

Opioids

Introduction to opioids

- Opioids are commonly used in the context of pain and palliative care.
- Junior doctors will often be asked prescribe these drugs and whether it is starting a patient on it for the first time, or writing up an admitting drug chart it is helpful to understand a bit more about opioids and what adverse effects to look out for.

Pharmacology of opioids

- **Types of Opioids**
 - **Natural opiates: codeine, morphine**
 - **Semi-synthetic opioids: oxycodone, hydrocodone, diamorphine, buprenorphine**
 - **Synthetic opioids: methadone, fentanyl**
- **Weak Opioids vs Strong Opioids**
 - **Weak:** codeine, dihydrocodeine
 - **Strong:** tramadol, morphine, oxycodone, fentanyl, buprenorphine, diamorphine, methadone
- **Morphine Metabolism**
 - Opiates are predominantly metabolised by the liver where they undergoes 1st pass metabolism
 - 2 main metabolites are M3G and M6G (morphine-3 or 6-glucononide)
 - Well tolerated in patients with mild to moderate hepatic impairment
 - Morphine metabolites are then excreted by the kidneys
 - Caution in patients with renal impairment as the metabolite will not be excrete as fast leading to risk of overdose over time

Prescribing opioids

- WHO principles of cancer pain management
 - **By the mouth** - preferred first line route
 - **By the clock** - persistent pain responds better to regular analgesia than PRN
 - **By the ladder** - WHO pain ladder
 - **For the individual** - see pain pages {link}
 - **Attention to detail** - review response regularly
- Morphine is the first line strong opioid of choice in palliative care.
- Consider what route is best to manage the pain
 - Oral route is first line but if the patient is vomiting or unable to take medications orally, subcutaneous injection may be preferred.
- Start with immediate release preparation (IR)
 - Once the person's opioid requirements are established you can switch them to a modified release preparation or patch.

Cautions with morphine (i.e. you can still prescribe it but be aware of how its effect might be different)

- Caution in patients with renal and hepatic impairment (not excreted so quickly – more risk of overdose)
- Caution in the elderly (tend to need lower doses, more inclined to become delirious with opiates)
- Caution in inflammatory bowel disorders (may increase complication rate including toxic megacolon)
- Caution in obstructive airways disease (can lead to respiratory depression, risking CO₂ retention)
- Caution in epilepsy (may lower the seizure threshold - uncommon)

Side effects of morphine

- Once started on an opioid remember to regularly review for common side effects which include the list below (*the * indicates toxicity: immediately review and discussion with specialist palliative care team*)
- Constipation and nausea
- Dry mouth
- Confusion*
- Drowsiness *
- Myoclonus *
- Hallucinations *
- Pinpoint pupils * (can be present in chronic opioid use)
- Respiratory depression if severe (RR<8) *

Peak plasma concentrations morphine

- Immediate release (oral) – levels usually peak within the first hour, effect lasts for 4 hours
- Modified release (oral) – levels usually peak at 2-6 hours and effect lasts for 12 hours.

Example starting prescription of morphine

- Ensure that you read local and national prescribing guidelines and refer to relevant formularies.
- NB: PRN doses should be approximately 1/6 of the total dose received in a 24 hour period
- **Moderate pain:**
 - Morphine Sulphate IR (oramorph) 2.5mg 4-6 hourly regularly (i.e. QDS or six times per day)
 - AND
 - Morphine Sulphate IR (oramorph) 2.5mg PRN max 2 hourly
- **Severe pain:**
 - Morphine Sulphate IR (oramorph) 5mg 4-6 hourly regularly (i.e. QDS or six times per day)
 - AND
 - Morphine Sulphate IR (oramorph) 5mg PRN max 2 hourly
- **NB.** if starting a regular opioid remember to start a laxative (e.g. Macrogol I sachet BD orally)

Dose calculations in opioids

- When calculating opioid doses, switching to an alternative opioid or switching route doses are usually referred to by their strength relative to oral morphine.
- It always helps to refer to a dose calculation chart when prescribing a new opioid to give you an idea of how much the patient is receiving in a 24 hour period.

Useful opioid dose calculations

- Codeine
 - Codeine 60mg = 6mg oral morphine (divide by 10)
- Tramadol
 - Tramadol 100mg = 10mg oral morphine (divide by 10)
- Morphine
 - Morphine sulphate 10mg iv = morphine sulphate 20mg PO (multiply by 2)
 - Morphine sulphate 10mg sc = morphine sulphate 20mg PO (multiply by 2)
- Oxycodone
 - Oxycodone IR 5mg PO = morphine sulphate IR 10mg PO (multiply by 2)
 - Oxycodone 5mg sc = morphine sulphate IR 20mg PO (multiply by 4)
- Patches
 - Patches have varying equivalent doses and a dose equivalent range is often cited.
 - Buprenorphine patch normally changed every 7 days

- Buprenorphine 10 micg/hour = 20mg morphine sulphate PO in 24 hours
- Buprenorphine 20 micg/hour = 45 mg morphine sulphate PO in 24 hours

- Fentanyl patch normally changed every 3 days (72 hours)
- Fentanyl 12micg/hour = 45 mg morphine sulphate PO in 24 hours
- Fentanyl 25 micg/hour = 90 mg morphine sulphate PO in 24 hours.

Toxicity

- This is quite commonly seen in the acute hospital setting or on the wards. The basic steps in management are the same but they differ slightly in naloxone dosing:

1. Opiate toxicity in patients on regular long term opioids

- Remember these patients are **opioid dependent** and may go into withdrawal if opioids are stopped completely – assess analgesic requirements and discuss with specialist palliative care team.
- This should be treated this as an emergency: contact the palliative care team immediately.
- Treat from an ABCDE perspective including:
 - Head tilt / jaw thrust / chin-lift +/- airway adjuncts if signs of airway compromise
 - Oxygen if sats <95%)
 - IV access
 - Check pupils and glucose
- Stop opioids and remove any patches (e.g. fentanyl or buprenorphine – ensure ALL have been removed)
 - If there is evidence of reduced GCS and respiratory depression it may be necessary to administer naloxone to reverse some of the toxic effects.
 - Respiratory depression can be defined as:
 - Respiratory rate <12 AND cyanosed or difficult to rouse
 - Respiratory rate <8
- The recommended dose for adults who are receiving chronic opioid/opiates is **100 to 200 micrograms (1.5 to 3 micrograms/kg) by intravenous injection.**
 - If there is little or no response this can be repeated every 2 minutes.
 - **NB. Higher doses of naloxone than this in chronic may result in a cardiac arrest**
 - Note that if the patient is not compromised from an airway or breathing perspective it may be appropriate to simply stop all opiates, remove any patches and wait for the opiate effects to wear off (naloxone may not be necessary)
- Treat the underlying cause of the toxicity e.g. infection/ acute renal failure secondary to dehydration

2. Opioid toxicity in patients who are not on regular long term opioids

- Assess from an ABCD perspective as above
- Stop any opioids that have been recently started – remember to look for any new patches
- If there is evidence of reduced GCS and respiratory depression (see above) you will need to give naloxone to reverse the toxic effects
 - The dose of naloxone recommended by the BNF *for patients not on long-term opiates* is 400 micrograms to 2mg via intravenous injection
 - If there is no response, the initial 400mcg dose can be repeated at intervals of two to three minutes to a maximum of 10mg