪ Mechanism of pain
  ▪ Presence of incidental pain
  ▪ Daily opioid use
  ▪ Cognitive function
  ▪ Psychological distress
  ▪ Tolerance
  ▪ Past history of drug or alcohol addiction

Edmonton Staging System for Cancer Pain


- **Prognosis for pain control**
  - Patients were defined, based on these features, as having a
    - Good prognosis
    - Intermittent prognosis
    - Poor prognosis
  
- **ESS found to be highly sensitive with poor specificity**
Classification System for Cancer Pain (ECS-CP)

- In response to ESS’ limitations, modifications were made

- Despite changes, some maintain there is no internationally accepted tool for cancer pain assessment
  Fainsinger, RL, Nekolaichuk, CL. Cancer pain assessment-can we predict the need for specialist input? Eur J Cancer. 2008; 44(8): 1072-7,
Appendix III: Pain Management Fast Facts

- Components for pain ASSESSMENT
- Types of PAIN
- Step Ladder of Analgesic Medication (WHO)
- Guidelines for ORDERING analgesics
- NEUROPATHIC pain
- COMMUNICATION
- Opioid dose INCREASE
Critical Components to Pain Assessment (1)

- Location(s)
- Description
- Type
- Impact on ADL
- Intensity
- Pattern: Continuous/Intermittent
- Onset
- Duration
Critical Components to Pain Assessment

- What makes pain better/worse
- Patient’s perception of pain
- Patient’s goal for pain relief
- Analgesics used in past
- Analgesics receiving in past 24 hours
Types of Pain (2)

- Visceral
- Muscle
- Bone
- Neuropathic
- Pleuritic
- Colic
• Commonly localized to site of the injury/tumor
• Pain can be referred to the somatic area supplied by same nerve root
• Clue to this kind of pain
  ▪ “I ache all the time.”
Muscle (2)

- May be difficult to isolate as cause may be due to an underlying disorder
  - Systemic cause
  - Metabolic cause
- Clue to this kind of pain
  - “I’m sore and stiff.”
  - “It feels like a Charlie-horse.”
Bone (2)

- Range from dull ache to deep and intense pain
- Commonly well localized
- May be worse on movement and weight-bearing
- May be worse at night
- May be masked by muscle pain
  - Due to involuntary, protective muscle spasm
- Clue to this kind of pain
  - “It hurts when I move.”
  - “It aches at night.”
Neuropathic (2)

• Constant, superficial, burning pain commonly caused by damage to the
  - Nerve
  - Plexus
  - Root
  - Spinal cord

• When specific nerve involved pain is reported in a relatively constant area of body surface, consistent with dermatome
  - May also be referred pain to the somatic region supplied by the involved nerve
Neuropathic (2)

• Clue to this kind of pain
  ▪ “It feels like my skin is **burning**.”
  ▪ “It feels like someone **stabbed** me.”
  ▪ “It’s a **shooting** pain.”

• More later…
Pleuritic (2)

- Pain with inspiration
- May present with shallow, guarding breathing
- Clue to this kind of pain
  - “The pain is worse when I breathe in.”
Colic (2)

• Partial or complete obstruction of a hollow viscus can lead to intermittent cramps

• Clue to this kind of pain
  ▪ “The pain comes and goes like cramps.”
Step Ladder: Moderate Pain (3)

- **Step 1: Treat with non-opioid analgesic**
  - Around the clock
    - Maximum dose for single ingredient extra-strength acetaminophen is 3 gm/day
      - 2 pills every 6 hours
    - Ibuprofen 400 mg q 4 hours
    - Choline magnesium trisalicylate: 1500 mg bid
    - Other NSAID’s
  - May be combined with adjuvant drugs if indicated
Moderate Pain (3)

• Around the clock
  ▪ Acetaminophen/hydrocodone: 325 mg/5
  ▪ Acetaminophen/hydrocodone: 325 mg/7.5
  ▪ Acetaminophen/hydrocode: 325 mg/10

• Stronger opioid to be considered when pain not controlled with these combinations at a total daily dose of 400 mg/day of codeine or 80mg/day of oxycodone
Severe Pain (3)

• Step 3: Failure to achieve adequate relief with Step 2

• Around the clock
  ▪ Morphine 15-30 mg q 4h titrate to pain
  ▪ Hydromorphone 2-4 mg q 4h titrate to pain
  ▪ MS-Contin or other long acting 30-60 mg q8-12h

