Pain Management in Advanced Cancer Patients

C. Woelk MD, CCFP, FCFP
Medical Director of Palliative Care – RHA Central Manitoba
Physician, Community Cancer Program – Boundary Trails Health Centre
Family Physician – Winkler, MB
woelk@cwwiebemedical.ca
Objectives

• To appreciate the complexities of pain and its management in advanced cancer.

• To understand the rationale for the use of a variety of opioids and routes of administration.

• To have an approach to deal with neuropathic and incident pain.

• To understand some of the practical aspects of pain management for patients choosing to die at home.
Disclosure of Conflicts

“Anything to declare?”
“Try this – I just bought a hundred shares.”
Understanding the Context of the Illness: Total Suffering

- Multiple Losses
- Communication issues
- Existential issues
“I feel like a sick rabbit, being chased by crows, who take one bite out of me at a time.”
Multiple Losses

People suffer from what they have lost of themselves in relation to the world of objects, events, and relationships.

“The Nature of Suffering and the Goals of Medicine” – Eric Cassel
What is a Person? Eric Cassel

- Persons have personality and character.
- A person has a past, a cultural background.
- A person has roles; No person exists without others.
- A person is a political being.
- Persons do things.
- Persons are often unaware of much that happens within them and why.
- Persons have regular behaviour.
- Every person has a body.
- Every person has a secret life.
- Every person has a perceived future.
- Every person has a transcendent dimension, a life of the spirit.

A Trajectory of Terminal Illness

![Graph showing the decline of functional status over time.](https://via.placeholder.com/150)
Communication Issues

• Delivering Bad News
• Discussing Prognosis
• Iatrogenic Suffering
"There’s nothing more that we can do"
Understanding the Context of the Illness

Communication Issues

What Dying People Want

David Kuhl
Existential Issues

• Sense of Abandonment
• Fear
• Why Me?
• Hope
• Dignity
I'm not as important as I thought I was. It used to be that I thought the world could not go on without me. But now when I get up in the morning, with so little energy, I see that it does just fine, with little of my input.
Understanding the Context of the Illness: Total Suffering - Woodruff

Total Suffering

- Physical Symptoms
- Psychological
- Social
- Cultural
- Spiritual
- Pain
Understanding the Context of the Illness: Total Suffering - Woodruff
Understanding the Context of the Illness: Total Suffering - Woodruff

- Pain
- Spiritual
- Physical Symptoms
- Cultural
- Psychological
- Social
Opioids in Advanced Cancer
World Health Organization Pain Ladder

- **Step 1**
  - Non-opioid
  - +/- Adjuvant

- **Step 2**
  - Opioid for mild to moderate pain
  - +/- Non-opioid
  - +/- Adjuvant

- **Step 3**
  - Opioid for moderate to severe pain
  - +/- Non-opioid
  - +/- Adjuvant

- Increasing Pain
# Opioids in Palliative Care

<table>
<thead>
<tr>
<th>Opioid</th>
<th>PO</th>
<th>IV/SC</th>
<th>PR</th>
<th>TD</th>
<th>TM</th>
<th>SR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone</td>
<td>+</td>
<td>(+)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>+</td>
<td>+</td>
<td>(+)</td>
<td>(+)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>+</td>
<td>(+)</td>
<td>(+)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sufentanil</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>+</td>
<td>(+)</td>
<td></td>
<td></td>
<td></td>
<td>(+)</td>
</tr>
</tbody>
</table>
Issues Related to Long Term use of Opioids

- Increasing doses
- Increasing toxicity
- Opioid rotation
Increasing Doses of Opioids in Advanced Cancer

• Length of presence of disease
• Worsening disease
• Complicated pain issues more likely
Concerns re escalating doses

Does the use of opioids hasten death?
Concerns re escalating doses

Does the use of opioids hasten death?

NO
Opioids, Survival and Advanced Cancer in the Hospice Setting

- 114 consecutive hospice patients, ages 13-71
- Analysis of survival, according to opioid use
- No significant relationship found between mortality and:
  - Dose on admission
  - Dose at death
  - Mean dose
  - Overall dose increase and decrease
  - Day by day dosage changes
Opioids, Survival and Advanced Cancer in the Hospice Setting

**Fig. 1.** Kaplan-Meier survival curves according to overall change in opioid dosage during hospice admission.
Concerns re escalating doses

- Side effects
- Tolerance
- Physical Dependence
- Opioid dosage
- Addiction
- Diversion
Concerns re escalating doses

Side effects

Tolerance

Physical Dependence

Opioid dosage

Addiction

Diversion
Managing Increasing Doses of Opioids

- Use opioids at appropriate frequency
- Increase the scheduled doses if the breakthrough doses are frequent
- Don’t forget to increase the breakthrough dose
- Watch for escalating use
Managing Increasing Doses of Opioids
Opioid Neurotoxicity

- Cognitive Dysfunction
- Myoclonus
- Hyperalgesia
- Allodynia
- Perceptual Disturbance
- Seizures
Risk Factors for Opioid Induced Neurotoxicity

• Opioid determinants of cognitive dysfunction:
  – High opioid doses
  – Route of delivery
  – Choice of opioid
  – Length of treatment with opioids
• Borderline cognition/delirium
• Dehydration
• Renal failure
• Psychoactive drugs
• Advanced age
Psychomotor Activity Classification of delirious episodes (n=94)

- Mixed: 76% (20 cases)
- Hypoactive: 2 cases
- Hyperactive: 2 cases
- Normal: 2 cases

