The Facts About Effectively Managing Intractable Cancer Pain

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Objectives

- Describe cancer pain
- Incidence of cancer pain
- Identify a team approach to treatment of cancer pain
- Define the roles of intrathecal drug delivery systems and neuromodulation in treating cancer pain
Sources of Pain in Cancer Patients

Cancer pain comprises:

- Acute pain
- Chronic pain
- Tumor-specific pain
- Treatment-related pain

Existence of pain due to cancer

More than two thirds of cancer patients report pain which they attribute to their cancer

Base: all screened – (individual base sizes shown on chart)

S4. Have you suffered any pain due to your cancer?

More than 50% of patients with the following types of cancer currently suffer from pain:

§ Lung
§ Pancreatic
§ Brain Tumour
§ Bone/Muscle
§ Blood Borne
§ Non-Hodgkins
§ Head/Neck
§ Leukaemia

www.paineurope.com
European Pain in Cancer (EPIC) Global Results Presentation, July 2007
Where We Are Today in Managing Cancer Pain?

- Minorities, women, and the elderly are particularly at risk for cancer-related pain.¹
- One survey found that while health care providers believe they are doing a good job at managing pain and its symptoms, families do not.²
- Cancer pain still pervasive in adults and children.³
- Cancer pain is undertreated in all settings where patients with cancer are managed.³

You Are The Patient’s Advocate

- Patients with cancer are often reluctant to report the extent of their pain\(^1\)
  - Fear that reporting pain will take physician time away from their treatment
  - Concern about addiction
  - Beliefs that “good” patients do not complain about pain
  - Concern about side effects with escalating doses

- Result = under-treatment of pain

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The Effects of Pain

- A majority of patients experience pain at some point during their course of cancer treatment.¹
- Cancer pain impairs quality of life and functionality.¹
- The cost of inadequate pain control and related side effects (of pain medications) is high, both in terms of impaired function and quality of life.²-⁴
- Pain interferes with all activities of daily living.⁵

Pain as the “Fifth Vital Sign”

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) issued a comprehensive description of patients’ rights and standards of care for pain management.

- **Recommendation:** make pain assessment/management priority in daily practice
- **Consider pain intensity the 5th vital sign:** measure along with temperature, pulse, respiration, and blood pressure
- **Patients’ rights:** full pain workup when pain is not easily characterized or treated

Start with a Comprehensive Pain Assessment

The National Cancer Institute recommends that the clinician help the patient describe pain¹:

- Location
- Changes in pattern
- Intensity or severity
- Aggravating and relieving factors
- Cognitive response to pain
- Goals for pain control

These are essential to the initial assessment:¹

- Detailed history¹
- Physical examination¹
- Psychosocial assessment²
- Diagnostic evaluation¹

Assessment Goals

- Characterize the pathophysiology of pain
- Determine intensity of pain
- Determine impact on patient’s ability to function

Cancer Pain Therapy: The Oncologist’s Perspective

- Systemic pharmacologic therapy
- Collaboration with pain medicine and palliative care specialists
- Good pain management facilitates good cancer management

Multidisciplinary Approach to Chronic Pain Management

- Pain specialists
- Psychologists
- Nurses
- Social workers
- Rehabilitation specialists

Complex Problem

- Physiological factors
- Social factors
- Psychological factors

Multidisciplinary Solution
Cancer Pain Management Strategies

- **Pharmacologic strategies**
  - Nonopioid analgesics
  - Acetaminophen
  - Nonsteroidal anti-inflammatory drugs
  - Opioid analgesics
  - Coanalgesics (adjuvant analgesics)
  - Corticosteroids

- **Physical strategies**
  - Massage
  - Exercise
  - Transcutaneous electrical nerve stimulation (TENS)
  - Acupuncture

- **Psychological strategies**
  - Hypnosis or relaxation with imagery
  - Cognitive-behavioral methods

- **Nerve blocks/Radiofrequency**
  - Radiation therapy
  - Chemotherapy

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Pharmacological strategies

- Non-opioid analgesics
  - Decadron and oral corticosteroids
    - Significant reduction in edema and good for acute metastatic disease and brain involvement
  - NSAID’s
    - Additive effect by inhibiting COX-1 and COX-2 pathways and possibly COX-3
  - Acetaminophen
    - inhibiting COX-1
  - Anti-epileptic medications
    - Gabapentin has a synergistic effect when combined with morphine (N Engl J Med 2005;352:1324-34)
  - Bisphosphonates
  - Cannabis
Psychological strategies

- Coping skills
- Biofeedback
- Meditation
- Family or group
Opioid Analgesics for the Treatment of Cancer Pain