• Breakthrough pain
  ▪ Use short acting preparation of same medication

• Opioid naïve and elderly patients
  ▪ Start with lower dose
General Guidelines (4)

• Document quality and type of pain to help determine medication management

• Administer medications routinely rather than prn
  ▪ Exception: If pain is intermittent, consider prn use

• Use least invasive route of administration, first
  ▪ Oral route is first choice
  ▪ If unable to tolerate po medications, consider buccal, sublingual, rectal and transdermal routes BEFORE
  ▪ IV or subcutaneous routes
General Guidelines (4)

• Begin with low dose and titrate carefully until comfort achieved
  ▪ For constant, moderate to severe pain, use long-acting medication
  ▪ Have short-acting medication available for breakthrough pain

• Reassess frequently, and adjust dose to optimize pain relief
  ▪ While monitoring and managing side-effects
General Guidelines (4)

• Only one combination analgesic (non-opioid/opioid) for breakthrough pain, e.g.
  ▪ Hydrocodone/acetaminophen
  ▪ Codeine/acetaminophen

• Only one opioid for continuous moderate to severe pain, e.g.
  ▪ Oxycodone

• Short-acting oral opioids ordered at intervals no longer than 4 hours
General Guidelines (4)

- Adjuvant medications for opioid non-responsive neuropathic pain
- Always have an order for breakthrough pain
  - Use an immediate release opioid at a strength equivalent to 10-20% of the 24 hour dose of the sustained release dose
    - Order q1-2 hour, prn
General Guidelines (4)

- Only one sustained-release preparation at a time
- Need bowel regimen to prevent constipation
General Guidelines (4)

• Plan to address pain that is known to be precipitated by activity
  ▪ Pharmacologic
  ▪ Non-pharmacologic

• Pain management flow sheet when pain is at moderate level or higher (5/10)
Genera Guidelines (4)

- Non-pharmacologic interventions are clearly identified as part of treatment plan
Neuropathic Pain (5)

• Quality
  ▪ Sharp
  ▪ Shooting
  ▪ Burning
  ▪ Numbness
  ▪ Tingling
  ▪ Hyperalgesia
    ▪ Slight stimulus like light touch is perceived as severe pain)
Neuropathic Pain (5)

• Frequency and Intensity
  ▪ Severe
  ▪ Continuous
  ▪ Often disturbs sleep
  ▪ Can fluctuate in intensity
  ▪ Can be reduced by diversional activities and mood elevation
  ▪ May be position dependent when nerve compression present
Neuropathic Pain (5)

• Examples
  - Arm pain with brachial plexus involvement
  - Leg pain with pelvic tumor involvement of lumbosacral plexus
    - May be bilateral with sacral involvement
    - Described as **aching and pressure-like**
    - Associated weakness in legs
    - **Burning and stabbing** leg pain
    - Numbness and tingling may be present
  - Diabetic neuropathy
Neuropathic Pain (5)

- Management options
  - Opioids: Some neuropathic pain will respond, partially
    - Lack of responsiveness, especially with drowsiness
  - Antidepressants, especially for burning and tingling pain
    - Desipramine po starting at 10mg qhs
    - Nortriptyline po starting at 10 to 30 mg hs
      - Allow at least 10 days before changing
Neuropathic Pain (5)

• Management Options
  ▪ Anticonvulsants
    ▪ Gabapentin po starting does 100 mg q8 h
    ▪ Pregabalin
    ▪ Clonazepam po starting dose 0.5 mg q 8 h
    ▪ Consider carbamazepine especially. for shooting pain
      ▪ 200 mg hs or
      ▪ Bid and titrate
Neuropathic Pain (5)

- Never give both nortriptyline (TCA) and carbamazepine (anticonvulsant)
  - Opposite effects
    - TCA lowers seizure threshold
    - Carbamazepine elevates seizure threshold
- If mixed pattern of shooting pain and burning pain use anticonvulsant
Based on nurse-physician communication:

- State the pain management **goal**
  - Pain rating and activities
- Summarize **current** pain ratings and effect of pain on activities
- List current analgesic doses and relevant side effects
- Suggest solutions, especially if dose escalation is being considered
Guidelines for Analgesic Escalation (7)

