Anticipatory prescribing and end of life considerations

Dr Stephanie Lippett
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Opiates

• Not all patients experience pain during their illness but symptoms are unpredictable

• Guidance suggests diamorphine but alternative opiates can be used

• Remember to write up sliding scales of doses as this allows the nursing team to step up/step down the analgesia as required
Opiates

• If the patient is symptomatic remember to give a stat dose of analgesia as well as commencing the syringe driver.

• When writing up a syringe driver you need to convert all regular and PRN oral doses of opiates taken in the last 24 hours.

• If the patient is on fentanyl-keep the patch on and use PRN s/c opiates for breakthrough.
Opiates

• Remember to increase the PRN dose of opiates when the regular dose is increased.

PRN S/C

doses = \(\frac{1}{6}\)th of total daily opiate dose

\[\frac{1}{5}\]th fentanyl patch dose (diamorphine) = \(\frac{1}{6}\) of total opiate dose

• PRN doses are usually written up for 4 hourly but at the end of life patients can require stat doses more frequently (1-2 hourly).

• When calculating doses be sensible and round down to a usable dose e.g. if \(\frac{1}{6}\)th = 6.66mg round down to 5mg.
The Syringe Pump

• Useful in certain circumstances
  • Vomiting patients
  • Patient no longer swallowing
  • For quick symptom control and dose titration

• Opiate Dose = total 24 hour oral opiate dose/2 (morphine/oxycodone) /3 (diamorphine)(+ any subcut doses).

• Opiate naive patients- start with PRN dosing and add into syringe driver if needs 2+ PRN doses.

• Usually stick with same opiate as oral prep
The Syringe Pump

- Keep same dose fentanyl patch on - replace every 72 hours as normal.
- Breakthrough doses need to take fentanyl patch into account as well as pump drugs
  - 1/6 pump dose + 1/6 of equivalent opiate dose of patch (diamorph=1/5 fentanyl patch)
  - Add both together to get total breakthrough dose
  - Patch breakthrough dose will remain constant
4 classes of opiates

- Phenanthrenes- most of the opiates we use codeine/tramadol/morphine/diamorphine/oxycodone
- Benzomorphans- loperamide
- Phenylpiperidines- fentanyl/alfentanil/pethidine
- Diphenylheptanes- methadone

Useful to know in patients with severe allergies-can change out of group
Choice of drug

- Effectiveness is much the same with all strong opiates
- Choice is based on
  - cost
  - local guidelines
  - mode of administration
  - availability
  - side effect profile
  - personal choice
  - renal impairment
  - volume in the syringe driver
Which opiate to choose?

- Recent nice guidelines not prescriptive-person centred care

- Morphine = cheapest
  - All conversion tables work on morphine equivalent

- Diamorphine = 1st line in Rochdale
  - Relatively cheap compared to other opiates
  - Dry powder amps
  - Useful when volume an issue in the syringe driver
  - Simple to work out fentanyl breakthrough dose
  - Various strength vials-5mg/10mg/30mg/100mg/500mg-
    consider dose patient is on (S/Driver and breakthrough)
  - 1/3 oral morphine dose- Reduce dose in renal impairment
    (eGFR <50) or use alternative opiate
Which opiate to choose?

- **Oxycodone**
  - More expensive
  - Useful if side effects of morphine not tolerated
  - Better renal profile than morphine but still not recommended in end stage renal failure. Reduced dose needs to be considered if eGFR<50
  - 1.5-2 x as potent as morphine (some anecdotal evidence suggests equal potency subcut)
  - ? Better for bone pain - evidence not convincing
  - Various strength ampules (10mg/ml, 20mg/2ml, 50mg/ml)
  - Volume can be an issue in the syringe driver with larger doses
Which opiate to choose?

• Fentanyl patches
  • Topical-useful for swallowing issues
  • Less constipating than other opiates (more lipid soluble therefore crosses BBB easier- lower doses required to give same effect of other opiates)
  • Overcomes some compliance issues
  • Sometimes accepted by patients reluctant to take anything with ‘morphine’ in the name.
  • 12-48 hours to reach max effect-only suitable for stable pain as titrating up the dose not easy
  • 17 hours to clear drug after removal of the patch-drug reservoir.
  • Better renal profile than morphine/oxycodone
Which opiate to choose?

• Fentanyl/ alfentanil injections
  – Do not rely on the kidney for excretion
  – Recommended when the eGFR is <30
  – Drugs of choice when eGFR < 20
  – Not removed by dialysis
Cost comparison

- Morphine
  - 10mg/ml 10 amps = £9
  - 30mg/ml 10 amps = £9
- Diamorphine
  - 10mg 5 amps = £15
  - 30mg 5 amps = £14
- Oxycodone
  - 10mg/ml 5 amps = £8
  - 50mg/ml 5 amps = £70
- Fentanyl patch
  - 12mcg 5 patches = £12
  - 100mcg 5 patches = £58
- Fentanyl inj
  - 100mcg/2ml 10 amps = £14
- Alfentanil inj
  - 1mg/2ml 10 amps = £7
  - 5mg/10ml 5 amps = £16
Drug Prescribing Issues

