

Guideline: Pain in Palliative Medicine

These guidelines have been drawn up to help establish initial appropriate palliation of patients with advancing disease; they also suggest when advice should be sought from your local Palliative Care Team. There is also a useful section in the front of the BNF: 'Prescribing in Terminal Care'.

Type of pain

Quality (type)

Severity

Radiation

Precipitating and relieving factors

Timescale for each separate site of pain

(Often several pains co-exist)

Pain charts and pain scoring scales are often useful

Cause of pain

Pain has many dimensions beyond those physically related to the disease; psychological, social and spiritual factors can be important. Thus the concept of TOTAL PAIN is useful in assessment.

Clarify the likely cause and type of pain:

- Somatic/Visceral pain (often dull, aching) - follow WHO analgesic ladder.
- Bone pain - consider NSAID ± opioids. Bisphosphonates can help. Radiotherapy referral should be considered.
- Neuropathic pain (burning, numbness or altered sensation) – trial of low dose antidepressants or anticonvulsants and discuss with Palliative Medicine (see below).
- Non-infective pleuritic pain, liver capsule pain, joint pain - consider NSAID or steroids.
- Myofascial pain, muscular pains or spasm - consider paracetamol, muscle relaxant and complementary therapies.
- Infection - consider antibiotics and analgesics.

Analgesic prescribing

For initial prescribing there is no need to look beyond the WHO ladder:

Step 1 – (usually mild) pain - non-opioids

e.g. paracetamol (1g qds), NSAIDs (ibuprofen 200 mg – 400 mg tds to qds consider gastro-protection e.g. lansoprazole 30 mg mane with all but the fittest patients – almost all cancer patients are at risk).

Step 2 – (usually moderate) pain - weak opioids

e.g. codeine, dihydrocodeine:

➤ often cause constipation and other opioid side effects.

Combined preparations fall into 2 groups:

➤ low opioid content – cocodamol (8/500), codydramol.

➤ higher opioid content - cocodamol 30/500 (Tylex, Solpadol)

Give group 1 and 2 drugs regularly but generally no more than qid. if containing paracetamol or NSAID. If the pain is still persists move to step 3 drugs.

In general codeine is 1/10th the potency of oral morphine.

Tramadol is often classed as a moderate strength opioid, but has similar potency to other strong opioids (100mg tramadol approx = 20mg morphine).

Step 3 – (usually severe) pain - strong opioids

e.g. morphine, diamorphine, fentanyl, oxycodone, hydromorphone, methadone.

Morphine

Use morphine as first line unless there is a history of previous adverse effects with it. Titrate the dose to obtain pain control with normal release morphine sulphate solution or tablets –

Morphine solution - Oramorph available in 2 strengths; 10mg/5ml, and a concentrated 100mg/5ml liquid. Alternatively use normal release morphine sulphate tablets 10mg, 20mg, or 50mg.

Titration of morphine to obtain pain control.

If changing from weak opioid, start with 10mgs every four hours and when required.

If elderly or group two analgesic has been omitted, start 5mg every four hours + prn.

If there is significant renal impairment you may need to reduce both dose and frequency, or discuss with Palliative Care Team using an alternative from the outset.

Using Morphine contd.

Monitor the patient's response every 12 - 24 hours; if still in pain increase by 30-50% until pain is controlled or patient develops side effects (remember not all pain responds completely to opioids).

i.e. 5 → 7.5 → 10 → 15 → 20 → 30mg.

NB if pain is not improving within 48hrs, contact Palliative Care Team for advice.

Once pain is controlled consider slow release morphine for maintenance.

To convert dose

- 6 x 4 hrly oral morphine = 24 hr morphine dose
- $\frac{24 \text{ hr morphine dose}}{2} = 12 \text{ hrly slow release morphine dose}$

For breakthrough pain

- if patient is on normal release morphine 4 hourly, give 100% of the 4 hourly dose as often as needed between doses if needed and consider increasing the regular dose while monitoring for signs of opioid side effects and/or toxicity.
- if patient is on slow release morphine 12 hourly, give one sixth of the 24 hourly dose as normal release as needed, and consider increasing the regular dose.

Patients who are vomiting or unable to swallow

- the opioid can be given as a continuous subcutaneous infusion of diamorphine via a syringe driver.

- to convert dose:

$$\frac{24 \text{ hr oral morphine}}{3} = 24\text{hr s/c diamorphine}$$

Subcutaneous boluses of 1/6th total daily dose are used p.r.n.

Other opioids

Alternative opioids and alternative modes of administration are used in the following circumstances:

- where the pain is clearly opioid responsive BUT
- where side effects (see below) limit the dose such that analgesia is not achieved
- where renal impairment might predictably cause accumulation of drug or metabolites
- where swallowing difficulty or vomiting makes oral administration ineffective

The rationale is not that an alternative opioid is stronger or better and so will succeed where morphine has failed. The hope is that a different side effect profile will better tolerated and thus allow increased doses to be used to achieve analgesia.

Switching is not appropriate if morphine has been used up to toxic doses (see below) without achieving pain relief.

