

## Morphine and oxycodone – what is the difference?

Morphine is considered internationally to be the opioid analgesic of choice in moderate to severe pain. It is used in many areas of medicine including musculoskeletal injury, post-surgery and in malignant disease.

Oxycodone is an opioid analgesic that became available in New Zealand in 2005. It has similar indications to morphine. This bulletin examines the similarities and differences between these two opioids and their place in clinical practice.

### Morphine

#### Indications

Morphine like other opioid analgesics is used peri-operatively and for acute, chronic, malignant and non-malignant pain.

#### Pharmacodynamics

Morphine is a mu opioid agonist with only minimal activity at other opioid receptors.

#### Pharmacokinetics

The oral availability of morphine is 20 - 40% which means that for every 10mg of morphine given orally 2 to 4mg reaches the systemic circulation. This is because of high first pass metabolism. Morphine has a short half life of 2 to 3 hours. Although morphine is extensively metabolised by glucuronidation, an active metabolite morphine-6-glucuronide is excreted renally ( $f_u = 0.9$ ). This may accumulate in patients with renal dysfunction and dose adjustment may be necessary.

#### Adverse effects

The adverse effects of morphine and opioids in general, include constipation, nausea and vomiting, drowsiness, confusion and hallucinations. As many of the adverse effects include central nervous system depression, this may be enhanced by other central nervous system depressants e.g. morphine plus cyclizine, particularly post-operatively. Tolerance develops over several days to the majority of adverse effects with the exception of constipation. The extent of the adverse effects varies with the opioid.

Patients should almost always be prescribed laxatives on initiation of opioids. Anti-emetics e.g. metoclopramide or haloperidol may also be required initially.

#### Formulations

Morphine is available as immediate release tablets (Severedol<sup>TM</sup> 10mg, 20mg) and liquid (RA-Morph<sup>TM</sup> 1mg, 2mg, 5mg, 10mg/mL), slow release tablets (LA-Morph<sup>TM</sup> 10mg, 30mg, 60mg, 100mg), slow release capsules (m-Eslon<sup>TM</sup> 10mg, 30mg, 60mg, 100mg, 200mg), suppositories (20mg, 30mg) and injections (morphine sulphate 10mg, 15mg, 30mg/mL, morphine tartrate 120mg/1.5mL, 400mg/5mL).

#### Dosing

Immediate release oral tablets and liquid are usually given four to six hourly. The slow release tablets or capsules are usually given twelve hourly as they release morphine slowly over this period. If converting from immediate release morphine to slow release the last dose of immediate release is usually given with the first dose of slow release. Many patients prescribed slow release morphine are also prescribed some immediate release tablets or liquids to be taken for "breakthrough" pain. The dose prescribed for each occasion is usually 1/5<sup>th</sup> to 1/6<sup>th</sup> of the 24 hour dose of slow release given four to six hourly.

#### When should morphine be used?

Morphine should be the first line opioid in most patients with moderate to severe pain. In patients with renal dysfunction, severe adverse morphine effects or morphine tolerance a change of opioid should be considered.

### Oxycodone

#### Indications

The indications for oxycodone are the same as for morphine and other opioids.

#### Pharmacodynamics

Oxycodone, like morphine is a mu opioid agonist with minimal activity at other opioid receptors.

#### Pharmacokinetics

The oral availability of oxycodone is approximately 80%, which means that for every 10mg of oxycodone given orally approximately 8mg reaches the systemic circulation. Oxycodone has a short half life of 3 to 4 hours, which is slightly longer than that of morphine. Oxycodone is metabolised by CYP2D6 to one or more active metabolites which are cleared renally. Dose adjustment may be necessary in patients with renal dysfunction. Concomitant administration of CYP2D6 inhibitors may affect the amount of analgesia produced and those patients who are 'poor' 2D6 substrate metabolisers may also be affected.

#### Adverse effects

Adverse effects of oxycodone are similar to those of morphine.

#### Formulations

Oxycodone is available as oral immediate release capsules (OxyNorm<sup>TM</sup> 5mg, 10mg, 20mg) and slow release tablets (OxyContin<sup>TM</sup> 5mg, 10mg, 20mg, 40mg, 80mg) only. An injection and oral solution may be available in the near future.

#### Dosing

Like morphine the immediate release capsules of oxycodone are usually prescribed four to six hourly. As oxycodone has a slightly longer half life many patients may be maintained on the six hourly dosing interval. The slow release tablets are prescribed 12 hourly. The slow release formulation is slightly different from that of morphine – oxycodone slow release tablets have an immediate release component followed by a slow release over 12 hours. This means that there is no need to give the last dose of immediate release with the first dose of slow release when converting from immediate to slow release oxycodone.

#### When should oxycodone be used?

Oxycodone may be a useful alternative to morphine in patients who have had severe adverse effects from morphine or in those who have developed tolerance to it i.e. useful in opioid rotation. Conversion between opioids is always difficult and there is little agreement internationally about the exact equivalence of oxycodone to morphine in both acute and chronic settings. In practice, as the oral availability of oxycodone is about twice that of morphine and the half life is similar, when converting from morphine to oxycodone halve the dose and titrate to pain. As oxycodone is metabolised by CYP2D6, patients who are taking CYP2D6 inhibitors (e.g. fluoxetine, terbinafine) or who have a slow CYP2D6 substrate metaboliser genotype should be monitored for toxicity. As the metabolites of oxycodone may be renally cleared, patients with renal dysfunction may experience some toxicity.