

## Morphine and Oxycodone - What is the difference?

Morphine is considered internationally to be the opioid analgesic of choice for the relief of 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 which has similar indications to morphine. Its place in therapy appears to be in patients in whom morphine use is ineffective or has resulted in adverse effects or tolerance. The use of oxycodone appears to be increasing within CDHB hospitals with \$57,090 being spent on it from July '09 to June '10 vs \$53,134 in the same period 08/09 and \$19,216 in 07/08 despite being considered second-line. Anecdotally the use of oxycodone as first-line therapy has become widespread throughout the CDHB.

### Morphine

#### Indications

Morphine, like other opioid analgesics, is used peri-operatively and for the relief of 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 largely 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. A major adverse effect is central nervous system depression, which may be enhanced by concomitant use of 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.

#### 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 of immediate release prescribed for each occasion is usually  $1/5^{\text{th}}$  to  $1/6^{\text{th}}$  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 moderate to severe renal dysfunction, severe adverse morphine effects, or morphine tolerance, a change of opioid should be considered. Seek specialist advice.

#### Formulations

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

Cost comparisons	immediate release	slow release	inj
10mg morphine	\$0.10-\$0.29	\$0.19	\$0.95
5mg oxycodone	\$0.15 -\$0.24	\$0.39	\$3.02* (10mg)

\*NB 10mg morphine inj is thought to be equivalent to 10mg oxycodone inj

### 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 70 to 80%, which means that for every 10mg of oxycodone given orally approximately 7 to 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 and 3A4 to one or more active metabolites that may accumulate slightly in patients with severe renal dysfunction. Concomitant administration of enzyme inducers and inhibitors may affect the amount of analgesia produced and those patients who are 'poor' 2D6 substrate metabolisers may also be affected. Dose adjustment may be necessary.

#### Adverse effects

Adverse effects of oxycodone are similar to those of morphine.

#### Dosing

Like morphine the immediate release formulations 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. "Breakthrough" doses of immediate release ( $1/10^{\text{th}}$  to  $1/12^{\text{th}}$  of the 24 hour dose initially) are also prescribed 4 to 6 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. Patients with renal impairment may experience less toxicity with oxycodone than with morphine.

#### Conversion from morphine to oxycodone

Conversion between opioids is always difficult and there is little agreement internationally on equivalent doses 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 oral morphine to oral oxycodone halve the dose and titrate to pain. When converting from morphine injection to oxycodone injection seek specialist advice. As oxycodone is metabolised by CYP2D6 and 3A4, patients who are taking CYP inducers or inhibitors or who have a slow CYP2D6 substrate metaboliser genotype should be monitored closely. As the metabolites of oxycodone may be renally cleared, doses should be decreased slightly in patients with severe renal dysfunction.

#### Formulations

Oxycodone is available as oral immediate release capsules (OxyNorm™ 5mg, 10mg, 20mg), immediate release liquid (OxyNorm™ 1mg/mL), slow release tablets (OxyContin™ 5mg, 10mg, 20mg, 40mg, 80mg) and injection (OxyNorm™ 10mg/mL, 1mL and 2mL).