

Palliative Care Pain Management

Practice Guidelines

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PALLIATIVE CARE PAIN MANAGEMENT

Statement of Intent

The NRAHS Palliative Care Pain Management Guidelines are the overarching guidelines for clinical practice in palliative care pain management within NRAHS.

Endorsement

The NRAHS Palliative Care Pain Management Guidelines were developed with substantial input from clinicians. The process of approval outlined by the NRAHS Clinical Standards Committee was adhered to and the following Northern Rivers Area Health Service Staff signed the final original copy:

Area Medical Director Palliative Care

Area Director of Nursing and Quality

Area Director of Medical Services

Area Chief Pharmacist

Alles 17/11/14 15 Nov 04.

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1. PAIN MANAGEMENT

1.1 PRINCIPLES:

- 1. Patients have a right to competent pain assessment and management.
- 2. Pain is often under-treated.
- 3. Pain relief in palliative care cannot be considered in isolation and must be part of a multidisciplinary approach which encompasses physical, psychosocial, and spiritual aspects of pain and suffering. All of these elements of "**total pain**" must be considered in pain that is difficult to control. The patient, families and care providers need to collaborate to achieve best result.
- 4. Pain is better controlled when patients, families and care providers understand that respiratory depression, addiction and the development of tolerance are not problems with the correct use of opioids.

5. The development of persistent side effects of opioid medication including respiratory depression, confusion and sedation are avoidable and require specialist palliative care advice.

- 6. Satisfactory pain control is achievable in most palliative care patients but 10-20% of patients with difficult pain will need early specialist referral, including those with
 - Neuropathic pain
 - Incident pain
 - Multiple pains
 - Opioid resistant pain
 - Intolerable side effects to analgesics.
 - "Total Body Pain" (i.e. severe pain that is physically and emotionally overwhelming)
 - A morbid fear of analgesics
 - Requests for euthanasia because of pain
- 7. The basic principles of palliative care pain management include:
 - **Believe** the patient
 - Help the patient take responsibility for their own pain management as much as possible
 - Make an accurate diagnosis of the causes of pain and plan management accordingly
 - Prevent pain where possible by ordering regular and prn medications
 - Start with simple oral analgesics
 - Re-evaluate regularly since the patients needs change as the illness progresses
 - Anticipate side effects and always prescribe regular aperients and prn anti-emetics.
- 8. The aim of Palliative Care pain management is to achieve a satisfactory level of comfort for the patient. This may not mean complete pain relief.

Reference: "Therapeutic Guidelines Palliative Care", 2001, pg 117, Therapeutic Guidelines Ltd.

2. PAIN ASSESSMENT

2.1 GUIDELINES:

- 1. Pain assessment should attempt to determine the mechanism producing the pain and factors influencing the pain experience including psychosocial factors.
- 2. There is usually more than one pain to be evaluated.
- 3. Patients may not report pain openly. Reasons include:
 - To avoid being hospitalised
 - To avoid starting morphine
 - To avoid acknowledging the disease may be worsening
 - Concerns about increasing medication for the mistaken fear of addiction and tolerance
 - The misconception that pain is inevitable with cancer
 - Patients may not relate to the word "pain", but may relate to words such as "discomfort" or "ache".
- 4. Reasonable pain control is achievable in most palliative care patients but 10-20% of patients with difficult pain will need early specialist referral, including those with
 - Neuropathic pain
 - Incident pain
 - Multiple pains
 - Opioid resistant pain
 - Intolerable side effects to analgesics.
 - "Total Body Pain" i.e. severe pain that is physically and emotionally overwhelming)
 - A morbid fear of analgesics
 - Requests for euthanasia because of pain

2.2 PROCEDURE:

1. Take a history

- i) Begin with "*Tell me about your pain*".
- ii) <u>Location</u>
 - A body chart will assist with localising the pain and will help patient's selfassessment. Location will help diagnose the cause of the pain. (See Appendix 15.2 Patient Self Assessment Pain Chart)
- iii) Exacerbating / Relieving Factors
 - What makes the pain worse or better?
- iv) <u>Analgesics</u>
 - What analgesics make the pain worse or better? What are the previous drugs, doses and side effects of those medications?
- v) Pain Character
 - What is the pain like? Eg. sharp, shooting, electric shock, burning (neuropathic pain).
 - If the patient has difficulty describing pain ask, "What would I have to do to myself to experience the pain you are feeling?"

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- vi) <u>Radiation</u>
 - Referred pain radiates, e.g. liver pain to the right shoulder blade. Neuropathic pain radiates, e.g. lumbar spine to the leg.
- vii) <u>Severity</u>
 - The pain score is the patients <u>self-report</u> of the pain experience and not an objective assessment.
 - Pain severity is usually measured using a
 - numerical scale.
 - 0 (no pain) \Rightarrow 10 (worst pain imaginable)
 - or a verbal descriptor scale eg
 - mild \Rightarrow moderate \Rightarrow severe
 - > Children may prefer a face scale.



- Be clear in what you are asking. Are you measuring?
 - \succ The pain right now?
 - > The worst pain in the last 24 hours?
 - > The average pain in the last 24 hours?
- Assessment, regular re-assessment and documentation of the patients pain score is essential.
- The patient should never be woken to have their pain assessed.
- Patients' pain should be assessed during movement and activity as well as at rest
- Assess and document effects of all interventions for pain control.
- viii) Function
 - How does the pain interfere with the patients life, e.g. mobility, activity, work, etc?
- ix) <u>Understanding</u>
 - What is the patients understanding of their pain?
- x) <u>Total Pain</u>
 - Pain is not a sensation but an **experience** that affects our whole being.
 - How we feel, our beliefs, culture and attitudes can profoundly affect our pain perception both positively and negatively. This is the concept of "Total Pain".
 - Therefore, explore psychosocial / spiritual issues particularly with chronic or severe pain, or pain that is not responding to treatment.
 - Pay particular attention to **sleep** disturbances, **anxiety** and **depression** (SAD), which may respond to support but may need pharmacological intervention.
- xi) <u>Collaborate.</u>
 - Patients may not be able to report their pain accurately, therefore it is always worth getting the opinion of someone who knows the patient well, e.g. the carer, GP community nurse, volunteer etc.

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2. Perform a Physical Examination

A physical examination will help to diagnose the cause of pain but must also include:

- Assessment of mobility
- Pain behaviour (wincing, grimacing, etc)
- Observation of non-verbal cues
- Assessment of side effects including nausea, constipation and drowsiness.
- Assessment of opioid toxicity including confusion, delirium, myoclonus or change in respiratory function.

3. Investigations

Restrict investigations to those that will influence the management decisions.

4. Re-evaluate

Re-assess regularly as the patients condition can change rapidly and warrant a change in management.

Reference: "Therapeutic Guidelines Palliative Care", 2001, pg 117, Therapeutic Guidelines Ltd.

3. ANALGESIC PRINCIPLES

This is a 4-step approach to the use of analgesics in the Palliative Care setting.

3.1. GUIDELINES:

Step 1 Reduce the noxious stimulus

- Take a history and focused physical examination with the aim of identifying the noxious stimulus that is causing the pain.
- Investigations may or may not be appropriate according to the patient's performance. Pain in cancer patients can be due to disease, side effects of treatment, debility or unrelated to cancer.
- Give regular paracetamol.
- If there is potentially an inflammatory process, consider non-steroidal antiinflammatory drugs, Cox 2 inhibitors, and or steroids if the risk of potential benefits outweigh the potential side effects (See NSAIDs 13.7).

Step 2 Raise the pain threshold

- Do a psychosocial assessment to try and identify pain "threshold" issues that are exacerbating pain.
- Most commonly consider S A D, (sleep, anxiety and depression). The patient will likely need psychosocial and spiritual support but pharmacological intervention must also be considered in the distressed patient.