Fentanyl

Available as 72 hours transdermal preparation which has specific uses.

It should be used only for stable pain and after opioid responsiveness has been established.

Possible indications:

- persistent severe side effects with morphine in opioid-sensitive pain, particularly nausea, vomiting and constipation, but also drowsiness and hallucinations.
- oral administration is not possible (instead of a syringe driver in longer term patients).
- poor compliance.
- poor renal function.

It is currently advised to titrate up the patient's opioid dose using normal release 4-hourly morphine. This can then be converted to the appropriate fentanyl patch for longer term pain control if desired.

A recommended conversion scheme from oral morphine to fentanyl patch is given below:

Oral 4-hourly morphine (mg)	Oral 12-hourly morphine (mg)	Fentanyl patch (mcg/hr)
<25	<70	25
25 – 35	70 – 110	50
40 – 50	115 – 150	75
55 – 65	160 – 200	100
70 – 80	210 – 240	125
85 - 95	250 - 290	150

Alternatively one can simply divide the total daily morphine dose (in mg) by three and use the nearest patch strength in mcg/hour, rounding down if pain is controlled, and up if it is not.

By this calculation diamorphine in mg/24 hours is fentanyl in mcg/hour.

Care is needed with pain management when starting or stopping fentanyl patches. It takes some 12 hours before a patch begins to work fully, and so alternative pain relief must cover this time.

A patch leaves some 12 hours of fentanyl behind following removal. The new analgesic must be timed accordingly to avoid opioid excess.

When converting back from fentanyl to morphine / diamorphine, allow for the greater potential of these to cause sedation, which may have been the reason for fentanyl in the first place - advice should be sought from Palliative Care Team.

As required doses are available as fentanyl lozenges (Actiq) with which experience is limited and results variable. Alternatively, if the patient can swallow, use oral morphine, or subcutaneous diamorphine if they cannot. Oral and injected oxycodone are alternatives – see below.

Oxycodone

An alternative opioid which may be used if the patient has persistent problems - dysphoria, hallucinations or drowsiness on therapeutic doses of morphine. Because it has dopamine antagonist properties it may cause less nausea. It has theoretical advantages in renal failure as it lacks active metabolites.

1mg oral oxycodone = 2mg oral morphine.

Oxycodone normal release preparation is available as liquid, concentrated liquid or capsules (Oxynorm);

and as sustained release 12hrly tablet preparation (Oxycontin), used 12 hourly (cf Zomorph).

It has recently become available in injection form, used in the same way as diamorphine is for those on oral morphine preparations. The conversion factor from oral to injected oxycodone is to divide by 2.

It is probably the current first choice when switching opioid from morphine or diamorphine.

Hydromorphone

It is best to seek specialist advice before using hydromorphone.

Another alternative opioid where CNS side effects from morphine are persistent or unacceptable. It is available as immediate release capsules, in just two strengths of 1.3 and 2.6 mg. These strengths were devised on the presumption that it is 7.5x more potent than oral morphine

ie oral morphine 10mg = oral hydromorphone 1.3mg.

Some have suggested the factor should be 5x.

It is also available as controlled release capsules. It can also be obtained in specialist hospices as an injection, but supplies are unreliable.

It has been used in renal failure to good effect, but does have an active, renally excreted metabolite -HM3G.

Methadone

Most would recommend that this drug be used only by specialists in Pain Relief or Palliative Care and even then only in a unit where staff are trained and experienced in its use.

Opioid Conversion Factors

Should there be a need to switch from one opioid or route to another, a chart of conversion factors is attached.

Opioids to avoid

Pethidine Injection

- only lasts for 2-2½ hours.
- toxic metabolite norpethidine accumulates causing convulsions when given regularly.

Common side effects of opioids

Constipation

Always prescribe aperients prophylactically at the outset .

e.g. senna and docusate in combination or a dantron combined with docusate (codanthrusate) or poloxamer (codanthramer).

More resistant constipation may be helped by the use of movicol or codanthramer strong.

In intestinal obstruction, stimulant laxatives should be avoided.

Nausea and Vomiting

In about one third of patients opioids cause nausea +/- vomiting via the brain chemoreceptor trigger zone (CTZ). Haloperidol 0.5 - 3mg at night (centrally acting dopamine antagonist) is therefore useful.

Metoclopramide also works. Domperidone ought to work, and is without central/extrapyramidal effects; it can also be given rectally.

If nausea, vomiting or constipation persist, consider fentanyl as described above.

CNS side effects

These are common – maybe 20% of patients, and do not necessarily represent toxicity. Initially drowsiness can be troublesome, though usually is short lived. More concerning are the dysphoria, and pschotomimetic effects which can render a given opioid intolerable.

They can be treated with drugs but it is more logical to explore alternatives, other than at the end of life where the issues and expectations are different.

Oxycodone, hydromorphone and fentanyl are all useful alternatives (see above). It is worth discussing this with the Palliative Care Team.