- Used most often in the management of severe pain because:
  - Effectiveness
  - Ease of titration
  - Favorable risk-to-benefit ratio

- Routes of administration
  - Oral
  - Transdermal
  - Parenteral: Intravenous or subcutaneous
  - Intraspinal: Epidural or intrathecal
    - Consider when other routes of administration cannot control pain or when side effects limit further dose escalation

2. Ibid., p 64.
Intervention techniques

- Vertebroplasty/ Kyphoplasty
- Radiofrequency
  - Splanchnic nerves
  - Peripheral nerves
  - C2 Cordotomy
- Intrathecal drug delivery systems
- Spinal cord neuromodulation
Radiofrequency

- Splanchnic nerves
  - Pancreatic cancer
  - Abdominal cancer
  - Chronic abdominal pain
- Case
  68 y/o male with history of neuroendocrine tumor with metastatic mass compressing celiac plexus and resistant abdominal pain.

Raj, Prithvi et al
Radiofrequency

- Peripheral nerves
- Case
  - 70 y/o female with history of facial squamous cell CA with radical facial resection and chronic neuropathic pain in left infraorbital region. Failed to respond to opioids, AED’s, NMDA medications
Advanced Strategies for Intractable Cancer Pain Management

10-20% Invasive Therapy Needed

80-90% Adequate Pain Control

Portenoy R. Oncology 1999;S2:7.
Spinal Anatomy

- Epidural Space
- Arachnoid Membrane
- Intrathecal Space (Subarachnoid Space)
- Dura
- Pia Mater
- Spinal Cord
- Nerve Root
Epidural vs. Intrathecal Space

Intrathecal Space
(Subarachnoid Space)

Epidural Space
Physiology of Spinal Opioids

- Nociceptors carry a “pain” signal to the dorsal horn.
- In the dorsal horn neurons release substance P.
- Substance P triggers ascending neurons that carry this signal to the brain.
- Opioids inhibit the release of substance P, blocking the pain transmission.
- Perceived pain is reduced.
# Epidural vs. Intrathecal Opioids

<table>
<thead>
<tr>
<th>Pros</th>
<th>Intrathecal</th>
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<tbody>
<tr>
<td><em>Reduced risk of respiratory depression and other serious complications</em></td>
<td><em>Faster onset of analgesia</em></td>
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<tr>
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<td><em>Lower risk of catheter failure</em></td>
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<td><em>Allows for CSF sampling</em></td>
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<td></td>
<td><em>Longer intervals between refills</em></td>
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<td></td>
<td></td>
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<tr>
<td>Cons</td>
<td></td>
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<tr>
<td><em>80-90% of drug is systemically absorbed</em></td>
<td><em>Potential CSF leakage leading to spinal headache</em></td>
</tr>
<tr>
<td><em>Possible dural fibrosis can occlude catheter</em></td>
<td><em>Increased risk of meningeal infection or neural injury</em></td>
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<td><em>Greater dose requirement</em></td>
<td><em>Risk of inflammatory mass</em></td>
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<td><em>Slower onset of analgesia compared to intrathecal delivery</em></td>
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What is successful pain management?

Success = Pain relief – Unmanageable side effects
Approximate Equivalent Daily Doses of Morphine Administered by Various Routes

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Relative Potency (mg)*</th>
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<tbody>
<tr>
<td>Oral</td>
<td>300</td>
</tr>
<tr>
<td>Intravenous</td>
<td>100</td>
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<tr>
<td>Epidural</td>
<td>20</td>
</tr>
<tr>
<td>Intrathecal</td>
<td>1</td>
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*Relative approximations based on clinical observations

Reduce Dose → Reduce Side Effects

1 mg intrathecal morphine = 300 mg oral morphine

Intrathecal Drug Delivery: Patient Selection Criteria

I. Symptoms of pain due to advanced stage cancer at presentation, with a minimum life expectancy of >3 months¹-⁴

II. Refractory to conventional pain management because of drug toxicity or unsatisfactory analgesia¹-⁴

III. Visual analog scale (VAS) of ≥ 5, despite 200 mg/day of oral morphine or the analgesic equivalent¹,³,⁴

Consider those on lower doses if opioid side effects are refractory to conservative treatment and severe enough to prevent upward titration.¹,³,⁴

IV. Consider early evaluation of intrathecal drug delivery for those with pelvic tumors who may have eventual nerve compression.²

Contraindications to Intrathecal Drug Delivery

- When infection is present
- When pump implant depth exceeds depth specified in pump labeling
- Intrathecal Drug Delivery Contraindications
  - When body size is not sufficient to accept pump bulk and weight
  - When contraindications exist relating to the drug
  - Drugs with preservatives
  - Do not use the patient control device, if applicable, to administer opioid to opioid-naïve patients or to administer ziconotide