Step 3 Consider opioids

- Consider early use of opioids , particularly for moderate or severe pain.
- Use them according to standard principles (see 4. Opioid Prescribing)

Step 4 Consider adjuvant analgesics

- In pain management it is standard practice to use adjuvant analgesic drugs for components of pain that are not completely opioid responsive, eg neuropathic pain and bone pain (see relevant guidelines). Due caution must be given to polypharmacy, drug interactions and side effects.
- Common adjuvant analgesics include steroids, anticonvulsants, antidepressants and NMDA antagonists (see relevant guidelines).

Reference: Lickiss, 2001, "Approaching Cancer Pain Relief", European Journal Of Pain, Vol 15, Supplement A, pg 5-14

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4. OPIOID PRESCRIBING

4.1 GUIDELINES:

(See also sections; 1.Palliative Care Pain Management Principles, 2.Pain Assessment and 3.Analgesic Principles before commencing patient on opioids.)

- 1. When opioids are indicated, morphine remains the drug of choice because of flexibility of dosage and routes available for its administration.
- 2. **Pethidine is NOT recommended** for palliative care patients or chronic use. Pethidine must be given 2-3 hourly for effective pain relief. Doses approaching 1gm per day may produce convulsions.
- 3. Pain is better controlled when patients, families and care providers understand that respiratory depression, addiction and the development of tolerance are not problems with the correct use of opioids. It is important to dispel myths, e.g. the use of subcutaneous syringe drivers means death is imminent and that the use of opioids shortens life.
- 4. Opioids must be used cautiously in impaired renal function (See section 7.1). Consult with Palliative Care Service for advice.
- 5. Side effects will occur and need to be managed (See section 7.1)
 - **Constipation** will occur and always requires regular aperients eg. Movicol 1-3 /day or Senna & Docusate 2 bd and titrate accordingly.
 - **Nausea** is minimised by starting with low dosage and increasing the dose according to pain response. It generally improves after 2-3 days. prn anti-emetics (metoclopramide 10mg) may help.
 - **Sedation** may occur but is minimised by starting with low dosage and increasing the dose according to pain response. It generally improves after 2-3 days.
- 6. Opioid Toxicity should be avoided where possible: (See section 7.1)
 - **Respiratory depression** is assessed with respiratory rate and pulse oximetry, and occasionally spirometry. It is a feature of opioid toxicity and necessitates a reduction or change in opioids. Consult with Palliative Care Service for advice.
 - **Visual hallucinations** are a feature of opioid toxicity and necessitate a reduction in or change in opioids. Consult with Palliative Care Service for advice.
 - **Myoclonus** is a feature of opioid toxicity and necessitates a reduction in opioids where possible. Consult with Palliative Care Service for advice.
- 7. Opioids are not effective sedatives and will cause confusion, agitation and distress if given as sedatives especially in the terminal phase. If sedation is necessary, a benzodiazepine or psychotropic drug should be considered. Consult with the Palliative Care Service.

8. Opioid Fomulations

Normal Release:

(Onset of analgesia approximately 20 minutes, Duration of analgesia approximately 4 hours)

- Oral Morphine (Ordine, Sevredol) Oxycodone (Endone, Oxynorm) Hydromorphone (Dilaudid), Codeine
- Subcutaneous Morphine, Hydromorphone

NB Subcutaneous : Oral Morphine Ratio is 1 : 2, i.e. 5mg SC = 10mg oral morphine

Controlled Release:

MS Contin, Oxycontin, Kapanol, Durogesic

9. Breakthrough Medication

- A breakthrough is a dose of normal release opioid given in between regular doses of opioids.
- It is given at any time if pain occurs and must never be substituted for the regular dose, eg if a breakthrough is given at 5.40pm and the regular dose is due at 6pm, the 6pm dose is still given.
- The breakthrough dose is 1/6 of the 24 hour dose. This is because normal release morphine lasts 4 hours and there are 6 lots of 4 hours in a 24 hour period.

i.e. if a patient is on 30 mg MSContin bd, Total 24 hour Oral Morphine Dose = 60mg

1/6 of 60mg = 10mg

Therefore the breakthrough dose is 10mg orally or 5mg subcutaneously

- 10. The optimal timing for normal release morphine is every 4 hours i.e. an adequate analgesic dose for a patient should last 4 hours. If morphine needs to be given more frequently e.g. every second hour, the patient is being underdosed and is more likely to experience pain.
- 11. The most effective method for achieving pain control with morphine is to start on an appropriate regular 4 hourly dose and adjust the dose over 24 48 hours until pain is controlled. This usually involves giving a number of breakthrough doses. The total 24 hour dose is then converted to an equivalent sustained release preparation. For best practice, use the Palliative Care Morphine Variable Dose Chart to titrate morphine.(See 5 Morphine Variable Dose Chart).
- 12. For patients already on opioids, it may be appropriate to increase the dose of controlled release morphine (taking into account breakthrough doses) rather than titrate on 4 hourly morphine. This is NOT appropriate for acute pain management; titration using 4 hourly morphine and breakthroughs is required.

Eg a patient on MSContin 30mg bd is taking 6 breakthrough doses of 10mg morphine.

MSContin: $2 \times 30 \text{ mg} = 60 \text{mg}$ Breakthrough Doses $6 \times 10 \text{mg} = 60 \text{mg}$

120mg (Total 24 hour Oral Morphine Requirements)

Therefore the new dose is : MSContin 60mg bd ($2 \times 60mg = 120mg$) New breakthrough dose is 1/6 of 120mg = 20mg orally or 10mg Subcutaneously

The controlled release dose should be increased if

- The patient's pain consistently returns before the next regular dose is due
- The patient's pain score remains high
- 3 or more breakthroughs are required in 24 hours

The controlled release dose should be decreased if

- The patient is pain free but drowsy.
- The above sequence in reverse order would be appropriate.

References:

- "Therapeutic Guidelines Palliative Care", 2001, pg 130-134, Therapeutic Guidelines Ltd.
- BMJ 1996; 312: 823-826. "Morphine in Cancer Pain, Modes of Administration".
- Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version, www.palliativedrugs.com
- Back Ian, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, www.pallmed.net

5. MORPHINE VARIABLE DOSE CHART

5.1 <u>GUIDELINES</u>

- 1. The morphine variable dose chart has been developed to facilitate safe morphine administration and improved pain control for palliative care patients.
- 2. The most effective method for achieving pain control with morphine is to start on regular 4 hourly normal release morphine and adjust the dose over 24-48 hours until the pain is controlled. This is applicable to opioid naïve patients and those patients on opioids who are experiencing severe pain problems.
- 3. The chart is written so that the ward nurse can assess the patient at least 4 hourly and titrate the morphine dose (up or down) without the need for the doctor to change the prescribed order.
- 4. Once the prescribed maximum dose is reached the patient must be reassessed by the doctor and a new chart written.
- 5. When the pain is controlled, the morphine is converted to a sustained release opioid for maintenance (See 6. Opioid Conversion Tables).