• Dose escalations are calculated as a percentage of the current dose, based on the patient’s pain rating.
  - For example, going from 1 tab to 2 tabs is a 100% increase
  - Most patients will not notice an increase in analgesia when the percentage increase is less than 25% above baseline
Guidelines for Analgesic Escalation (7)

- **Assuming normal renal function, e.g.**
  - Mild to moderate pain (3-6/10)
    - Dose escalation is 25-50% of current dose
  - Moderate to severe pain (7-10/10)
    - Dose escalation is 50 to 100% of current dose

- **Long-acting opioids**
  - Don’t increase the long-acting drug more than 100% at any one time
    - Regardless of number of breakthrough doses used
Guidelines for Analgesic Escalation (7)

Frequency of dose escalation

- Depends on drug half-life
- Short-acting opioids can be safely escalated every two hours
  - Does NOT apply to combination drugs
Guidelines for Analgesic Escalation (7)
Frequency of dose escalation

• Sustained-release/long-acting opioids can be escalated every 24 hours
  ▪ Morphine
  ▪ Oxycontin

• Fentanyl Patch can be escalated no less than every 72 hours
Appendix IV: Inflammatory Management

• Anti-inflammatory medication for
  - Bone pain
  - Generalized aches
  - Terminal fever

• If increasing doses of opioids do not relieve pain, pain may be primarily inflammatory in nature
NSAID Use

• Consider naproxen or salsalate
• Indomethacin can be delivered by
  ▪ Gel or Rectally
  ▪ May be useful at terminal stage for fever and inflammatory control
• Consider proton-pump inhibitor
  ▪ Omeprazole 20 mg daily one-half hour prior to first meal
Dexamethasone

- Dexamethasone considered for
  - Inflammatory pain
  - Swelling
  - Tumor pressure
  - Liver capsule pain
  - Bone pain
  - Increase appetite

- Dosing
  - Start at 2mg bid
  - Increase, as needed, up to 8 mg four-times per day, depending on need and tolerance
Appendix V: Approximate Equivalent Doses of Oral Analgesics for Less Severe Pain

Robert Brindley, KP, Martinez Medical Center, Hospice Program

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PO(mg)</th>
<th>SALIENT FEATURES</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASPIRIN (ASA)</td>
<td>600</td>
<td>Excellent analgesic; non-opioid, anti-inflammatory, affects platelets, GI toxicity.</td>
</tr>
<tr>
<td>CODEINE</td>
<td>30</td>
<td>Weak opioid.</td>
</tr>
<tr>
<td>HYDROCODONE*</td>
<td>5</td>
<td>Weak opioid. 6x more potent than codeine. Alternative to codeine. In Hycodan liq 5mg/5ml &amp; tabs + Atropine.</td>
</tr>
<tr>
<td>MEPERIDINE (Demerol)</td>
<td>50</td>
<td>Weak opioid, high addiction liability; poor absorption, short duration.</td>
</tr>
<tr>
<td>PROPOXYPHENE HYDROCHLORIDE (Darvon)</td>
<td>65</td>
<td>Weak opioid. Could accumulate like methadone. Caution with use in the elderly. (Darvocet-N 100/650mg also generic 100/325mg or 100/500mg)</td>
</tr>
<tr>
<td>PROPOXYPHENE NAPSYLATE (Darvon-N)</td>
<td>100</td>
<td>Weak opioid. Could accumulate like methadone. Caution with use in the elderly. (Darvocet-N 100/650mg also generic 100/325mg or 100/500mg)</td>
</tr>
<tr>
<td>TRAMADOL (Ultram)</td>
<td>50</td>
<td>Parent drug/metabolite occupy opioid receptors. Also increases norepinephrine and serotonin. Prescription, but not classified as opioid. Max dose = 400mg/day. 50mg tab = 1 Ty1 w/Cod 30mg.  Associated with seizures. (Ultracet 37.5mg/325mg APAP)</td>
</tr>
<tr>
<td>IBUPROFEN (Motrin, Advil, various)</td>
<td>400</td>
<td>Similar to aspirin, 600-800mg Q6hr for anti-inflammatory. Aspirin equivalent doses get same GI side effects. Liq 100mg/5ml; Max dose 3,200mg/day. IV (Caldolor) 400, 800mg @100mg/ml. Dilute to 4mg/ml and give over 30 minutes every 6 hours.</td>
</tr>
<tr>
<td>NAPROXEN (Naprosyn)</td>
<td>250</td>
<td>Similar to aspirin; liquid 125mg/5ml; up to 750mg (max 1,500mg/day) Q12hr as anti-inflammatory.</td>
</tr>
<tr>
<td>ACETAMINOPHEN (Tylenol)</td>
<td>650</td>
<td>Minimal anti-inflammatory action. Max dose 4gm/day; 3gm/day in elderly. Liver toxic.</td>
</tr>
<tr>
<td>SODIUM SALICYLATE</td>
<td>1000</td>
<td>Similar to aspirin. Non-acetylated so minimal effect on platelets or renal function.</td>
</tr>
<tr>
<td>CHOLINE SALICYLATE (Arthrapan)</td>
<td>870mg/5ml</td>
<td>Liquid mint flavor. 10-15ml Q6hr for anti-inflammatory dose. Non-acetylated. Little effect on renal function or platelets. Non-prescription (For tablets use Trilisate 750mg Q6hr - prescription drug)</td>
</tr>
</tbody>
</table>