Opioid toxicity

Careful use of opioids following the above guidelines makes this unusual. However opioid toxicity should be considered if the patient is:

- restless, confused or has hallucinations – (may be intolerance, not necessarily toxicity).
- drowsy.
- has small pupils.
- has myoclonic jerks.
- has a decreased Respiratory Rate (<12/min) (although this may occur naturally in a dying patient)

All opioids can do this, and an alternative opioid is not the answer.

If opioid toxicity is suspected

Stop the patient's opioids and discuss with your senior colleagues and / or the Palliative Care Team immediately.

Monitor the patient's respiratory rate hourly.

If possible avoid giving naloxone to anyone established for any length of time on opioids, unless to save the life of someone with respiratory depression; although it will reverse the patient's respiratory depression, it will also reverse any analgesia with major pain and distress as a result.

It should be used diluted and titrated according to response and may need to be given as an infusion as a bolus only lasts for about an hour. This is particularly important if the patient is on long acting opioids, or is renally impaired and thus retaining opioids and metabolites.

Remember: Respiratory depression may be prolonged for up to 36 hours if the patient was on a slow release preparation.

Ask senior colleagues for help, including an anaesthetist.

Once respiration has returned to normal and pain begins to return give a breakthrough dose (i.e. 50% of the four hourly dose). Then recommence opioids with a 30-50% dose reduction.

Neuropathic pain – outline

It is probably best to seek specialist advice.

In about half of the cases the pain will be controlled reasonably well using the WHO ladder approach,

ie paracetamol, NSAID and opioids in combination.

For the rest the choice is between an antidepressant and an anticonvulsant or both.

Burning pain is said to respond best to tricyclics, usually amitriptyline, beginning with 10mg at night and titrating slowly.

For shooting pain it is thought that anticonvulsants may be best, and gabapentin is currently the most widely used. Opinions differ as to starting dose (100 – 300mg) and speed of escalation. These are grey areas in terms of evidence and can be difficult clinically as a result.

A final plea

- All analgesia is best given by mouth where possible.
- Injected drugs are not more potent, and are only more effective if swallowing or vomiting are issues.

- Intravenous analgesia using morphine is a fine way of patient and doctor managing post op pain. It is not a strategy for medium and long term pain control.
- Intramuscular analgesia is to be avoided in all circumstances. It hurts, causes bruising and bleeding, and risks damage to sciatic nerves and the like. And most palliative care or chronically ill patients have little or no “M” to put injections “I”.
- Subcutaneous injections are the recommended route for continuous infusion (except PCA) and for prn doses.
- Diamorphine is the recommended drug largely because it is a powder of which large doses can be dissolved in tiny volumes of water.

OPIOID CONVERSION CHART

PO codeine	PO morphine	SC diamorphine	PO oxycodone	SC oxycodone	PO Hydromorphone	TD fentanyl	New opioid and route
	x 10	x 30	x 20	X 40	X 50	nr	PO codeine
÷ 10		x 3	x 2	X 4	x 5	X 3	PO morphine
÷ 30	÷ 3		÷ 1.5	X 1.3	x 1.7	X 1	SC diamorphine
÷ 20	÷ 2	x 1.5		X 2	X 2.5	X 1.5	PO oxycodone
÷ 40	÷ 4	÷ 1.3	÷ 2		X 1.25	÷ 1.3	SC oxycodone
÷ 50	÷ 5	÷ 1.7	÷ 2.5	÷ 1.25		÷ 1.7	PO hydromorphone
nr	÷ 3	X 1	÷ 1.5	X 1.3	X 1.7		TD fentanyl

Doses are expressed as mg/24 hours, except fentanyl which is mcg/hour.

- Find the new opioid and route you are changing to on the RIGHT of the table
- Where the lines cross, read the conversion factor:
 x = multiply current opioid by this factor
 ÷ = divide current opioid by this factor
 nr = not recommended

****IMPORTANT POINTS TO NOTE** :**

- Equivalent doses of strong opioids cannot be exact and are therefore only a guide.
- When converting for reasons of toxicity remember to reduce the dose.
- As the dose of morphine increases e.g. >2 g/24 hrs, dose conversions will become **LESS** accurate. This could be due to an increased concentration of the metabolite M3G. M3G is thought to neutralize the analgesic effect of morphine by a non-opioid mechanism. Therefore when converting at high doses give only ½ to ¼ of the calculated equivalent dose, depending on whether there is opioid toxicity.
- Fentanyl patch strengths cover a range of other opioid doses. Use the patch strength nearest the arithmetic answer, rounded **DOWN** unless pain is not controlled then round up.
- Buprenorphine TD is not yet widely used. The approximate morphine equivalence is:-
 - 35 patch = 30-60mg morphine/24 hours
 - 52.5 patch = 60-90mg
 - 70 patch = 90-120mg
 - 2x70 patch = 120-240mg
 - round down unless pain is not controlled, then round up.
- Hydromorphone is manufactured as if the conversion factor from oral morphine is 7.5, hence the IR strengths of 1.3 and 2.6, equivalent to 10 and 20mg of morphine respectively. Some suggest a conversion factor of 4, not 5, depending on whether the switch is from morphine to hydromorphone, or vice versa.