5.2 PROCEDURE

- 1. Assess the patients understanding of opioids and reassure about safety, efficacy and how you will manage side effects, particularly constipation and sedation.
- 2. **Regular aperients must be prescribed** e.g. Macrogol (Movicol) 1 3 sachets /day or Docusate plus Senna 2 bd and titrated accordingly.
- 3. <u>Choose the route</u>
 - The optimal route of administration of morphine is by mouth. If the oral route is not available, e.g. with severe nausea, vomiting, constipation or the patient is unable to tolerate oral medications, then the subcutaneous route is used. The subcutaneous dose is half the oral dose, e.g. 10mg oral morphine = 5mg s/c morphine.
 - The intramuscular route is not used because it is painful and the IV route is inconvenient and has no advantages over the subcutaneous route.
- 4. Choose the dose
 - There is no standard dose of morphine. The dose may range from 2.5mg 4 hourly to more than 200mg 4 hourly. However, the majority of patients will not need more than 30mg 4 hourly.
 - If patients are needing doses >100mg 4 hourly, referral to Palliative Care Service is required. Dose conversions for higher doses will become progressively more erroneous and need specialist supervision.
 - If the patient is not on an opioid then 5-10mg orally is a reasonable starting dose.
 - If the patient is elderly or frail, 2.5mg is a reasonable starting dose.
 - If the patient is already on an opioid, use the opioid conversion table to calculate the appropriate 4 hourly dose.
 - The dose is adjusted (up or down) according to analgesic response. The adjusted dose is usually 25 –50% of the original dose ie 10mg can be increased by 2.5 5mg to 12.5 15 mg
 - The recommended sequence of doses is:

 $2.5\text{mg} \rightarrow 5 \rightarrow 7.5 \rightarrow 10 \rightarrow 15 \rightarrow 20 \rightarrow 30 \rightarrow 40 \rightarrow 60 \rightarrow 80 \rightarrow 100 \rightarrow 130 \rightarrow 150 \rightarrow 200\text{mg}.$

The dose should be increased if

- The patient's pain consistently returns before the next regular dose is due
- The patient's pain score remains high
- 3 or more breakthroughs are required in 24 hours

The dose should be decreased if

- The patient is pain free but drowsy.
- The above sequence in reverse order would be appropriate.
- A rapid reduction in opioids (eg halving the total dose) may result in opioid withdrawal.

5. Breakthrough dose

- A breakthrough dose is given at any time if pain occurs.
- The breakthrough dose is the same as the 4 hourly dose and must never be substituted for the regular dose, eg if a breakthrough is given at 5.40pm and the regular dose is due at 6pm, the 6pm dose is still given.

6. Maximum dose

- This is the maximum regular 4 hourly dose that the nurse can give.
- A recommended maximum dose is appropriately 3x the starting dose
- If the patient is in pain and requires a larger dose, the doctor must review the patient and write a new morphine variable dose chart.
- 7. Anti-emetics
 - Prescribe anti-emetics as a PRN order, e.g. Metoclopramide 10mg qds or Haloperidol 0.5mg (maximum 5mg per day).
- 8. Frequency of Assessment
 - Assessments must be documented
 - Patients on the Palliative Care Morphine Management chart need to be assessed at least every 4 hours during the day.
 - Patients with a pain score of 8–10 must be assessed every 20 minutes and analgesia given until their pain reduces to a more acceptable level.
 - Do not wake patients to assess pain.
 - Patients on slow-release opioids or who have stable pain must be assessed at least once per nursing shift and pain score documented.
- 9. Conversion to Slow Release Opioids
 - Once the pain is stable, the 4 hourly morphine is converted to a sustained release opioid for maintenance.
 - See 6. Opioid Conversion Tables for equivalent doses.

6. OPIOID CONVERSION TABLES

APPROXIMATE EQUIVALENT ORAL DOSES 10mg oral morphine = 2mg Hydromorphone

ng oral morphine =	2mg Hydromorphone
	6mg Oxycodone
	40mg Tramadol
	80mg Pethidine
	80mg Codeine
	140mg Dextropropoxyphene

N.B. 1 Panadeine Forte = 4mg oral morphine (Approximately)

SUSTAINED RELEASE PREPARATIONS

Opioid	Trade Name	Unit Doses (mg)	Frequency
MORPHINE	MS Contin	5, 10, 15, 30, 60, 100, 200	12 hrly
	MS Contin Suspension	20, 30, 60, 100, 200	12 hrly
	Kapanol	10, 20, 50, 100	12 hrly or 24 hrly
	MS Mono	30, 60, 90, 120	24 hrly
OXYCODONE	Oxycontin	5, 10, 20, 40, 80	12 hrly
		25mcg/hr, 50mcg/hr,	
FENTANYL	Durogesic	75mcg/hr, 100mcg/hr	Every 72 hrs

SLOW RELEASE EQUIVALENT

4 hourly dose of Morphine		12hrly Morphine MS Contin or Kapanol	24hrly Morphine MS Mono or Kapanol	12hrly Oxycodone (OxyContin)	Fentanyl (mcg/hr)
S/C	ORAL				
2.5	5mg	15	30	10	Not recommended
5	10	30	60	20	25
7.5	15	45	90	30	25
10	20	60	120	40	25
15	30	90	180	60	50
20	40	120	240	80	75
25	50	150	300	100	75
30	60	180	360	120	100
40	80	240	480	160	125
50	100	300	600	200	175

EXAMPLE If the patients pain is controlled on 20mg oral morphine every 4 hours, convert to

- MS Contin 60mgbd
- Kapanol 60mg bd
- MS Mono 120mg daily
- OxyContin 40mg bd
- Fentanyl Patch 25mcg/hr / 72 hours

FENTANYL PATCH CONVERSION

4 hourly dose Oral Morphine	24hr Oral Mor	phine	Fentanyl Patch mcg/hr
10 – 20mg	60 – 134	\rightarrow	25
25 – 35mg	135 – 224	\rightarrow	50
40 – 50mg	225 – 314	\rightarrow	75
55 – 65mg	315 – 404	\rightarrow	100
70 – 80mg	405 – 494	\rightarrow	125
85 – 95mg	495 – 584	\rightarrow	150

Reference Palliative Care Formulary 2nd Edition 2002, Radcliffe Press

7. MANAGING OPIOID SIDE EFFECTS

7.1. <u>GUIDELINES</u>

- 1. Opioid induced side effects can be minimized by titrating morphine on the lowest appropriate dose and increasing slowly to maximise analgesia and minimise side effects.
- 2. Patients experiencing intolerable side effects with one opioid, may benefit from switching to another eg from morphine to oxycodone, or from changing route, eg from oral to subcutaneous.
- 3. Patients who develop opioid toxicity without a change in medication dose, may be developing **renal failure.** Reduce the dose and frequency of opioid. Consider rehydration if appropriate. Consider changing opioid to fentanyl or methadone which are safer in renal failure. Referral to Palliative Care Service is recommended.
- 4. Consultation with the Palliative Care Service is recommended for persistent intolerable side effects.

7.2. SPECIFIC SIDE EFFECTS

1. Constipation

- Constipation will always occur and requires regular aperients
 - Movicol 1- 3 per day
 - OR
 - > Senna & Docusate 2 bd and titrate accordingly
- (See Constipation Guidelines)

2. Nausea

- Nausea may be an issue initially but usually settles after several days.
 - Use prn anti-emetics (subcutaneously if severe)
 - Metoclopramide 10mg qds
 OR
 - Haloperidol 0.5 5mg nocte

3. Sedation

- Sedation may occur but is minimised by starting with low dosage and increasing the dose according to pain response.
- Sedation usually abates after a few days.
- If the patient is pain free and drowsy, reduce the opioid dose.

7.3. OPIOID TOXICITY

- 1. Visual hallucinations and delirium are features of opioid toxicity and necessitate a reduction in opioids.
 - Prescribe Haloperidol 0.5mg subcutaneously every 30 minutes until patient settles.
 - (See Delirium Guidelines)
- 2. Myoclonus is a feature of opioid toxicity and necessitates a reduction in opioids.
 - Myoclonus is less of a feature with Fentanyl.
 - Clonazepam 0.5-2mg bd (Beware Clonazepam is a long acting drug and may cause prolonged sedation and confusion in the frail and elderly).