*VICODIN IS A COMBINATION OF HYDROCODONE 5MG PLUS ACETAMINOPHEN 500MG, Vicodin ES = 7.5/750 -- Anexsia 5/325, 5/500 and 7/5/650. Lortab 2.5/5, 5/10, 7.5/500. Also liquid Lortab 2.5mg/5ml c 167mg acetaminophen. One Vicodin 5/500mg APPROX = 3.5mg oral morphine.

*NORCO IS A COMBINATION OF HYDROCODONE 5, 7.5, or 10MG PLUS ACETAMINOPHEN 325MG
Approximate Equivalent Doses of Oral and IM Analgesics for Severe Chronic Pain Upon Repeated Dosing

<table>
<thead>
<tr>
<th>DRUG</th>
<th>IM(mg)</th>
<th>PO(mg)</th>
<th>MAJOR DIFFERENCES FROM MORPHINE/COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MORPHINE</td>
<td>10</td>
<td>20</td>
<td>IV-2hrs, IM-3hrs, IR PO/PR-4hrs ER Oramorph SR (15,30,60,100mg) MS Contin (15,30,60,100,200mg)-12hrs Kadian (20,30,50,60,100mg) Avinza (30,60,90,120mg)-24hrs Supp. 5,10,20,30mg oral Liq 2, 4 or 20mg/ml-easy titration.</td>
</tr>
<tr>
<td>HYDROMORPHONE (Dilaudid)</td>
<td>2</td>
<td>4</td>
<td>2,4,8mg tab, 3mg supp, PO/PR-4hrs, oral Liq 1mg/ml Semisynthetic alternative to morphine. High potency inject 10mg/ml Exalgo tabs (8,12,16)-24hrs.</td>
</tr>
<tr>
<td>OXYCODONE*</td>
<td>10</td>
<td></td>
<td>PO-4hrs. 5,10,15,20,30mg tab, 5mg cap, liq 1&amp; 20mg/ml Oxycontin-12hrs (10, 15,20,30,40,60,80mg tab).</td>
</tr>
<tr>
<td>HEROIN (diamorphine)</td>
<td>6</td>
<td>12</td>
<td>Not available in the U.S. PO 4hrs. Converted to morphine in body.</td>
</tr>
<tr>
<td>METHADONE (Dolophine)</td>
<td>10</td>
<td>12.5</td>
<td>High PO to IM ratio - IM 4-5hrs, PO 6-8hrs, IM 10mg/ml Tab 5,10,40mg Liq 1,2,10mg/ml. Adjust dose every 3-5 days. Very difficult to titrate or calculate oral morphine equiv. Ratio changes based on morphine daily dose.</td>
</tr>
<tr>
<td>LEVORPHANOL (Levo-Dromoran)</td>
<td>2</td>
<td>2.5</td>
<td>2mg tablets. High PO to IM potency. PO 6-8hrs. Difficult to titrate.</td>
</tr>
<tr>
<td>OXYMORPHONE (Opana)</td>
<td>1</td>
<td>5 ?</td>
<td>5,10mg IR, 5,7,5,10,15,20,30,40mg ER tabs-12hrs, poor po absorption,1mg/ml inj.</td>
</tr>
<tr>
<td>TAPENTADOL (Nucynta)</td>
<td>60</td>
<td></td>
<td>50, 75, 100mg 1/3rd Morphine potency-Acute pain-Serotonin Syndrome/Seizures Max daily dose 600mg (100mg every 4hrs)-700mg first day.</td>
</tr>
<tr>
<td>FENTANYL (Sublimaze/Duragesic Patch)</td>
<td>0.1</td>
<td>50mcg</td>
<td>Transdermal. Injectable very short acting. Used intrathecally. Patch Q72hrs (25mcg/hr = 10mg MS PO Q4hrs). Difficult to titrate. Actiq (Lozenge on a stick) 200,400,600,800,1200,1600mcg for cancer BTP. Fentanyl buccal tab 100,200,400,600,800mcg.</td>
</tr>
<tr>
<td>PENTAZOCINE (Talwin)</td>
<td>60</td>
<td>180</td>
<td>Opioid agonist-antagonist. can produce withdrawal in opioid dependent patients, dysphorias, hallucinations common. Representative of Nalbuphine (Nubain), Butorphanol (Stadol), Dezocine (Dalgan), Buprenorphine (Buprenex).</td>
</tr>
<tr>
<td>MEPERIDINE (Demerol)</td>
<td>100</td>
<td>300</td>
<td>Erratically absorbed PO. Short duration of action either route. IM painful. Risk of seizures due to metabolite normeperidine which has a long half-life &gt;200hrs.</td>
</tr>
<tr>
<td>HYDROCODONE</td>
<td>35</td>
<td></td>
<td>6X stronger than codeine. Vicodin 5/500mg approx equal to APAP/codeine 30mg.</td>
</tr>
<tr>
<td>KETOROLAC (Toradol)</td>
<td>10-90</td>
<td></td>
<td>NSAID, good analgesic, not good anti-inflammatory. IV/IM/PO Q6hrs short term use only, 5 days total. IM loading dose 30mg then 15mg Q6. Affects platelets. PO max 40mg/day. 10mg PO = APAP/Cod 30mg. Any inj dose = 12mg MS inj.</td>
</tr>
</tbody>
</table>

