Palliative Care and the Critical Role of the Pharmacist

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Education/ Palliative Care
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Overview

• What is palliative care
• Role of a pharmacist in palliative care
• Issues in palliative care
  – Syringe drivers
  – Ketamine infusion
  – Methadone for pain
• Resources available in palliative care
What is palliative care?

• Term ‘palliative care’ has been used since mid-1970s
• No consensus on the definition used
• To complicate matters further - hospice, end-of-life care and terminal palliative care are used interchangeably
• Terminology review (Pastrana 2008) noted that palliative care definitions may include and/or differ based on:
  – the theoretical principles underpinning care provision
  – the goals of care
  – the target group
  – the structure of care provision
  – the tasks to be undertaken
  – the expertise of the care providers
Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.
WHO definition of Palliative Care

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten or postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death;
- offers a support system to help the family cope during the patient's illness and in their own bereavement;
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;
- will enhance quality of life, and may also positively influence the course of illness;
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.
Statistics

**Figure 1.1: Deaths and proportion of population aged 65 years and over, observed (1986 to 2006) and projected (2016 to 2056)**

*Note: Data for this figure are shown in Appendix Table A1.1. The projected data shown are from “Series B”. Sources: ABS 2008a, 2008b, 2010a, 2010b.*
Why is it important?

• In developed countries there is a high probability that death will occur with warning as a result of chronic disease or malignancy

• Depending on a person’s position on the disease and overarching goals of care, medications are prescribed to:
  – actively treat disease
  – reduce or eliminate symptoms
  – stop or slow a disease process
  – prevent a disease or symptom
Impact on patients

• 4 components of ‘work’ relating to burden of treatment rather than the illness itself
  – Learning about the treatment and their consequences
  – Engaging with others to organise care
  – Adhering to treatments and lifestyle changes
  – Monitoring treatments

• 8 medications on referral to a palliative care unit
Why a pharmacist?

• Symptom management
• Medications, interactions, side effects
• Advice on medications that may no longer be needed
• Informing the family on the use of medications
• Maintaining a reasonable stock of medication for patients
• Following up patients after discharge to carers were able to manage medications at home
• Supporting patients and families
• Providing extra information about medications to GPs
Palliative care pharmacist

- Palliative care emphasises a multidisciplinary approach to improve quality of life and relieve symptoms
- Work closely with other healthcare professionals to detect, prevent and resolve medication-related problems
- Assessments, medication reviews, patient counselling, follow-up, home visits and participate in outpatient clinics
- Expertise in therapeutic use of medication
- Complex medication regimens
- Involved with off-label or off license prescribing
Palliative care pharmacist

• Symptoms
  – Pain, anxiety, constipation delirium, depression
dyspnoea, insomnia, nausea and vomiting
• Pharmacological approach is specific
  – Right choice of drug, dosage, detection of side-
effects, interactions, over or under-utilisation
• Pharmacist recommendations
  – Change dose, change medication, change route,
  change time of administration, initiate new medication
  and stop existing medication
Early Palliative Care

Original Article

Early Palliative Care for Patients with Metastatic Non–Small-Cell Lung Cancer


Editorials

Managing patients with advanced cancer: the benefits of early referral for palliative care

Ian E Haines

Palliative care is becoming fundamental in the starting line-up of care choices

or Australian patients with advanced, incurable illness, particularly cancer, the option of referral to specialist palliative care services can seem to be a random and discretionary default that is sometimes called on when all possibilities for life-saving treatment have been exhausted or cannot easily be accessed. Palliative care services (distinct from palliative chemotherapy) provide a broad range of inputs to patients and their carers and can include specialized medical and nursing manage...
Palliative Care and Chemotherapy

- More and more available each year
- New trials
- Consider interactions
  - Cytochrome P450
  - Potential for prolong QT
  - Electrolyte abnormalities
The ‘Grey’ Area

• The palliative care population are often excluded from clinical trials
• Best available evidence may therefore be principles based application of pharmacology, physiology and understanding the experience of the patient in front of you
• Develop the skills to interpret the grey evidence
1: Continuous subcutaneous infusion (CSCI)
CSCI: Considerations

• Why has it been started?
• Will these volumes fit in the syringe?
• Medications and compatibility (consider diluents)
• What references are available?
• Does the advice change depending on the patient?
CSCI: Indications