- 3. **Respiratory depression** is assessed with reduced respiratory rate, pulse oximetry, and occasionally spirometry. It is a feature of opioid toxicity and is usually accompanied by sedation.
 - Stopping the opioid immediately, giving oxygen and waiting for the respiratory depressant effects to wear off is usually adequate. The patient usually rouses to verbal stimulation.
 - In rare circumstances, if the patient is thought to be severely compromised after opioids eg unrousable, respiration rate < 8/min and cyanosed, then the Naloxone Administration guidelines should be considered.
 - However, for palliative care patients, over dosing with naloxone may give total opioid antagonism and the patient will wake up in agony and have acute opioid withdrawal.
 - Therefore naloxone must be titrated cautiously and where possible with advice from the palliative care service.

NB Respiratory depression secondary to opioids is generally an acute event and should not be confused with Cheyne-Stoke breathing in the dying process.

References:

- 1. "Therapeutic Guidelines Palliative Care", 2001, Therapeutic Guidelines Ltd.
- 2. Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version, <u>www.palliativedrugs.com</u>
- 3. Back Ian, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, www.pallmed.net

8. MORPHINE RESISTANT PAIN

8.1 GUIDELINES

- Some pains are resistant to morphine, which may result in a patient with severe pain as well as opioid toxicity.
- For pain that appears resistant to morphine, see section 3. Analgesic Principless i.e.
 - 1. Reduce the noxious stimulus
 - 2. Raise the pain threshold (Consider sleep disturbance, anxiety, depression)
 - 3. Use opioids appropriately
 - 4. Use adjuvants if indicated
- Use an alternative opioid or alternative route of administration (eg change oral to subcutaneous).
- Consider neuropathic pain and bone pain (See Relevant Guidelines)
- When patients are on high doses of morphine ie greater than 500mg morphine per day, their pain may become worse with continued use of morphine. This may be due to high concentrations of morphine's main metabolite M3G, which is said to neutralise the analgesic affect of morphine by a non-opioidergic neuro-excitatory mechanism. Therefore when converting at high dose levels it is necessary to refer to the Palliative Care Service for specialist advice.
- Early consultation with the palliative care service is recommended.

References:

- 1. "Therapeutic Guidelines Palliative Care", 2001, Therapeutic Guidelines Ltd.
- 2. Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version,
- www.palliativedrugs.com
 Back Ian, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, www.pallmed.net

9. MORPHINE MISCONCEPTIONS

9.1. GUIDELINES

Patients and carers may have misconceptions about opioids, which they will need reassurance about:

• Addiction

Psychological addiction and drug seeking behaviour are rare. Physiological dependence after long-term use however is likely to develop i.e. suddenly stopping opioids will cause a "withdrawal" phenomenon. This is true of many drug classes, not just opioids.

• Tolerance

"If I take it now, what will I take when I really need it?"

Tolerance may occur in the long term, but can be managed by switching to an alternative opioid (eg from morphine to oxycodone), or simply increasing the amount of opioid

• Impending Death

"Morphine will hasten my death".

There is no evidence that the correct use of opioids hastens death. In fact, adequate pain relief not only improves quality of life but also contributes to lengthening life.

References:

1. "Therapeutic Guidelines Palliative Care", 2001, Therapeutic Guidelines Ltd.

- 2. Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version, <u>www.palliativedrugs.com</u>
- 3. Back Ian, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, www.pallmed.net

10. NEUROPATHIC PAIN

10.1 GUIDELINES

- 1. Neuropathic pain is due to nerve damage either centrally or peripherally.
- 2. If associated with cancer it usually involves an inflammatory process therefore an opioid and NSAID should be trialled first before adding an adjuvant analgesic.
- 3. A third of neuropathic pains are opioid sensitive, a third partially sensitive, and a third not sensitive.
- 4. Adjuvant agents (e.g. tricyclic anti-depressants) should be introduced at the lowest dose and titrated up to clinical response.
- 5. As more than one agent may be needed a methodical approach is required paying particular attention to side effects and drug interactions.
- 6. Early referral to palliative care service is recommended to prevent the development of chronic neuropathic pain.

10.2 PROCEDURE

1. Patient Assessment (See 2 Pain Assessment Guidelines).

a. <u>History</u>:

- Pay particular attention to features of neuropathic pain, e.g.
- Burning pain
- Stabbing pain
- Spontaneous pain
- Shooting pain "like an electric shock"
- Ache "like a toothache"
- Pins and needles, unpleasant sensations or tingling
- Phantom pain

b. Examination:

Perform a full neurological examination with attention to

- pain in an area of numbness
- allodynia (pain from a non-painful stimulus) e.g. gently stroking the skin reproduces pain.

c. Investigations:

• May or may not be appropriate according to the patients condition.

2. Analgesic Approach

- a. Consider radiotherapy for cancer related neuropathic pain
- b. Prescribe paracetamol 1g qds
- c. Titrate opioids (See 4 Opioid Prescribing Guidelines)
- d. Consider using TENS
- e. If pain not controlled, add either
 - Diclofenac 25 50mg tds OR
 - Dexamethasone 8mg mane
 OR
 - Celecoxib 100-200 mg bd

- The choice depends on the pharmacodynamic risks for the patient (See 13.7 NSAIDs and Steroids)
- > Use Dexamethasone if nerve compression suspected
- Trial for 3 5 days.
- f. If pain not controlled, consider
 - Amitriptyline 10 25mg nocte OR
 - Nortriptyline 10mg nocte
 - > Adverse effects of Tricyclic antidepressants:
 - Sedation
 - Postural hypotension
 - Anticholinergic side effects
 - Aggravation of pre-existing heart block.
 - NB Nortriptyline has fewer anticholinergic side effects than amitriptyline and is twice as potent
 - Trial for 3 5 days
- g. If pain is not controlled, consider adding an anticonvulsant eg
 - Carbamazepine 100mg bd
 OR
 - Sodium Valproate 200-600mg bd
 - ٠
- h. If pain is not controlled, consult with the palliative care service for consideration of
 - Gabapentin 300mg nocte. Maximum dose 2400mg in 4 divided doses. (Reduce dose in renal impairment.)
 - Ketamine infusion
 - Lignocaine infusion
 - Nerve blocks
 - Intrathecal / Epidural anaesthesia
 - Neurosurgery

3 Re-evaluate

• Re-evaluate as the pain may change over time depending on treatment or disease progression. Management will need to be changed accordingly.

References:

- 1. "Therapeutic Guidelines Palliative Care", 2001, pg 139, Therapeutic Guidelines Ltd.
- 2. Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version, www.palliativedrugs.com
- 3. Back Ian, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, www.pallmed.net

11. MALIGNANT BONE PAIN

11.1 GUIDELINES:

- 1. The most common cancers associated with bony metastases are breast, prostate and lung.
- 2. The bones most commonly involved are those of the spine, pelvis, ribs and femur.
- 3. Bony metastases produce:
 - Pain (> 70%)
 - Poor mobility
 - Fractures (< 10%)
 - Nerve root compression
 - Spinal cord compression (medical emergency)
 - Bone marrow failure due to massive infiltration (rare in solid tumours)
- 4. The pathophysiology of bone pain is not fully understood. It can be related to involvement of the periosteum and may also be related to inflammatory processes.
- 5. **Radiotherapy** is the gold standard for treatment of bone pain secondary to metastases and will produce clinical improvement in approximately 80% of patients whether a radiosensitive tumour or not (e.g. melanoma). Improvement usually occurs within two weeks and can last several months.

