

Anticipatory prescribing and end of life considerations

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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 = $1/6^{\text{th}}$ of total daily opiate dose

$1/5^{\text{th}}$ fentanyl patch dose (diamorphine) =

$1/6$ of total opiate dose

- PRN doses are usually written up for 4hourly 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 $1/6^{\text{th}} = 6.66\text{mg}$ 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
 - $\frac{1}{6}$ pump dose + $\frac{1}{6}$ 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 ampoules (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 10amps = £9
- Diamorphine
10mg 5amps =£15
30mg 5 amps=£14
- Oxycodone
10mg/ml 5amps = £8
50mg/ml 5amps = £70
- Fentanyl patch
12mcg 5 patches =£12
100mcg 5patches = £58
- Fentanyl inj
100mcg/2ml 10 amps = £14
- Alfentanil inj
1mg/2ml 10 amps = £7
5mg/10ml 5amps = £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 $\frac{1}{6}$ 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 dual use for sedation and no incompatibilities unlike some of the anti-emetics

Levomepromazine 2

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)
 - 1/4 PRN dose-mild breathlessness
 - 1/2 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.

- GLYCOPYRROLONIUM. 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