- Persistent nausea and vomiting
- Dysphagia
- Intestinal obstruction
- Coma
- Poor absorption of oral medications
- Avoid intermittent bolus injections
CSCI: Volumes

• Dependent on the device used
• Total volume of the medications
• Rate of the delivery
• Greater dilutions reduce:
  – Risk of incompatibility
  – Impact of priming
  – Injection site reactions
• May need shorter infusion times if volumes exceed the maximum 24hr volume (high doses of high volume medications: metoclopramide, morphine and midazolam)
CSCI: Diluent (WFI v 0.9% saline)

0.9% saline
- Adv: isotonic, less infusion site pain/reactions
- Disadv: incompatible with drugs (cyclizine), less data available

WFI
- Adv: more data for common drugs (hydromorphone, ketamine, octreotide)
- Disadv: large volumes is hypotonic therefore possible site reaction
CSCI: Compatibility

- Concentrations, brand, diluent, duration of infusion, temperature, light exposure, order of mixing and device
- Compatibility information might be presented as: physical, observational, laboratory or chemical

- No data? - pH of medications should be considered.
- Similar pH drugs are more likely to be compatible than differing ones (most drugs are acidic)
- But dexamethasone, frusemide, ketorolac and phenobarbital are alkaline
- Adding dexamethasone last reduces the precipitation risk
CSCI: References

- Eastern Metropolitan Region Palliative Care Consortium [www.emrpcc.org.au/resources](http://www.emrpcc.org.au/resources)
- Palliative Drugs [www.palliativedrugs.org](http://www.palliativedrugs.org)
- The Syringe Drive: Continuous Subcutaneous Infusions in Palliative Care (Dickman)
- Handbook on Injectable Drugs (Trissel)
- [www.pallcare.info](http://www.pallcare.info)
Syringe driver survey database search page

Please select the drug combination to search for below, browse the index, submit an entry or go back to SOSD home page

Drug 1
- Alfentanil
- Dexmedetomidine
- Fentanyl
- Hydrocodone
- Hydromorphone
- Methadone
- Morphine hydrochloride
- Morphine sulphate
- Morphine tartrate
- Oxycodone
- Sufentanil
- Baclofen
- Bupivacaine
- Clonazepam
- Chloral hydrate
- Cyclizine lactate
- Dexamethasone (sodium phosphate salt)
- Dexamethasone (phosphate salt)
- Diclofenac sodium
- Flunitrazepam
- Glycopyrronium (glycopyrrolate)
- Grapeseed
- Haloperidol
- Hydrocortisone
- Hyoscine butylbromide
- Hyoscine hybride bromide (scopolamine bromide)
- Ketamine
- Ketorolac tromethamine
- Levobupivacaine

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CSCI: The patient

- Disease trajectory
- Discharging home
2: Ketamine infusion

• Mechanisms include:
  – Interrupts N-methyl-d-aspartate (NMDA) receptor blockade
  – Interrupts cholinergic transmission
  – Inhibits the reuptake of noradrenaline and 5-hydroxytryptamine

• Suggested benefits:
  – Decrease of central sensitisation
  – Reduction of hyperalgesia
  – Reverse of opioid tolerance

• Evidence to support the use of ketamine in chronic cancer pain has been extrapolated from other settings and uncontrolled studies

• All studies reported adverse-effects
Controversial ‘Pulse’ Ketamine Infusion


• Day 1: 100mg ketamine CSCI
• Day 2: 300mg ketamine CSCI
• Day 3-7: 500mg ketamine CSCI


• Same as protocol as above
• Multi site, double blinded, randomized control, placebo control study
Would you recommend it?

CANCER PAIN & PALLIATIVE CARE SECTION

Review Article
Ketamine for Pain in Adults and Children with Cancer: A Systematic Review and Synthesis of the Literature

Amy Lee Bredlau, MD,* Rajbala Thakur, MD,† David Nathan Korones, MD,‡ and Robert H. Dworkin, PhD§

*Departments of Pediatrics and Neurosciences,
3: Methadone for pain

- Wide interindividual variation / variable plasma half-life
- Mixed opioid properties: mu, NMDA, pre-synaptic block of serotonin re-uptake
- QT prolongation / fatal cardiac arrhythmias
- Social stigma associated with methadone
- Metabolised by several cytochrome P450 iso-enzymes (CYP3A4, CYP 2B6, CYP2D6, CYP2C9, CYP2C19 & CYP 1A2)
- Rotation to methadone is reserved for patients who fail to respond to other opioids
- Several methods exist but none are superior
Why is there a concern?