6. Bone pain is usually opioid responsive (contrary to common belief).

- 7. There is no definitive evidence that NSAIDs are better than opioids for bone pain. When prescribing NSAID's, the drugs with the lowest gastrointestinal toxicity are
 - COX-2 Inhibitors e.g. celecoxib
 - Ibuprofen,
 - Diclofenac
 - Naproxen.

NSAIDs with higher gastrointestinal toxicity include

- Piroxicam,
- Indomethacin,
- Ketorolac.

(See 13.7 NSAIDs)

11.2 PROCEDURE

- 1. <u>Patient Assessment</u> (See 2.Pain Assessment Guidelines)
 - a. History
 - Pain is usually a dull ache, which is well localised and increases with moving, standing and walking.
 - There may be other features depending on the nature of the metastases, e.g. neuropathic pain, spinal cord compression (**medical emergency**), incident pain or muscle spasm (See relevant Guidelines).
 - If there is a fracture, pain will be of sudden onset and may not be associated with trauma.
 - b. Examination:
 - There is usually local tenderness as well as incident pain.

- c. Investigations:
 - Restrict investigations to those that will influence management decisions.
 - <u>X-rays</u> are very useful. They are abnormal if more than half of the cancellous bone is destroyed.
 - <u>Bone scanning</u> is more sensitive but less specific. Bone scanning can detect small metastases (2mm) but may be negative in purely lytic lesions, e.g. multiple myeloma. Bone scans will show abnormality wherever there is osteoblastic activity, e.g. arthritis, infection, trauma and Paget's disease.
 - <u>MRI</u> is the investigation of choice in suspected spinal cord compression or if there is suspicion of soft tissue involvement (**MEDICAL EMERGENCY**)

2 Analgesic Approach

- a. Consider radiotherapy.
- b. Prescribe Paracetamol 1g qds.
- c. Titrate opioids (see 4 Opioid Prescribing Guidelines).
- d. Consider physiotherapy referral for advice on movement and bracing.
- e. Use short acting analgesics eg inhaled nitrous oxide or transmucosal fentanyl* prior to painful activities (eg showering).
- f. If pain is not controlled, add a NSAID e.g.
 - Diclofenac 25 50 mg tds OR
 - Celecoxib 100 200mg bd
- g. Consider dexamethasone especially if there is suspicion of nerve root entrapment and / or neuropathic pain.
- h. Cautious use of steroids is advised if concomitant administration of NSAID's due to GI toxicity (See 13.7 NSAIDs).
- i. If pain not controlled consult with the palliative care service for consideration of:
 - Strontium 89

Useful for multiple bony secondaries in prostate cancer. There is an 80% response rate within 2-3 weeks and lasts 4-6 months. Strontium 89 can cause myelosuppression. Specialist advice should be sought before using.

- <u>Bisphosphonates</u> e.g. Pamidronate or Zoledronic acid The bisphosphonates inhibit osteoclast activity and are therefore useful in bone pain secondary to lytic lesions e.g. myeloma and breast cancer for which they are licensed. There is some evidence emerging of their use in other cancers particularly prostate cancer although they are not licensed for use for pain control currently. They are licensed for use for malignant hypercalcaemia. Specialist advice should be sought before prescribing.
- Local infiltration with steroid and local anaesthetic.
- Nerve blocks e.g. rib pain.
- Surgical fixation of unstable bone (think incident pain and fracture prophylaxis).
- Acrylic cement for unstable fractures of vertebrae or pelvis.

Epidural / intrathecal infusions. •

3. Re-evaluate

The pain may change over time depending on treatment or disease progression, and • management will change accordingly

*Transmucosal fentanyl is called "Actiq" and is available as a non-PBS medication via the Special Access Scheme.

References:

- "Therapeutic Guidelines Palliative Care", 2001, Therapeutic Guidelines Ltd.
 Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version,
- www.palliativedrugs.com
- 3. Back Ian, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, www.pallmed.net

12. INCIDENT PAIN

12.1 GUIDELINES:

- 1. Incident pain is pain associated with movement
- 2. Incident pain is difficult to manage and consultation with the palliative care service is recommended.
- 3. The risk is that breakthrough doses are given for pain that is severe but short lived. Once movement has ceased, the pain stimulus is removed and the patient then becomes opioid toxic.
- 4. Incident pain is usually due to bone metastases (See. Bone Pain Guidelines).
- 5. It is not always possible to achieve complete pain relief, but at the very least, the aim should be for the patient to have a reasonable night's sleep and be comfortable at rest.

12.2 PROCEDURE:

- 1. <u>Patient Assessment</u> (See 2. Pain Assessment Guidelines)
 - a. <u>History</u>
 - There may or may not be pain at rest.
 - There is severe pain on movement, i.e. the pain is predictable.
 - There pain is usually well localised and may have other features e.g. neuropathic pain, muscle spasm or spinal cord compression (Medical Emergency – See Guidelines)
 - The pain may have an acute onset, especially if there is a fracture (which may not be due to trauma)
 - b. Examination
 - There is usually local tenderness and pain with movement.
 - There may be features of neuropathic pain.
 - There may be features of opioid toxicity (sedation, myoclonus, respiratory depression)

c. Investigations:

- Restrict investigations to those that will influence management decisions.
- <u>X-rays</u> are very useful. They are abnormal if more than half of the cancellous bone is destroyed.
- <u>Bone scanning</u> is more sensitive but less specific. Bone scanning can detect small metastases (2mm) but may be negative in purely lytic lesions, e.g. multiple myeloma. Bone scans will show abnormality wherever there is osteoblastic activity, e.g. arthritis, infection, trauma and Paget's disease.
- <u>MRI</u> is the investigation of choice in suspected spinal cord compression or if there is suspicion of soft tissue involvement (**MEDICAL EMERGENCY**).

2. Analgesic Approach

- Consider radiotherapy.
- Prescribe Paracetamol 1g qds
- Titrate opioids (see 4.Opioid Prescribing Guidelines)
- Consider physiotherapy referral for advice on movement and bracing.
- Use short acting analgesics eg inhaled nitrous oxide or transmucosal fentanyl* prior to painful activities eg showering (See 13.2 Transmucosal Fentanyl)

- If pain is not controlled, add a NSAID e.g.
 - Diclofenac 25 50 mg tds
 OR
 - Celecoxib 100 200mg bd
- Consider dexamethasone especially if there is suspicion of nerve root entrapment and / or neuropathic pain.
- Cautious use of steroids is advised if concomitant administration of NSAID's due to GI toxicity (See 13.7 NSAIDs)
- If pain not controlled consult with the palliative care service for consideration of:
 - ➢ Strontium 89

Useful for multiple bony secondaries in prostate cancer. There is an 80% response rate within 2-3 weeks and lasts 4-6 months. Strontium 89 can cause myelosuppression. Specialist advice should be sought before using.

> <u>Bisphosphonates</u> e.g. Pamidronate or Zoledronic acid.

The bisphosphonates inhibit osteoclast activity and are therefore useful in bone pain secondary to lytic lesions e.g. myeloma and breast cancer for which they are licensed. There is some evidence emerging of their use in other cancers particularly prostate cancer although they are not licensed for use for pain control currently. They are licensed for use for malignant hypercalcaemia. Specialist advice should be sought before prescribing.

- Local infiltration with steroid and local anaesthetic.
- Nerve blocks e.g. rib pain.
- Surgical fixation of unstable bone (think incident pain and fracture prophylaxis).
- Acrylic cement for unstable fractures of vertebrae or pelvis.
- Epidural / intrathecal infusions.

3. <u>Re-evaluate</u>

• The pain may change over time depending on treatment or disease progression, and management will change accordingly

*Transmucosal fentanyl is called "Actiq" and is available as a non-PBS medication via the Special Access Scheme.

