Opioid Use in the Management of Pain and Breathlessness for the Palliative Care Setting

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DFCM Open April, 1, 2013
PURPOSE

• This set of slides is meant to accompany the one-page document “Pharmacologic Management of Pain, Breathlessness and Nausea in the Palliative Care Setting”

• The focus for this set of slides is on the use of opioids for both pain and breathlessness and intended to provide more detailed information as well as a case example
Objectives

• Review the use of opioids in the management of cancer-related symptoms
  • Pain and Breathlessness
• Describe common opioid side effects and associated prevention/management strategies
• List commonly held beliefs/concerns re: opioids that are myths
Case - Mr. M

- 54 yo male, rectal cancer, metastases to lung
- C/o constant LBP - 8/10, deep, dull, achy in character, no aggrav or allev factors
- 2\textsuperscript{nd} pain, increasing, radiates down left leg, ("more of a shooting feeling"), 10/10 with movement, 0/10 at rest
- Increasingly short of breath with mild activity
- Percocet 1-2 po q4h prn (10/day "when pain is severe"; questionable benefit)
Pain Management

- Approach to the management of cancer-related pain is **VERY different** from the management of chronic pain.
- Patients (and family members) often require a tremendous amount of education (repeated and reinforced) to **undo** the fears HCPs unintentionally perpetuate.
- “I want to save using this until I really need it”
- “I don’t want him to become hooked”
- “I don’t want to become an addict”
Pain Management

• Pain continues to be under-managed in all stages throughout the cancer illness trajectory

• Opioids are the **MOST effective medical intervention** in the management of cancer-related pain, even WITH classic neuropathic descriptors

• Includes post-treatment symptom syndromes
  • 25% of new patient referrals to Odette outpatient Palliative Care Clinic (eg. peripheral neuropathies)
Breathlessness Management

• SOB continues to be under-managed in all stages throughout the cancer illness trajectory
• Opioids are the MOST effective medical intervention in the management of breathlessness, regardless of underlying disease or condition
Breathlessness Management

**Opioids:**

- Strong evidence from multiple studies and meta-analyses confirm the usefulness of oral and/or parenteral opioids to provide significant clinical benefit in the setting of acute, sub-acute and chronic breathlessness
- Incident breathlessness is relieved rapidly with the use of breakthrough opioids
- Nebulized opioids have not shown to be of any greater benefit than systemic opioids
Opioids:

- Respiratory depression is a commonly feared side effect of opioids
- Some studies show ↓ in resp rate with use of opioids in naive patients
- Not found to be clinically significant as neither hypercapnia nor hypo-oxygenation resulted
- **NO** evidence for respiratory depression when using opioids for the relief of breathlessness with appropriate titration to reach the effective dose
Opioid Options?

- Pain and Breathlessness - Two options:
  - Maximize what is being done
  - Do something different

- 10 Percocet's/day - further increase limited by total daily dose of acetaminophen

- Suggest rotating to either a hydromorphone or a morphine based regimen to better manage nociceptive pain and address current inflexibility in breakthrough dosing

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# Opioid EQUIANALGESIC Table

<table>
<thead>
<tr>
<th></th>
<th>Codeine</th>
<th>Morphine</th>
<th>Oxycodone</th>
<th>Hydromorph</th>
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<tbody>
<tr>
<td><strong>PO</strong></td>
<td>100mg</td>
<td>10mg</td>
<td>5mg</td>
<td>2mg</td>
</tr>
<tr>
<td><strong>SC/IV</strong></td>
<td>5mg</td>
<td></td>
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<td>1mg</td>
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</tbody>
</table>

Fentanyl patch 25 micrograms q 72 hrs = 50 mg po morphine q 24 hrs

Methadone = complex conversion, requires license

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1 Percocet (5mg PO oxycodone) =
10mg PO morphine = 2 mg PO hydromorphone
From here, its pure math…

Oxycodone 50mg q24h = Morphine 100mg q24h = Hydromorphone 20mg q24h

MS Contin 45mg BID (30mg + 15mg) OR
Hydromorph Contin 9mg BID (6mg + 3mg)

Morphine 10mg po q1h prn for pain or SOB OR
Hydromorphone 2mg po q1h prn

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The approach to the use of opioids for breathlessness is **NO** different than the approach to the use of opioids for pain.
Neuropathic Pain