*PERCOCET-5 = Oxycodeone 5mg plus acetaminophen 325mg. Tylox = Oxycodeone 5mg plus acetaminophen 500mg. Percodan = 4.5mg oxycodeone plus 325mg ASA. APPROX = 12MG ORAL, MORPHINE. Some other strengths Roxicet 5/500mg, 7.5/325 or 500mg & Percodon-Demi 2.5/325mg.
Appendix VI: Breakthrough Pain

• Fentanyl formulations
  ▪ May be drug of choice for quick onset and short duration pain control
    ▪ Oral transmucosal
    ▪ Buccal tablet and soluble film
    ▪ Sublingual
    ▪ Intranasal spray
  ▪ When considered for BTP, should be administered to **opioid-tolerant patients** receiving doses of oral morphine equivalents of at least 60 mg
Breakthrough Pain

- Intravenous morphine is an effective method to provide fast analgesia for BTP
  - Provides immediate and total availability of drugs
- Comparing IV morphine and transmucosal fentanyl for BTP
  - IV morphine was significantly more effective than fentanyl 15 minutes after administration, while no differences were found at 30 minutes
  - The outcome was independent of the opioid doses used for background analgesia
Breakthrough Pain: Morphine versus Fentanyl

• IV Morphine Compared to Oral Transmucosal Fentanyl
  ▪ Adverse effects were comparable and never troublesome, even in patients receiving high BTP doses
Appendix VII: Methadone

• Strong points
  ▪ Excellent absorption
  ▪ High lipid solubility
  ▪ High potency
  ▪ Long half-life
  ▪ Decreased opioid cross-tolerance
  ▪ Low cost
  ▪ May benefit patients with both somatic and neuropathic pain
Methadone

- Methadone may be desirable in the setting of renal failure
- Prescribing should be done by physicians experienced with use of methadone
Methadone

• Caution
  ▪ Drug interactions especially those that involve cytochrome p450 systems
    ▪ Antifungals
    ▪ Some antibiotics
    ▪ Antivirals
  ▪ May modestly increases QTc interval at higher doses
    ▪ EKG monitoring
  ▪ Marked individual variation in pharmacokinetics
Methadone