References:

- 1. "Therapeutic Guidelines Palliative Care", 2001, Therapeutic Guidelines Ltd.
- 2. Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version, <u>www.palliativedrugs.com</u>
- 3. Back lan, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, www.pallmed.net

13. ANALGESICS

13.1 FENTANYL PATCHES (Duragesic):

- Fentanyl is a potent synthetic opioid.
- The membrane in the transdermal patch provides a rate-limiting delivery system that allows a standardised amount of fentanyl to cross each hour from patch to skin.
- Once the patch is applied to the skin the drug diffuses into the subcutaneous tissues and forms a reservoir. It is then absorbed into the systemic circulation and takes 17-24 hours to reach optimal plasma levels.
- The patch then provides a constant analgesic dose for a further 48 hours.
- It is worth remembering that a reservoir of fentanyl cumulates in the skin under the patch, and significant blood levels persist for 24 hours, sometimes more, after removing the patch. This is significant if fentanyl is being discontinued.
- Consider Fentanyl patches as the "Queen Mary" of the analgesic world i.e. very slow to get up to speed and equally slow to stop.

Indications

- 1. Intolerable side effects with morphine eg constipation, nausea, sedation and confusion
- 2. Patient preference.
- 3. Renal failure.
- 4. Dysphagia
- 5. Poor compliance with oral medication

Conversions

The patch comes in 4 sizes – 25mcg/hr, 50, 75 and 100. When transferring a patient from morphine to Fentanyl there is a conversion table of equivalent doses shown below.

4 hourly dose Oral Morphine	24hr Oral Mor	ohine	Fentanyl Patch mcg/hr
10 – 20mg	60 – 134	\rightarrow	25
25 – 35mg	135 – 224	\rightarrow	50
40 – 50mg	225 – 314	\rightarrow	75
55 – 65mg	315 – 404	\rightarrow	100
70 – 80mg	405 - 494	\rightarrow	125
85 – 95mg	495 – 584	\rightarrow	150

FENTANYL PATCH CONVERSION

Starting on the patches

- Systemic analgesic concentrations are reached within approximately 12 hours, therefore if converting from:
 - 4 hourly morphine, give regular doses for the first 12 hours after applying the patch
 - 12 hourly morphine, apply the patch and the final dose of SR morphine at the same time
 - 24 hourly morphine, apply the patch 12 hours after the final SR morphine
 - a syringe driver, continue the syringe driver for about 12 hours after applying the patch.
 - Steady state plasma concentrations of fentanyl are achieved after 36 48 hours therefore the patient should use breakthrough analgesia liberally in the first 3 days
 - When using the manufacturers recommended starting dose (see above), approximately 50% of patients need to increase the patch strength after the first 3 days

<u>Notes</u>

- Fentanyl patches are not recommended if the patient is on less than 40mg oral morphine a day.
- Fentanyl patches are for patients with stable pain only and not to be used for titrating opioids.
- When changing from morphine to Fentanyl the patient can experience opioid withdrawal e.g abdominal cramps, sweats and flu-like symptoms. This is abated with giving prn 4 hourly morphine and should only last a few days.
- 10 20% of patients find that the patches provide analgesia for 48 hours and not 72 hours. In these instances it is appropriate to replace the patch every 48 hours rather than increasing the patch size.
- Due to the heat in summer the patches can slide off. Do not use Opsite over the patch to keep it in place, this will cause a faster delivery of Fentanyl and possible overdose. Instead stick micropore tape around the outside of the patch and not directly over the drug reservoir.
- Direct heat e.g. a hot water bottle will increase absorption.
- Cut hair rather than shave the skin before applying a patch as shaving will disrupt the top fatty layer of skin and therefore increase the rate of absorption.
- Change the position of the new patch every time, to rest the skin for 3 6 days.
- In moribund patients it is probably safer to continue fentanyl patches and give additional opioids parenterally rather than ceasing the patch and converting to morphine. This is due to the wide variability in analgesic equivalent doses.

13.2 TRANSMUCOSAL FENTANYL:

- Used for incident pain for patients already on regular strong opioids.
- Fentanyl Lozenges (on a stick) are available as ACTIQ on the Special Access Scheme.
- The drug is rapidly absorbed through the buccal mucosa with onset of analgesia within 5 10 minutes.
- Maximal effect is reached within 20 40 minutes with duration of action 1 3 hours
- The optimal dose is determined by titration and cannot be predicted by the patients regular dose of opioid.
- Specialist advise is recommended.

13.3 TRAMADOL:

- Tramadol has a dual analgesic action. It is a synthetic analogue of codeine that binds to μ -opioid receptors and inhibits norepinephrine and serotonin reuptake.
- It is not commonly used for cancer pain because of its ceiling dose of 400mg / day and drug interactions with anti-depressants.
- 10mg oral morphine is approximately equivalent to 40 mg oral tramadol.
- 10mg subcutaneous morphine is approximately equivalent to 100mg subcutaneous tramadol
- It interacts with Serotonin reuptake inhibitors and tricylic antidepressants to lower seizure threshold and concomitant use is not recommended.

13.4 OXYCODONE:

- Oxycodone is a potent synthetic opioid.
- 10mg oral morphine is equivalent to approximately 6mg oral oxycodone.
- 10mg subcutaneous morphine is equivalent to approximately 15mg sc oxycodone
- Oxycontin continuous preparation has a biphasic absorption i.e analgesia is achieved within 1 hour and sustained over 12 hours.
 - Endone tabs = oxycodone (5mg)
 - Oxynorm caps = oxycodone (5, 10, 20mg) NORMal Release
 - Oxycontin tabs = CONTINuous realease oxycodone (5, 10, 20, 40, 80)
 - Oxynorm Liquid 1mg/ml (PBS)
 - Oxynorm Concentrate 10mg/ml (not PBS)

13.5 HYDROMORPHONE (Dilaudid):

- Hydromorphone is a potent opioid.
- 10mg oral morphine is equivalent to approximately 2mg oral hydromorphone
- 5mg oral hydromorphone is equivalent to approximately 1mg subcutaneous hydromorphone,
- There is wide individual variability in dose equivalence for hydromorphone and given its potency, specialist advice is required.

13.6 METHADONE:

- Methadone is a potent synthetic opioid with mixed properties. It is a μ receptor agonist, possibly a δ-opioid receptor agonist, an NMDA receptor antagonist and a pre-synaptic serotonin re-uptake blocker.
- The pharmacology of methadone is complex and very variable.
- It can take 10 12 days to reach steady state concentrations.
- Dose conversions from other opioids are not static and appear to be a function of previous opioid exposure.
- In an opioid tolerant patient 10mg oral morphine = 1mg oral methadone. This is not true for opioid intolerant patients
- The use of methadone in palliative care requires specialist supervision.

13.7 NSAIDs (Non-Steroidal Anti-inflammatory Drugs):

- In palliative care, NSAIDs are indicated for
 - > Mild to moderate pain due to tissue injury and inflammation
 - Bone pain
 - Neuropathic pain
 - Neoplastic fever
 - Headache
 - Biliary and ureteric colic
- Despite their usefulness, they have serious adverse side effects that necessitate cautious prescribing. Some of the major adverse effects of NSAIDs include
 - ≻ <u>GIT</u>
 - Gastritis, ulcers and erosions, Major GI haemorrhage, Nausea & vomiting
 - Renal
 - Renal failure, oedema,
 - ➢ <u>CVS</u>
 - Raised BP, fluid retention
 - ≻ <u>CNS</u>
 - Headaches, confusion, hallucinations, depression, tremor, tinnitus
 - Haematological
 - Anaemia, bone marrow depression, \downarrow platelet aggregation
 - <u>Hepatic</u>
 Hepatotoxicity, hepatitis
 - <u>Respiratory</u>
 Precipitation of asthma
- NSAIDs and COX inhibition.
 - NSAIDs are essential analgesics especially for pain associated with inflammation. Inflammation results in increased prostaglandin (PG) production locally and also in the CNS.
 - Increased PGs in the CNS results in central sensitisation and increased pain. NSAIDs inhibit cyclo-oxygenase (COX), the main enzyme in the synthesis of PGs from arachidonic acid.
 - NSAIDs inhibit PG production both at the site if injury and in the CNS, ie they have both a peripheral and central action. However, inhibition of PG synthesis does not account for the total analgesic effect of NSAIDs.

