



Opioid rotation for severe pain

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How do you get the best pain relief for your patients with cancer related pain? Opioids are widely used to treat cancer pain and are most effective when toxicity is managed and patients and their families understand and accept the pain-management plan.

Underlying principles

Common factors interfering with optimal opioid use are:

- Failure to maintain regular dosing (round the clock)
- Not providing a fast acting PRN medication (breakthrough/rescue treatment)
- Mistakes in dose equivalence
- Poor management of side effects

Good pain relief depends on sound medical assessment: the history (incl. site, severity and type of pain); examination; investigations; and formulation of a plan that is reviewed regularly review to ensure effectiveness.

Pain falls broadly into two types; nociceptive and neuropathic. The former tends to respond to simple analgesics such as paracetamol, NSAIDs and opioids. The latter often needs adjuvant medications such as a tricyclic antidepressant or an anticonvulsant.

Remember also the role of radiotherapy and sometimes chemotherapy in pain relief. Nerve blocks and spinal analgesia also have a place in very resistant pain.

Opioid rotation (switching) has become common practice to manage either:

- Severe side effects such as nausea, delirium, myoclonus or hallucinations, or
- Inadequate pain relief.

Morphine was the mainstay of opioid therapy (and is still the most widely prescribed worldwide) but we now have more choices. These choices bring benefits to the patient but at times cause more confusion for us as we prescribe drugs less familiar to us.

Why rotate?

Opioids work by binding to opioid receptors in the peripheral and central nervous system. Three major receptor subtypes exist - mu, kappa and delta. They each demonstrate specific binding affinities and are found in varying proportions in different sites.

Morphine is a strong mu receptor agonist with some action also at kappa receptors. Other opioids bind differently, so that rotating (switching) from one opioid to another gives a different binding affinity and a different profile of efficacy and toxicity.

Incomplete cross tolerance between opioids means that the dose of a new opioid may need to be less than the calculated equipotent dose of the previous opioid, to avoid toxicity or overdose.

Opioid alternatives, beyond morphine

These now include:

Oxycodone (Oxycontin™ a slow release BD preparation; and as Oxynorm™ and Endone™

both immediate release formulations).

Fentanyl (Durogesic™ patches, changed third daily; and Actiq™ lozenges for breakthrough pain).

Hydroxymorphone (immediate release tablets, liquid, or injection – no slow release preparation yet in Australia).

Methadone (tablets and injections; no specific slow release preparation; because of the long half life care is needed to prevent accumulation and toxicity).

Key Points

- Rotating opioids may reduce side effects and/or improve pain control.
- Use the dose of morphine in mg per 24 hours as the basis for dose conversion.
- Switch with care, reducing the new drug dose by approximately 25%.
- More than one rotation may be needed during the treatment of the patient.
- Document clearly the reason for rotation.

N.B. 1300 558 655 Palliative Care Specialist on call - ring to discuss patients and topics such as rotation of opioids or to check dose calculations.

References available on request

CASE EXAMPLE

Mrs B (aged 56) has breast cancer and multiple bone secondaries. She was previously treated with hormonal therapy, chemotherapy and palliative radiotherapy to her spine. Her pain has escalated over the past 3 weeks so that she is now on MS Contin™ tablets (SR morphine) 160mg BD plus Sevredol™ tablets (immediate release morphine) 30 mg PRN, taken about 3 times a day. She has good pain relief but has developed delirium. On examination, there is no evidence of an infection, brain metastases, UTI or abnormal biochemistry (including calcium).

The decision is made to rotate her opioid. You consider two options: either convert to (a) oxycodone, or convert to (b) fentanyl. A new breakthrough pain plan will also be required.

Option (a):

1. Calculate the total daily dose of opioid in mg of morphine per 24 hours. Mrs B currently uses 410 mg morphine per day.
2. Oxycodone is approximately 1.5 times as potent, so the equivalent dose will be 280 mg per day.
3. In rotating opioids reduce the new drug dose by 25 % so the starting dose of oxycodone will be 210 mg per day. This will best be delivered as 100mg Oxycontin™ BD

Option (b):

1. Mrs B currently averages 410 mg morphine per day.
2. Equivalent fentanyl dose is approximately 125 microgram/hour patch, changed third daily. This is based on a 25 microgram patch delivering the equivalent of 60-90mg oral morphine per 24 hours.

3. Rotating opioid requires 25% decrease in new drug dose, so the starting dose of fentanyl will be a 100 microgram/hour patch. Care needs to be taken to allow for the slow onset of action of the patch - it will take at least 12 hours to reach therapeutic levels and many days to achieve steady state.

Calculation of PRN (breakthrough/rescue) dosing:

1. Generally a dose of 1/6 to 1/12 of the total daily opioid dose is used as the suggested PRN dose.
 - a. For oxycodone, PRN dose is 1/6 to 1/12 of 210mg i.e. 20 to 35 mg Oxynorm™. Oxynorm could also be used for PRN dosing for a patient on a patch.
 - b. If you choose to use Actiq™ lozenges it is less easy to predict the required dose. Current PBS authority guidelines demand that you start on the 200 microgram lozenge and titrate up.