Table I. Summary of Published Morphine-to-Methadone Conversion Ratios

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<th>Bruera 1996&lt;sup&gt;16&lt;/sup&gt;</th>
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<th>Ripamonti 1998&lt;sup&gt;15&lt;/sup&gt;</th>
<th>Hagen 1999&lt;sup&gt;29&lt;/sup&gt;</th>
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<td>10:1 for M &lt; 1000 mg/d</td>
<td>5.42:1 for M &lt; 1165 mg/d</td>
<td>4:1 for M between 30 and 90 mg/d</td>
<td>4.6:1 for M ≤ 300 mg/d</td>
<td>3:1 for M &lt; 100 mg/d</td>
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<td>15:1 for M &gt; 1000 mg/d</td>
<td>16.84:1 for M &gt; 16.84 mg/d</td>
<td>6:1 for M between 90 and 300 mg/d</td>
<td>12.7:1 for M &gt; 300 mg/d</td>
<td>5:1 for M between 101 and 300 mg/d</td>
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<td>ratios</td>
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Abbreviations: M, morphine.
Switching to methadone – Option 1

‘Stop and Go’ approach

• PO morphine to PO methadone
• Give methadone loading dose which is 1/10 of the 24hr PO morphine dose (max 30mg methadone)
• Give methadone 3hrly prn which is 1/30 of the 24hr PO morphine dose (max 30mg methadone)

Examples:
Morphine 300mg/24hr PO = loading dose of methadone 30mg PO and 10mg 3hrly prn

Morphine 1200mg/24hr PO = loading dose of methadone 120mg PO and 40mg 3hrly prn. These are both capped at 30mg
Option 1

• On day 6: amount of methadone used over the last two days is noted and divided by 4 to give a 12hrly daily dose with 1/6-1/10 of the 24hr dose available as prn

Example:
Methadone 80mg used in previous 48hrs = 20mg twice a day with 5mg 3hrly prn

• If needing prn more frequently than 3hrly then an alternative opioid should be available
Switching to methadone – Option 2

Edmonton model for switching from (slow transition)

• Day 1: Decrease morphine dose by 30% and replace with methadone PO 8hrly using 10:1 ratio
• Day 2: If pain controlled, decrease the original dose of morphine by another 30%. Only increase methadone if pain not controlled
• Day 3: Discontinue the last 40% of morphine and continue 8hrly methadone plus 10% of daily methadone dose as a prn
• Treat transient pain with rescue doses of short acting opioids.
Addition of Methadone to Another Opioid in the Management of Moderate to Severe Cancer Pain: A Case Series

Elaine Wallace, MD\textsuperscript{1} Julia Ridley, MD\textsuperscript{1,2} John Bryson, MD\textsuperscript{1,3} Ernie Mak, MD\textsuperscript{1,2} and Camilla Zimmermann, MD, PhD\textsuperscript{1,4}

Abstract

\textit{Background}: Previous research has reported improved pain after adding methadone to another opioid, but did not quantify this benefit using a validated outcome measure.

\textit{Objective}: To assess quantitatively the effectiveness of adding methadone to another opioid for moderate to severe cancer pain.
To conclude

• The principle and practice of palliative care has changed and therefore the role of the palliative care pharmacist is evolving
• Symptoms are becoming more complex but the evidence / information is still limited
• We have the PK/PD knowledge and therefore ideally located to help review (or extrapolate) data regarding medications
• We should be adding to the evidence
Useful Palliative Care Resources

- Palliative Drugs [www.palliativedrugs.org](http://www.palliativedrugs.org)
- Eastern Metropolitan Region Palliative Care Consortium [www.emrpcc.org.au/resources](http://www.emrpcc.org.au/resources)
- The pharmacy Guild of Australia – initiated steps to enhance the role of community pharmacist in palliative care
References