COX exists in 2 forms; COX-1 is present in all tissues and is referred to as "constitutive", COX-2 is generally detectable in various tissues but is massively induced by inflammation.



- The classification of NSAIDs is based on their relative ability to inhibit COX-1 and COX-2.
- The idea behind developing COX-2 inhibitors was to have a NSAID devoid of GI toxicity. However, GI toxicity depends on multiple factors, not just COX – 2 selectivity.
- Cox –2 inhibitors available in Australia include celecoxib (COX-1 sparing).
- Cox-2 inhibitors have a lower rate of GI toxicity than other NSAIDs in the short term but t here is conflicting evidence that long term use affords lower GI toxicity. The other adverse effects remain the same.
- Cox-2 inhibitors also have a theoretical pro-thrombotic tendency therefore caution should be exercised when prescribing specific COX-2 inhibitors in susceptible patients (including those with cancer).

Risks of complicated peptic ulcer disease in patients taking NSAIDs compared with nonusers of NSAIDs

Past history of peptic ulcer disease	9.5 - 17
Age >60 years	3 - 13
High dose NSAID	8
Multiple NSAID	9 - 23
Irregularity of feeding	14
Presence of alcohol related diagnosis	5
Concomitant corticosteroids	4 - 10
Concomitant anticoagulants	12 - 16
Concomitant aspirin	8

Ie a patient with a history of peptic ulcer disease on NSAIDs has a 9.5-17 times greater risk of developing GI bleed than a patient with a history of Peptic ulcer disease not on NSAIDs.

- 1. Avoid in patients at risk of GI bleed if possible (see risk factors above)
- 2. Use drugs with a "safer" GI profile:

Lower GI toxicity risk

Cox-2 inhibitors	
Ibuprofen	
Diclofenac	
Naproxen	

Higher GI Toxicity Risk

Piroxicam Indomethacin Ketoralac

- 3. Prescribe a gastro-protective drug prophylactically if the patient is at risk Eg proton pump inhibitor, Omeprazole 20mg / day
- 4. Avoid in patients with renal impairment if possible.
- 5. Avoid the combination of NSAID, ACE inhibitor and diuretic.
- 6. If the NSAID has no analgesic effect, consider swapping to an alternative NSAID from another class.

References:

- 1. "Therapeutic Guidelines Palliative Care", 2001, Therapeutic Guidelines Ltd.
- 2. Palliative Care Formulary 2nd Ed, 2002, Chapter 5, electronic version, www.palliativedrugs.com
- 3. Back lan, 2001, "Palliative Medicine Handbook", 3rd Edition, Pain Chapter. Electronic version, <u>www.pallmed.net</u>

14. PALLIATIVE CARE KETAMINE INFUSION

14.1 GUIDELINES:

- 1. These guidelines refer to Palliative Care patients only. For the use of Ketamine in acute pain states and its use in the setting of bone marrow transplantation, please refer to separate protocols.
- 2. For palliative care patients Ketamine can only be used under specialist supervision.
- 3. Ketamine is a phencyclidine like drug. It is a dissociative anaesthetic used mainly as an IV anaesthetic induction agent. It has also been shown to have analgesic properties at sub-anaesthetic doses.
- 4. The analgesic action is mediated mainly at the spinal level where it acts as an N-methyl-D-aspartate (NMDA) receptor antagonist

5. <u>Indications:</u>

- neuropathic pain
- phantom limb pain
- ischaemic pain
- incident pain
- to decrease dose of opioid
 - > when effective doses of opioids are prevented by toxicity
 - > where there is rapid pain escalation.

6. Adverse Reactions:

- skin reactions at site of SC infusion
- intracranial hypertension (by increasing cerebral blood flow)
- cardiovascular excitability
- psychomimetic effects
 - confusion
 - ➤ delirium
 - vivid unpleasant dreams
 - hallucinations
 - feelings of detachment from the body
 - impaired cognition and memory
- The psychomimetic side-effects are less frequent in subanaesthetic doses.
- In some cases they may necessitate withdrawal from therapy.
- 7. Benzodiazepines have proven to be the most effective agents for the prevention of these side effects.

8. Contraindications:

- Absolute
 - raised intracranial pressure
 - seizures

Relative

- hypertension
- cardiac failure
- previous CVAs

14.2 EQUIPTMENT:

- Graseby infusion pump
- 10 or 20ml minimum volume extension set
- butterfly needle, 23 or 25G

- luer lock syringe
- drawing up needle
- ampoule(s) of Ketamine
- ampoule(s) of sodium chloride 0.9%
- unsterile gloves
- film dressing
- sharps container

14.3 PROCEDURE:

- Commencement of Subcutaneous Infusion please refer to syringe driver protocol
- A Registered nurse is required to manage Ketamine infusions.
- 1. Record BP, pulse and temperature.
- 2. Wash hands according to infection control principles.
- 3. Draw up and check the prescribed Ketamine solution as per Drug Administration Procedure. Because Ketamine is irritant, draw up to the largest volume possible. Ensure all appropriate labels are attached.
- 4. Attach syringe containing Ketamine solution to infusion set, prime and clamp line. Ensure all connections are secure and no air is in line.
- 5. Don gloves.
- 6. Site butterfly needle subcutaneously and attach infusion set.
- 7. Program pump according to the infusion orders on the drug chart.
- 8. Unclamp infusion line and start pump.
- 9. Record commencement of infusion on drug chart.
- 10. Assess 4 hourly for 24 hours for changes in BP, pulse, temperature and skin reaction at infusion site. If there is a significant changed in BP or pulse, the infusion must be ceased and the doctor informed.
- If psychomimetic side effects occur, reduce the dose of Ketamine and give a single dose of benzodiazepine as ordered e.g. Clonazepam 0.5mg orally or Midazolam 2.5mg SC.
- 12. Routine observations required 3 times per day (not overnight).
- 13. Ketamine is acidic and very irritant to subcutaneous tissues. Check subcutaneous site **12 hourly** for irritation and change at least alternate days.
- 14. When Ketamine is used in cases of opioid tolerance, there will need to be a concomitant decrease in the opioid dose to avoid opioid toxicity. Opioid doses should usually be decreased by 1/3 daily, or more if patient drowsy and pain free.

14.4 DOSAGE and MONITORING:

- Initial starting dose for infusion is 50-100mg S/C over 24 hours.
- Increase by 50-100mg each day until pain relief or maximum dose of 500mg/day.
- Infusion usually ceased after 5 days.