• Disordered function of the nervous system anywhere from the periphery to the cerebral cortex; VERY common component of “malignant pain”, poorly managed
• Pain may be described as sharp, burning, “pins and needles”, shooting (or none of the above!)
• 1st and 2nd line Tx: opioids, TCAs, anticonvulsants
• Specifically: gabapentin, pregabalin, nortriptyline
Gabapentin

• Gabapentin titration:
  
  • Day 1 - Initiate 300 mg at HS for 3 days
  • Day 4 - Increase to 300 mg BID for 3 days
  • Day 7 - Increase to 300 mg TID
  • Continue to titrate based on response to a maximum of 3600 mg daily*

*If normal creatinine clearance – dose reduce if not
PREGABALIN

• “Lyrica”
• Developed to maintain biologic activity of gabapentin & improve pharmacokinetic properties
• Initiate 50-75mg BID to a maximum 300mg BID
• Reduce if CrCl<60 mL/min
• Onset of action as early as 1 week
• Similar efficacy observed with BID and TID dosing
• At dose > 75mg BID, more cost effective than gabapentin
• No head to head efficacy data
A Plan FOR MR. M

Choose to begin Hydromorph Contin 9mg BID and Hydromorphone 2mg q1h prn

Phone follow up in 3 days, LBP somewhat improved (using 8 BTs per day), radiating pain remains unchanged

Titrate Hydromorph Contin based on BT use and add neuropathic adjuvant

Encouraged Mr. M to use a BT dose prior to activity to prevent breathlessness

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General Info: Opioid Naive

- **Principles for either pain or breathlessness management**
- Start with small doses
- Morphine 2.5mg s/c or 5.0mg po q1h prn
- Morphine equivalent for HM or oxycodone
- If ≥ 2 doses per day, start low dose of standing and leave BT
• Use IR preparations only
• Use of a breakthrough or rescue dose may indicate either inadequate dosing or incident pain
  □ H10% of the total daily dose
• Frequency (how often made available): oral preparations q1h prn and s/c q30min prn
  (based on time to max serum concentration)
• Use an IR opioid when initiating
• For constant pain, if pt using IR routinely q4h and symptom not controlled, titrate dose qd
• If pt requires IR routinely (i.e. q4h), consider adding up total daily dose and divide into two SR doses q12h
• If symptom not controlled by SR and associated breakthrough doses of IR, may titrate dose q48h
Managing Opioid Side Effects

• Constipation – must prevent for all patients requiring routine opioid; senna 1-4 bid and/or lactulose 15-45ml qd-qid (may add in stool softener but no efficacy if used in isolation)

• Nausea – haloperidol 0.5-1.0mg q4h prn or prochlorperazine 10mg q6h prn

• Sedation – transient at initiation; if persists and pt remains in pain, opioid may not be the cause AND/OR consider addition of neuropathic adjuvant
Managing Opioid Side Effects

• If symptom is refractory, consider opioid rotation or use alternate route of administration (i.e. subcut)
• With signs of toxicity (confusion, agitation, hallucinations, myoclonus, RR decline), change to IR formulation and ↓ standing dose by 50%
• Toxicity uncommon in patients with pain well managed on routine opioids
• Naloxone is rarely required, only if RR significantly declined, VERY uncommon once taking opioids routinely

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Opioid Myths

MYTH 1 - “Aren’t these too strong?”

- Potency (opiate receptor affinity; accounts for “difference” in # of mg)
- Equianalgesic dosing
- Titrate to effectiveness
- “All opioids are in the same category in terms of strength. Its about figuring out which one and what dose works the best for you and your pain.”

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MYTH 2 - Opioids cause addiction

• Physical dependence is an expected result of long-term opioid treatment but SHOULD NOT BE CONFUSED WITH ADDICTION

• Physical dependence = withdrawal syndrome

• Addiction is a chronic neurobiologic disease with genetic, psychosocial and environmental factors

• Helpful to patients to differentiate reason for use i.e. physical pain versus “psychological pain”
Opioid Myths

MYTH 3 - Opioids = Rapid tolerance

- Tolerance = state of adaptation, diminished effect of drug over time
- Clinically significant tolerance is unusual
- In patients with progressive disease, if increased doses of opioids are necessary and unexpected, consider investigating
Resources for Further Info

For cancer-related pain and breathlessness:

https://www.cancercare.on.ca/toolbox/symptools/

For chronic non-malignant pain:

http://nationalpaincentre.mcmaster.ca/opioid/

Canadian Family Physician article on Opioids for Pain and Breathlessness

http://www.cfp.ca/content/56/6/544.full.pdf+html?sid=25a1c936-94f0-4b3e-80b2-f5ed3dc776dd

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