• Computer generated oramorph- 6 hourly oramorph dose BUT some patients need another dose after 30-60 mins

• Out of hours drug availability- anticipate in hours

• When the opiate dose in the syringe driver increases the dose of the breakthrough opiate may need to be increased- breakthrough doses are calculated 1/6 of the total daily opiate
Things to remember

• Consider psychological/spiritual/social issues when pain difficult to control

• symptom control issues -contact hospice for advice/ OPD review.
Anticipatory prescribing

- Midazolam- 10mg/2ml amps x10
- Glycopyrronium- 600mcg/3ml amps x10
  (200mcg/1ml amps ok for breakthroughs but use a lot of amps for S/Driver)
- Levomepromazine 25mg/1ml amps x10
- Opiate- opiate naïve = x10amps, if on opiate no. of amps depends on dose needed
  (need to calculate enough for several days + breakthrough doses)
Nausea and vomiting

- 50% of patients with advanced cancer experience problems with N&V
  (Twycross, Introducing Palliative Care. 1999)

- Think about a reversible cause and manage this

- Target anti-emetic to suit the most likely cause

- Consider route of admin-? Need syringe pump
Nausea and vomiting

- If oral antiemetic working, consider continuing with it subcut-don’t fix what isn’t broken

- Nice advocate Individualised anticipatory prescribing

- Levomepromazine often chosen re duel use for sedation and no incompatibilities unlike some of the anti-emetics
Other possibilities

• **Metoclopramide** - useful when gastric stasis is a problem but shouldn’t be used in patients with intestinal obstruction

• **Cyclizine** - broad spectrum anti-emetic but can precipitate with large doses of diamorphine and should be used with caution in patients with severe heart failure

• **Haloperidol** - useful for drug induced emesis but can precipitate at large concentrations.
Breathlessness

- Breathlessness = a subjective experience of breathing discomfort

- 70% of patients with cancer suffer from breathlessness in the last few weeks of life (Twycross, Introducing Palliative Care, 1999)

- 25% experience severe symptoms in the last week
Management of breathlessness

• Correct the correctable
  • Antibiotics-infection/COPD
  • Inhalers/nebulizers-bronchospasm
  • Oxygen-hypoxia
  • Steroids-obstruction/ lymphangitis/ asthma
  • Radiotherapy-obstruction
  • Drainage of fluid-ascites/effusion
  • Diuretics-CCF/ascites/ lymphangitis
  • Anticoagulation-PE
Management of Breathlessness

• Supportive non drug treatments
  • Anxiety management/ psychological support
  • Energy conservation
  • Fan/open window
  • Positional advice
• Drug treatments
  • Anxiolytics-reduce panic and anxiety
  • Oxygen-not always needed as patient not always hypoxic. Can be subjectively beneficial without hypoxia

• Drug treatments
  • Opiates-reduce respiratory drive and perception of breathlessness
    QDS oramorph (+PRN for pain)
    ¼ PRN dose-mild breathlessness
    ½ PRN dose –moderate breathlessness
    100%-150% PRN dose-severe breathlessness
  • Sedation in severe breathlessness/terminal agitation
Opiates

• Opiates can also be used to help breathlessness- off licence use

• Dose is the same as the breakthrough PRN dose of whichever opiate is written up for pain relief but can use smaller doses if symptoms not severe.

• Work by decreasing the rate of breathing (decrease the ventilatory response to hypercapnia/hypoxia and exercise). They do not cause respiratory depression if given orally/IM or s/c.
Opiates

• Because of this mechanism of action they are safe for all end stage breathlessness (including COPD)

• Initial treatment includes supportive measures like opening windows/fan/repositioning/considering O2 etc. and treating reversible causes with non aggressive measures like nebulizers/dexamethasone

• Other drugs that can be useful, esp. when anxiety is a large factor, include Lorazepam 0.5mg prn oral/sublingual or midazolam (doses as for restlessness) s/c.
Terminal restlessness

Aka-  terminal agitation
agitated delirium
terminal anguish
terminal distress

Occurs in up to 80% of patients near the end of life and is a collection of signs of central nervous system irritability
Features

- Decreased level of consciousness
- Restlessness
- Agitation
- Distressed vocalizing
- Twitching
- Myoclonic jerking
- Recurrent fitting
- Memory loss
- Disorientation/confusion
- Hallucinations/paranoia
management

• Distressing for the family and so it is important to explain and reassure

• Important to consider an underlying cause as it may be reversible

• Supportive measures and sedative medication are often needed
Supportive measures

• Reassure patient and family
• Familiar surroundings and faces
• Lighting and noise reduction
• Risk assessment-ensure patient/carer safety
• Look for and manage reversible cause
• Assess medication-is there a need to continue?
Sedative medication

Various medications can be used depending on symptoms and co-existing problems

- **Benzodiazepines (BDZ)** - diazepam/lorazepam/midazolam/temazepam - useful for anxiety and to aid sleep

- **Levomepromazine** - useful for agitation/paranoia esp. where antiemetic required. NB sedative dose higher than usual antiemetic dose (25-200mg)
Sedative medication

- **Haloperidol**-useful for agitation/paranoia/fear esp. where antiemetic needed

- **Barbiturates**(phenobarbitone)-last resort medications. Useful for severe intractable insomnia/fitting/BDZ paradoxical agitation
Midazolam

- Chosen as one of the end of life drugs because of its various uses

- Used for terminal restlessness/myoclonal jerks and fitting

- Doses differ for the different uses—doses start lower for terminal restlessness/myoclonic jerks.
Respiratory secretions.

