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THE JIMMY S BILIMORIA FOUNDATION

PALLIATIVE CARE
GUIDELINES
FOR A HOME SETTING IN INDIA

OPIOIDS

INTRODUCTION

This guideline presents recommendations for the use of opioids in the management of pain in adult patients with life-threatening illness, like cancer.

Choosing opioids

- The choice of opioid should depend on the severity of pain (see Table 1) and the WHO analgesic ladder
- Opioids are the drugs of choice for moderate to severe pain associated with life-threatening illness like cancer
- Assess and address fears and worries of patient and family around the use of opioids
- The opioid of choice for severe cancer pain is oral morphine (see Table 2)
- Consider prescribing laxatives (stimulant and/or softener) and anti-emetics along with opioids to prevent constipation and nausea, respectively.

Table 1: Opioids commonly used for cancer pain	
Opioids for mild to moderate pain	**Opioids for moderate to severe Pain**
Codeine Sulphate Tramadol HCl	Morphine sulphate Tapentadol* Fentanyl Buprenorphine Methadone
*Not used as first line in palliative care	

Table 2: Opioids for moderate to severe pain	
First Line	Morphine sulphate
Second Line	Fentanyl, Tapentadol, Buprenorphine
Third Line	Methadone

Switching opioid

- Common reasons for considering switching of opioids are:
  - ➢ Inadequate pain control after adequate titration

- Unacceptable adverse effects from a specific opioid which limits dose escalation
- Significant decline in renal function
- Unable to take oral route
- Allergy

- The conversion ratios between different opioids are approximate and should be used as a guide only (see Table 3)
- When oral morphine is available, low dose morphine can be used for moderate pain instead of weak opioids
- When switching opioids, reduce dose by up to 30% if the patient is opioid toxic, frail or elderly; and re-titrate gradually
- When converting from a second-line opioid, use 2/3rd of the calculated dose and re-titrate if necessary
- Where there is no direct conversion between opioids, use oral morphine equivalents i.e. convert the opioid to the equivalent of the oral morphine dose and, thereafter, to the required opioid
- Monitor closely if the patient has renal/hepatic impairment and choose an appropriate medication after checking the information on individual medications
- Prescribe an appropriate medication and dose to treat the breakthrough pain

Table 3: Approximate opioid potency ratio (oral morphine = 1)

Opioid	Potency ratio with morphine	Duration of action
Codeine	1/10	3 - 6 hours
Tramadol	1/5	4 - 6 hours
Buprenorphine transdermal patch	100	7 days
Fentanyl transdermal patch	100-150	72 hours
Tapentadol	1/3	4 - 6 hours

Opioids

Opioids are naturally occurring semi-synthetic and synthetic drugs which produce their effects by combining with opioid receptors and are stereo specifically antagonised by Naloxone.

A. Opioids for mild to moderate pain

Tramadol

- **Indications**
  - Moderate pain
  - Pain control is not achieved with WHO Step 1 analgesics
- **General Principles**
  - Start with Tramadol 50mg PO q6h with rescue doses of the same strength for breakthrough pain as often as necessary
  - Increase the dose of Tramadol gradually if necessary, up to a maximum of 400 mg/24 hours
  - In renal failure patients, start with 50mg PO q12h, dose adjustment is necessary based on the creatinine clearance
  - Available in the following strengths: 50mg (tablet, capsule), 100mg (tablet), 100mg (Injectable in 2 mL ampoule)
  - Available in combination with acetaminophen (Ultracet/ Calpol T), each tablet contains 37.5mg tramadol with 325mg acetaminophen
- **Precautions**
  - Tramadol is associated with seizures in the following circumstances:
    - The total daily dose exceeds 400mg
    - After rapid intravenous injection of tramadol
    - With concurrent use of medications which decrease seizure threshold e.g. TCAs, SSRIs, antipsychotics
    - If there is a history of seizures
  - Serotonin toxicity has been reported when using tramadol concurrently with medications that interfere with presynaptic serotonin re-uptake
  - It can increase the risk of suicide in emotionally unstable patients, if they are on tranquilisers or antidepressants
  - Patients should be monitored for side-effects such as nausea, vomiting, and constipation. An antiemetic and laxative should be prescribed prophylactically.
- **Contraindication**
  - Concurrent use of MAO inhibitors or within 2 weeks of cessation
  - Severe hepatic impairment
  - Severe renal failure (creatinine clearance less than 10ml/minute)
  - Uncontrolled seizures

B. Opioids for moderate to severe pain

Oral morphine

- **Indications**
  - Moderate to severe pain
  - Pain control is not achieved with WHO Step 1 and step 2 analgesics
- **General Principles**

- If opioid naïve, start with immediate release morphine at 5mg PO q4h with rescue doses of the same strength for breakthrough pain as often as necessary; smaller doses should be used in the elderly/frail
- Reassess the daily requirement after 24 - 48 hours and the regular dosing should be adjusted as necessary (*refer to the Guideline - Pain Management - Opioid titration*)
- Immediate release tablets and sustained release tablets can be administered rectally when no other route of administration is available
- Immediate release tablets are available in following strengths: 10 mg, 20 mg, 30mg
- Sustained release tablets (q12h) are available in two strengths: 10mg, 30mg

- **Precautions**
  - Sedation is common at the start of the treatment - explain to the patient and the family that it usually resolves within a few days
  - Nausea is common initially- start on metoclopramide 10mg tid or haloperidol 1.5mg at hsod or bd for the initial 3 - 5 days
  - Constipation is seen in most patients - prescribe laxatives prophylactically (stimulant and/or softener)
  - Dry mouth occurs in some patients - advise frequent sips of iced drinks, saliva replacements, or saliva stimulants