• Caution
  - Late toxicity due to drug accumulation is possible after start of treatment or after a dosage increase
  - In converting an opioid to methadone, a 75% reduction of the equivalent dose is recommended
  - The half-life of methadone varies from 12 hours to more than 100 hours
Non-oral Routes of Methadone Administration

- **Rectal**
  - Absorption may be variable
  - Avoid in patients with
    - Anorectal lesions
    - Severe thrombocytopenia

- **Transmucosal**
  - Optimal for breakthrough pain due to
    - Rapid absorption
Non-oral Routes of Methadone Administration

• IV and subcutaneous
  ▪ Used for acute titration
  ▪ Used in situations where other routes not available

• Neuraxial: Epidural or intrathecal
  ▪ May cause less side effects
  ▪ May be more effective in complex pain syndromes
    ▪ Neuropathic pain
    ▪ Plexopathy pain

• Long-term catheter systems
Appendix VIII: PCA Use

• PCA may be successfully used as the main indication for the treatment of breakthrough pain
  ▪ Supplement continuous infusion of opioids with the self-administration of additional boluses
    ▪ At pre-set doses and intervals.
    ▪ The as-needed dose should be about 15–20% of the daily dose of morphine.
PCA Use

- Optimal PCA infusion use can
  - Meet the needs of patients by
    - Allowing improved pain relief without increasing side-effects and
    - Using lower doses to maintain the same pain relief compared with externally controlled doses.
Appendix IX: Advanced Procedures

- **Radiofrequency ablation**
  - Via frictional heating or cryotherapy (leads to tissue necrosis)
  - May be useful in osteolytic mets
- **Subarachnoid neurolytic block**
  - May also be considered for extremity and thoracic wall pain in terminally ill patients
- **Neurectomy**
- **Rhizotomy**
- **Cordotomy**
  - May also be considered for lower extremity intractable pain
Advanced Procedures: Celiac Plexus Blocks

• Access plexus percutaneously
  ▪ Inject neurolytic substance (phenol or alcohol)
    ▪ Alcohol is preferred because it is less toxic to the tissues and vascular structures
  ▪ Duration and completeness of analgesia are not usually predictable

• Pain control must usually be integrated with pharmacological therapy
Advanced Procedures: Celiac Plexus Blocks

- Few clinical trials, with few patients
  - Confirm that analgesia appears to be in favor of celiac block during the first weeks after the start of treatment
    - Benefit may last for only 2–4 weeks.
    - May lead to sparing of analgesic use and decrease in opioid side-effects
Celiac Plexus Blocks: Side-effects

- Occur in 30-60% of patients
  - Orthostatic hypotension
  - Transient diarrhea are common side-effects encountered

- Lesser side-effects include
  - Transient dysesthesia
  - Reactive pleuritis,
  - Transient hematuria caused by renal puncture.
Cauda Equina Rhizotomy

• Indications
  ▪ Treatment of perineal pain
    ▪ When the patient has clear symptoms of somatic pain
    ▪ Disease recurrence
    ▪ Macroscopic areas of vulvovaginal or peri-rectal erosion
  ▪ Evident trigger points
  ▪ Difficulty in urinating related to pre-existing bladder dysfunction and already has a colostomy.
Cauda Equina Rhizotomy

- In 39 patients with perineal pain treated with this technique
  - Mean duration of pain relief was 5.4 months
  - Bladder sphincter complications occurred in 19 patients (49%)
  - No anal sphincter complications
    - 79% of patients had a colostomy
• Produces complete analgesia of the contralateral hemisomus from C5 to S5.

• Technically difficult
  ▪ Especially when a high dermatomic level of analgesia is required.
  ▪ In expert hands, the rate of complications is limited to
    ▪ 1% mortality
    ▪ Bladder dysfunction
    ▪ 8–20% loss of strength in the homolateral lower limb.
Percutaneous Cervical Cordotomy

- Done under local anesthesia
- Patient must be very cooperative.
- Prognosis should not be more than 1 year
  - Due to risk of postcordotomy dysesthesic pain
- The incidence of complications is higher for bilateral cordotomy
  - Therefore not recommended