Reference Palliative Care Formulary 2nd Edition 2002, Radcliffe Press

15. APPENDIX

15.1 Palliative Care Morphine Variable Dose Chart

15.2 Patient Self Assessment Pain Chart

15.1 PALLIATIVE CARE MORPHINE VARIABLE DOSE CHART

Explanatory notes only – PLEASE READ FULL GUIDELINES

- This morphine variable dose chart has been developed to facilitate safe morphine administration and improved pain control for palliative care patients.
- The chart is applicable to opioid naïve patients and those patients on opioids who have severe uncontrolled pain.
- Normal release morphine is prescribed 4 hourly and extra doses are called "breakthroughs".
- The chart is used so that the ward nurse can assess the patient at least 4 hourly and titrate the morphine dose (up or down) without the need for the doctor to change the morphine order.
- When the pain is stable, the 4 hourly morphine is converted to a sustained-release opioid for maintenance. (See Opioid Conversion Table on Back Page)

1. ROUTE

- Morphine is always prescribed orally.
- If the oral route is not available, then the subcutaneous route is used.
- The subcutaneous dose is <u>half</u> the oral dose e.g. 10mg oral morphine = 5mg sc morphine.

2. DOSE

- There is no standard dose of morphine
- If the patient is not on an opioid then 5-10mg orally is a reasonable starting dose.
- If the patient is frail or elderly, 2.5mg orally is a reasonable starting dose
- If the patient is already on an opioid use the conversion chart on the back page to calculate the 4 hourly starting dose.
- The dose is then adjusted over 24 48hrs according to patient response.
- If the patient is on more than 100mg morphine 4 hourly, consult the palliative care service for advice

The recommended sequence of doses is:

2.5mg - 5 - 7.5 - 10 - 15 - 20 - 30 - 40 - 60 - 80 - 100 - 120mg 4 hrly.

The dose should be increased if

- The patients pain consistently returns before the next regular dose is due
- The patient's pain score remains high
- 3 or more breakthroughs are required in 24 hours

The dose should be decreased if

• The patient is pain free but drowsy

4. BREAKTHROUGH DOSE

- A breakthrough dose is given at any time if pain occurs, irrespective of the regular dose.
- It is always the same as the 4 hourly dose.

6. MAXIMUM DOSE

- This is the maximum regular 4 hourly dose that the nurse can give.
- A recommended maximum dose is approximately 3x the starting dose
- If the patient is in pain and requires a larger dose, the doctor must review the patient and write a new morphine variable dose chart.

7. APERIENTS

- Regular aperients <u>must</u> be charted and titrated according to patient response e.g. Movicol 1-3/d or Docusate & Senna 2 bd
- •

8. ANTI-EMETICS

• Should be charted as a PRN order, e.g. metoclopramide 10mg qds

Morphine is not a sedative and can cause severe confusion, agitation and distress if given as a sedative in the terminal phase. If sedation is necessary, a benzodiazepine or psychotropic drug should be considered and consultation with the palliative care service is advised.

U/R NAME:	ALLERGIES					
Route: Oral / Subcutaneously (10mg oral =	5mg subcutaneous)					
Dose: mg every 4 hours and as required (indicate on chart if dose is a breakthrough dose)						
 Increase dose if 3 (three) or more breakthrough doses are required in a 24 hour period or pain score is consistently high. Decrease dose if patient is pain free but drowsy. The following dose sequence is recommended when making dose adjustments: 						
2.5 - 5 - 7.5 - 10 - 15 - 20 - 30 - 40 - 60 - 80 - 100 - 120 - 160 - 200						
Maximum Dose before contacting MO:mgs						
Doctor's Signature: Date: / /						
Print Name:						
Ensure aperients and anti-emetics are prescribed.						

PAIN ASSESSMENT CHART

DATE	TIME	DOSE	ROUTE	PAIN SCORE 0-10	MENTAL SCORE A,D,S, C,U	PAIN SITE	BREAK THROUGH	COMMENTS	SIGN	PAIN LEVEL ½ HOUR AFTER MEDICATION

DATE	TIME	DOSE	ROUTE	PAIN SCORE 0-10	MENTAL SCORE A,D,S, C,U	PAIN SITE	BREAK THROUGH	COMMENTS	SIGN	PAIN LEVEL ½ HOUR AFTER MEDICATION

OPIOID CONVERSION TABLES

APPROXIMATE EQUIVALENT ORAL DOSES

10mg oral morphine =	2mg Hydromorphone
	6mg Oxycodone
	40mg Tramadol
	80mg Pethidine
	80mg Codeine
	140mg Dextropropoxyphene

N.B. 1 Panadeine Forte = 4mg oral morphine (Approximately)

SUSTAINED RELEASE PREPARATIONS

Opioid	Trade Name	Unit Doses (mg)	Frequency
MORPHINE	MS Contin	5, 10, 15, 30, 60, 100, 200	12 hrly
	MS Contin Suspension	20, 30, 60, 100, 200	12 hrly
	Kapanol	10, 20, 50, 100	12 hrly or 24 hrly
	MS Mono	30, 60, 90, 120	24 hrly
OXYCODONE	Oxycontin	5, 10, 20, 40, 80	12 hrly
		25mcg/hr, 50mcg/hr,	
FENTANYL	Durogesic	75mcg/hr, 100mcg/hr	Every 72 hrs

SLOW RELEASE EQUIVALENT

4 hourly dose of Morphine		12hrly Morphine MS Contin or Kapanol	24hrly Morphine MS Mono or Kapanol	12hrly Oxycodone (OxyContin)	Fentanyl (mcg/hr)
S/C	ORAL				
2.5	5mg	15	30	10	Not recommended
5	10	30	60	20	25
7.5	15	45	90	30	25
10	20	60	120	40	25
15	30	90	180	60	50
20	40	120	240	80	75
25	50	150	300	100	75
30	60	180	360	120	100
40	80	240	480	160	125
50	100	300	600	200	175

EXAMPLE If the patients pain is controlled on 20mg oral morphine every 4 hours, convert to

- MS Contin 60mgbd
- Kapanol 60mg bd
- MS Mono 120mg daily
- OxyContin 40mg bd
- Fentanyl Patch 25mcg/hr / 72 hours

FENTANYL PATCH CONVERSION

4 hourly dose Oral Morphine	24hr Oral Mor	phine	Fentanyl Patch mcg/hr
10 – 20mg	60 – 134	\rightarrow	25
25 – 35mg	135 – 224	\rightarrow	50
40 – 50mg	225 – 314	\rightarrow	75
55 – 65mg	315 – 404	\rightarrow	100
70 – 80mg	405 – 494	\rightarrow	125
85 – 95mg	495 – 584	\rightarrow	150

Reference Palliative Care Formulary 2nd Edition 2002, Radcliffe Press

15.2 PATIENT SELF-ASSESSMENT PAIN CHART

Name: -----

R R R R R R R R R R R R R R R R R R R										
Descript	ive wor	<u>ds to d</u>	lescribe	e your p	<u>bain</u>					
Throbbing Burning Aching Blinding Frightful Unbearable Nauseating Cruel) 	Crushin Cutting Stinging Tiring Intense Annoyin Radiatin Punishir	g I Ig Ig	Stabl Sma Pene Shoc Sear Tend Copi Exha	bing rting etrating ing ler ng usting	Hurting Vicious Spread Torturii Relaxe Naggin Gnawir Sicken	ling ng d g ng ing	Dull Com Hapı Split Piero Pain Cont Mise	fortable by ting cing Free tent trable	
Describe	your pai	n								
What mak What mak Pain Level	es the pa es the pa I	in bette in wors	r? e?							
0	12	2	3	4	5	6	_7_	8	_9	10
No Pain					Moderate pain					Worst possible pain
Date/Time	Site of p	bain	Pain score	Descrip pain	tion of	Pain leve hour after medicatio	½ r on	Comments		Bowels

	Site of pain	Pain score	Description of pain	Pain level ½ hour after medication	Comments	Bowels
_						

Date/Time	Site of pain	Pain score	Description of pain	Pain level ½ hour after medication	Comments	Bowels
_						

Date/Time	Site of pain	Pain score	Description of pain	Pain level ½ hour after medication	Comments	Bowels
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