Fentanyl transdermal patch

Can be considered in patients with stable pain in the following situations:

- **Indications**
  - Unacceptable side effects from morphine
  - Renal failure
  - Where oral or subcutaneous routes are inappropriate or unacceptable
  - Non-compliance to oral medications
- **General principles**
  - Apply patch to dry, non-inflamed, non-irradiated, non-hairy skin area, on chest, back, flank or upper arm
  - Record the time and location of the patch application
  - For the first twelve hours after initiating a Fentanyl patch, continue use of appropriate regular dosing of the oral or subcutaneous opioid until the plasma levels are adequate.
  - Patches should be changed every 3 days, at the same time of day
  - New patch should be applied to a different site to the previous patch; to rest the underlying skin for 3 - 6 days
  - Used patches should be kept out of reach of children and pets
  - The used patches should be folded in half and discarded in the medical toxic waste or flushed down the toilet, as the used patch contains active medicine

- It is less constipating than morphine; halve the dose of laxatives when switching to Fentanyl
- Use Table 4 to determine the equivalent dose of Fentanyl Patch and appropriate rescue dose for breakthrough pain
- Available in four different strengths: 12. 12.5, 25 and 50 mcg/ hour

- **Precautions**
  - Heat can increase the absorption of Fentanyl; avoid exposure to heat sources
  - Pyrexia can increase the absorption of Fentanyl; use anti-pyretic measures
  - Do not cut the patch delivery system
- **Contraindication**
  - Poorly controlled pain
  - Opioid naïve patients
  - In acute pain management

Table 4: Approximate TD Fentanyl-oral morphine dose conversion chart		
24-hour oral morphine dose	**Fentanyl patch dose (mcg per hour)**	**Rescue dose of immediate release morphine**
30 to 59mg	12	5 to 10mg
60 to 89mg	25	10 to 15mg
90 to 119mg	37	15 to 20mg
120 to 179mg	50	20 to 30mg
180 to 239 mg	62	30 to 40mg
240 to 299mg	75	40 to 50mg
300 to 359mg	87	50 to 60mg
>360mg	100	60mg

Tapentadol

- **Indications**
  - Unacceptable side effects from morphine

- Renal failure
- Moderate to severe pain
- Pain control is not achieved with WHO Step 1 and step 2 analgesics

- **General principles**
  - Start with 50mg PO q4h - q6h if patient has moderate pain and is opioid naïve; a higher dose can be considered if pain is severe and patient had been on strong opioids
  - If the starting dose does not relieve pain, a second dose can be repeated after one hour
  - If necessary, increase the dose to 100mg q4h or 150mg q6h
  - Maximum dose of 600mg/24 hours (700mg in the first 24 hours)
  - Use conversion ratios (see Table 3) to determine the equivalent dose of Tapentadol
  - Available in three different strengths: 50 mg, 75 mg, 100 mg (immediate release tablets)
- **Precautions**
  - Patients should be monitored for side-effects such as nausea and vomiting, and constipation; an antiemetic regular or prn and a laxative should be prescribed prophylactically
  - Serotonin toxicity has been reported when using Tapentadol concurrently with serotoninergic medication
  - Seizures
- **Contraindication**
  - Concurrent use of MAO inhibitors or within 2 weeks of cessation of one
  - Severe hepatic impairment
  - Severe renal failure (creatinine clearance less than 10 ml/minute)
  - Seizures

Buprenorphine transdermal patch

- **Indications** - *refer to Indications under Fentanyl patch (see above)*
- **General principles -** *refer to General principles under Fentanyl patches (see above)* with the following changes:
  - Opioid naïve patients could be started on 5 mcg/hour patch
  - Patches should be changed every 7 days, at the same time of day
  - New patch should be applied to a different site to the previous patch; to rest the underlying skin for 9 days
  - Fentanyl patch is 1.4 times stronger than buprenorphine patch
  - Use Table 5 to determine the equivalent dose of buprenorphine Patch and appropriate rescue dose for breakthrough pain; (doses given are approximate)
  - Available in three different strengths: 5, 10 and 20mcg/ hour

- **Precautions** - *refer to Precautions under Fentanyl patch (see above)*
- **Contraindication** - *refer to Contraindications under Fentanyl Patch (see above)*

Table 5: Approximate TD Buprenorphine-oral morphine dose conversion chart		
24-hour oral morphine dose	**Buprenorphine patch dose (mcg per hour)**	**Rescue dose of Immediate release Morphine**
1 mg	5	2.5mg
30mg	10	5mg
60mg	20	10mg
90mg	30	15mg
120mg	40	20mg
180mg	60	30mg
240mg	80	40mg
300mg	100	60mg

Methadone

- **Indications**
  - Neuropathic pain and mixed pain not responding to combinations of NSAIDs, strong opioids and adjuvant analgesics
  - Unacceptable side-effects from morphine
  - Switching to other alternate opioids is not possible
  - End stage renal failure
- **General principles**
  - Available in two strengths - 5mg and 10 mg tablets; 5mg/ml suspension
- **Precautions**
  - Practitioners should have complete knowledge of pharmacology of methadone
  - Close monitoring of the patient when switching from another opioid, especially when the patient is on a higher dosage of opioids

- Start low and go slow when titrating upwards
- Monitor carefully when changing the dose of methadone
- Use caution when administering methadone to patients who are at risk of QT prolongation and history of cardiac disease in patient or family
- Be aware of drug interactions when prescribing methadone

- **Contraindication**
  - Concurrent use of methadone with MAO inhibitors, serotoninergic drugs, medications that prolong QT intervals
  - Severe liver dysfunction

Opioid titration (*refer to the Guideline - Pain Management – Opioid titration)*

Opioid toxicity (*refer to the Guideline - Pain Management)*

References

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