For a complete list of contraindications, refer to the manufacturer labeling for the specific device.
Scientific Evidence

- Five cancer related studies looking at treatment of IDD for refractory pain.
Smith et al

- 202 patient, multicenter trial with initial VAS >5 despite oral equivalent of morphine 200 mg/d, life expectancy >3 months, baseline VAS 7.5, mixed pain
- Intervention-IDD
- Outcome
  - Data collected at 2, 4, 6, 8, 10 and 12 weeks
  - Monitored VAS, toxicity, QOL, mortality
- Results
  - 84.5% IDDS achieved success compared to 71.8% CMM
  - VAS decreased by 2 points 52% IDDS to 39% CMM
  - Increased survival 53.9% IDDS to 37.2% CMM
- Conclusion IT morphine can decrease side effects, systemic medications and improve QOL
- Complications
  - 194 serious complications split evenly between 2 groups no death
Rauck et al

- 149 patient enrolled, 119 implanted for refractory cancer with patient therapy monitor
- Intervention - IDD with PTM
- Outcome
  - Supplemental opioid use
  - Pain relief
  - Opioid complications
  - Success defined by 50% or > reduction in one of the aforementioned
- Results
  - Numeric analog scale decreased 31% and maintained
  - Systemic opioid use at 13 months was 0%
  - Global assessment was excellent in 87%
- Conclusion IDDS improved pain control, reduced toxicity and improved survival
- Complications were difficult to assess due to only 15 patients lasting 13 months
43 consecutively treated cancer patients

Intervention IDD

Outcome

- Verbal rating scale
- Best pain reduction
- Final pain reduction

Results

- VRS was 61.1%
- No more than moderate pain reduction

Conclusion IT morphine is an effective treatment for neuropathic and nociceptive cancer pain

Complications

- Catheter, hematoma
53 patients terminal metastatic disease mean age 62

Intervention IDDS with morphine

Outcome
- Parental narcotic use
- Analgesic index, mobility, over outcome

Results
- All improved
- 65% reported good to excellent results

Conclusion
- Long term safety and efficacy of IDD is justified

Complications
- Nothing unexpected
35 patients intractable cancer

Intervention IDD

Outcome

- Numeric rating scale
- Enteral opioid consumption
- Self report daily activities

Results

- 48% reported 0-3 on NRS
- >50% reduction of opioids
- 80% patient had good to excellent relief

Conclusion- use of chronic IT morphine is justified

Complications

- No morbidity
Medications available

- FDA approved - first line
  - Morphine
  - Baclofen
  - Ziconotide

- Not FDA approved - second line
  - Fentanyl
  - Morphine/hydromorphone + ziconotide
  - Morphine/hydromorphone + bupivacaine/clonidine

- Third line
  - Clonidine
  - Morphine/hydromorphone/fentanyl\bupivacaine + clonidine + ziconotide

- 4\textsuperscript{th} line
  - Sufentanil
  - Sufentanil +bupivacaine + clonidine + ziconotide

- 5\textsuperscript{th} line
  - Ropivacaine, buprenorphine, midazolam, meperidine, ketorolac

- 6\textsuperscript{th} line
  - Experimental agents like gabapentin
Which medication to use

- Hydrophilic better than hydrophobic
- Morphine > hydromorphone > fentanyl > bupivacaine > clonidine
- Know where catheter tip is
# Recommendations for cancer pain patients based on disease state

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<thead>
<tr>
<th>Patient category</th>
<th>Patient characteristics</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>Patient category 1</td>
<td>Comprises those patient whose life expectancy is significantly compromised by their disease and the goal of therapy is palliative</td>
<td>A pretrial/internalization psychological evaluation should be considered optional. It should be done at the discretion of the physician, with focus on identifying cancer-and/or pain-related psychological factors potentially amenable to psychological intervention that may facilitate patient adjustment and analgesia rather than to clear the patient psychologically for IT therapy</td>
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<td>Patient category 2</td>
<td>Consists of patients whose disease process has been arrested, but wherein there is significant probability of recurrence</td>
<td>A pretrial/internalization psychological evaluation is encouraged with an emphasis on periodic psychological consultation/intervention to assist with changes in disease process/recurrence and coping</td>
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<tr>
<td>Patient category 3</td>
<td>Comprises patients whose cancer has been eradicated by surgery or other therapies, but who have residual chronic pain secondary to the medical tx</td>
<td>Patients should undergo a pretrial/internalization psychological evaluation approached in much the same way as those with chronic noncancer pain. Whenever possible the primary caregiver should be included to assess the type and degree of support</td>
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