• Respiratory secretions in the last days or hours of life are not uncommon.
• They can be distressing for relatives but are unlikely to distress the patient unless they are pronounced and the patient has awareness of them.
• These secretions are difficult to treat, once established, therefore attempts to PREVENT them can be more effective than treating an established problem.
General measures.

• There are non-medical measures that might help:
  • REPOSITIONING can be helpful.
  • Try tipping the bed head-up if the rattle is in the pharynx, to assist drainage.
  • REASSURANCE and EXPLANATION to relatives.
  • The relatives may be acutely aware of any changes while they wait with their loved one. Explanation that, mostly, secretions won’t be distressing the patient can help.
Medical (drug) measures.

- Anticholinergic (antimuscarinic) drugs will reduce secretion of fluids like saliva and intestinal juices.
- THEY DO NOT REMOVE SECRETIONS THAT ARE ALREADY PRESENT.
- There is only moderate to low evidence from studies that pharmacological treatments help secretions at end-of-life.

Remember: they will cause a dry mouth, so could add symptoms to the patient. Good on-going mouth care is important.
Anticholinergic drugs.

- **GLYCOPYRRONIUM.** This is non-sedating.

- **HYOSCINE HYDROBROMIDE.** This is sedating.

- **HYOSCINE BUTYLBROMIDE** (e.g. Buscopan). This is non-sedating.
Glycopyrronium.

• Glycopyrronium is given as s/c doses 200 micrograms (mcg) PRN up to every four hours and used in syringe driver.
• Maximum 1200 mcg/24 hours.
• More potent than hyoscine hydrobromide as an anti-secretory but in practice has about the same efficacy as it. Either will REDUCE the rattle in about 1/2 to 2/3 of patients.
• Lower doses can be effective if renal impairment co-exists.
• It is not sedating.
Hyoscine hydrobromide.

- Hyoscine hydrobromide is given s/c 400mcg PRN up to every 4 hours and can be used in a syringe driver.

- Maximum 2000 mcg/24 hours.

- Similar efficacy to Glycopyrronium but it is SEDATING.
What if secretions persist despite medications?

- IF MAXIMAL DOSES of either Glycopyrronium or Hyoscine DO NOT WORK, THEN DRUG MEASURES PROBABLY WON’T.

- It might be worth considering a swap, but using both together is unlikely to bring more benefit and is more likely to cause side effects.
Suction.

• Suction should be considered only in severe cases where the secretions are accessible.
• The patient needs to be unconscious to tolerate it and it could be argued that they would be unlikely to be distressed by the secretions
• Anecdotally, suction seems to stimulate more secretion itself.
Things to remember

• Terminal restlessness—very distressing for families. Patients can deteriorate very quickly—anticipatory drugs at home.

• Carry DNACPR form/prescribing authorisation sheets in bag—saves having to go and find one

• Consider stage of illness—before referring on for management and treatment if PPC is home
Things to remember

• Fitting risk- starting dose of midazolam in driver is higher (20-30mg) as is PRN dose (increase range to 10mg).

• Drug provision- need to take into account concentration and volume in syringe pump (e.g. glycopyrronium) as well as PRN doses needed (amount of vials prescribed).

• Compatibility/ volume issues -2 syringe drivers
Drug Prescribing Issues

• **Drug provision**-need to consider how long the drug will last for-how many vials in the syringe pump + breakthrough doses
• **Anticipatory prescribing**-need to consider current oral dose and range of dose when prescribing
• Consider if the drug is working for the pain if needing PRNs +++ (? Neuropathic agent/NSAID needed) Don’t automatically increase syringe driver dose
Drug Prescribing Issues

- Consider drug availability out of hours-prescribe enough to last until in hours

- Remember to leave the prescribing advice in the house so meds can be administered and regularly review (re-sign monthly)

- Take the prescribing advice/conversion tables with you when you get called out to a terminally ill patient
finally

Some important things to remember

• The advice is a guide and not set in stone—NICE guidelines advise individualised prescribing

• Prescribe in anticipation as symptoms are unpredictable and patients deteriorate quickly

• Prescribe a range of doses when writing up the medications and indicate a starting dose—saves time

• Remember to recalculate opiate PRN doses when the regular doses are changed
finally

Some important things to remember

• Remember to regularly update special notes with BARDOC—can undo all the good work done to achieve a good death if forgotten.

• DOLS/DOLIC—patients who die under a deprivation of liberty order no longer automatically need referral to the coroner.