Delirium in advanced cancer

• Reversible in 40%-60% of cases
Reversed and Non-Reversed Causes of Delirium


C. Woelk MD
Strategies to Prevent Opioid-Induced Cognitive Dysfunction and Delirium

Lawlor PG. The Panorama of Opioid-Related Cognitive Dysfunction in Patients with Cancer. Cancer 2002;94:1836-53

- Educate family regarding recognition of potential neurotoxic features such as myoclonus
- Objectively monitor cognition
- Adjust dose in elderly patients
- D/C or minimize dose of all unnecessary medications
- Adjust doses for impaired renal function
Strategies to Prevent Opioid-Induced Cognitive Dysfunction and Delirium

Lawlor PG. The Panorama of Opioid-Related Cognitive Dysfunction in Patients with Cancer. Cancer 2002;94:1836-53

- Maintain adequate hydration and use diuretics cautiously
- Perform multidimensional assessments
- Identify poor prognostic identifiers for pain control: neuropathic and incident pain, somatization, tolerance, addiction history
- Optimize non-pharmacologic therapies
- Adopt a proactive, preventative, early intervention approach
Managing Patients with Opioid-Related Delirium

Lawlor PG. The Panorama of Opioid-Related Cognitive Dysfunction in Patients with Cancer. Cancer 2002;94:1836-53

• Educate family: psychomotor agitation, perceptual disturbance, delusions and communication difficulties

• Establish goals of care, based on clinical situation, previously expressed wishes and family wishes

• Monitor delirium severity objectively

• Consider opioid dose reduction or change in drug

• D/C or minimize use of all unnecessary medications
Managing Patients with Opioid-Related Delirium

Lawlor PG. The Panorama of Opioid-Related Cognitive Dysfunction in Patients with Cancer. Cancer 2002;94:1836-53

- Consider all other contributory causes, esp. reversible ones
- Assess renal function and dose drugs accordingly
- Assess hydration and consider supplementing
- Treat delirium with neuroleptic drugs, e.g. Haldol, Nozinan
- Environmental manipulation: minimal noise, reorientation, presence of family members
- Prevent recurrence / anticipate risk factors
Issues Related to Long Term use of Opioids

• Opioid rotation
  – When effect seems to wear off (Tolerance)
  – In opioid neurotoxicity
  – Routine
Importance Aspects of Neuropathic Pain

• Identifying neuropathic pain

• Challenges in management
Neuropathic Pain: *Symptoms and Signs*

- **Paresthesias** – spontaneous, intermittent, painless abnormal sensations
- **Dysesthesias** – spontaneous or evoked unpleasant sensations
- **Allodynia** – pain elicited by non-noxious stimuli when applied to the symptomatic area
- **Hyperalgesia** – exaggerated pain response to a mildly noxious stimulus applied to the symptomatic area
- **Hyperpathia** – delayed and explosive pain response to a stimulus applied to the symptomatic area
Neuropathic Pain: *Therapeutic Options*

- Opioids
- Tricyclic Antidepressants (TCA’s)
- Selective Seratonin Reuptake Inhibitors (SSRI’s)
- Mixed Seratonin-Noradrenaline Reuptake Inhibitors (SNRI’s)
- Anticonvulsants
- N-Methyl-D-Aspartate blockers
- Topical Agents
- MORE ??
Reliability and Net benefit for Treatments of Painful Neuropathies
Methadone: Advantages

- High oral bioavailability
- Rapid onset of analgesic effect
- Long half life, requiring infrequent dosing
- Lack of [known] active metabolites
- Low rate of induction of tolerance
- Low cost
Methadone: Challenges

- Dose-dependent variable conversion rates with other opioids
- Large interindividual variations in pharmacokinetics
- High potential for accumulation, leading to late toxicity
- Potentially toxic interactions with other drugs
- Tightly regulated drug restrictions
Ketamine

• NMDA blocker
• Anaesthetic agent used in subanaesthetic doses
• “Vitamin K” – significant abuse potential
• Oral / Transdermal use?
Incident Pain
Managing Incident Pain

• Identifying / Defining incident pain

• Using medications effectively to treat it
Incident Pain

- Pain related to a particular incident
  - e.g. movement, dressing change

- Incident pain is *usually predictable*, *but* difficult to treat due to the pain’s *strong intensity* and *short duration*. 
Incident Pain - Management

- Sublingual or Intranasal Fentanyl and Sufentanil are short acting, high potency opioids useful for incident pain
- Start low, and increase the dose gradually until the optimum dose is found
- Protocol available at:
  [http://palliative.info/IncidentPain.htm](http://palliative.info/IncidentPain.htm)
## Incident Pain - Management

<table>
<thead>
<tr>
<th></th>
<th>Dose (mcg)</th>
<th>Volume (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>25</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>2</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>20</td>
<td>0.4</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>2</td>
</tr>
</tbody>
</table>
Intranasal administration
Wishing to Die at Home

• Prescription issues
  – Triplicates
  – Availability for refills
  – “Come get it” is not an option

• Preventing / anticipating problems
  – Pain crises
  – Spinal cord compressions
  – Neurotoxicity
  – All are difficult to manage at home, so trying to avoid them works better

• Create a team
Summary

• Anticipate pain in advanced cancer 
  (though it may not always occur)
• Plan ahead to deal with it
• Opioids are a cornerstone of management and 
  are safe when used appropriately
• Be aware of the indicators of pain which may 
  be more difficult to control
• Address neuropathic and incident pain