

## Morphine and Oxycodone - Similarities, Differences and Conversions

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 \$66,297 being spent on it in the financial year July 2010 to June 2011 (vs \$57,090 from July 2009 to June 2010) despite being considered by many as a second-line opioid. Anecdotally, the use of oxycodone as first-line therapy has become widespread throughout the CDHB hospitals and on discharge.

### The Similarities

#### Indications

- relief of acute, chronic, peri-operative, malignant and non-malignant pain

#### Pharmacodynamics

- agonistic (stimulating) of mu opioid receptors with minimal activity on other opioid receptors.
- efficacy of both drugs is the same

#### Adverse effects

- constipation (90%)
- nausea and vomiting
- drowsiness
- confusion
- hallucinations
- CNS depression (enhanced by other CNS depressants e.g. cyclizine)

NB Tolerance develops over several days to effects and the majority of adverse effects with the exception of constipation. Co-prescription of laxatives should always be considered on initiation of most opioids. Anti-emetics such as metoclopramide or haloperidol may also be required initially.

#### Dosing (oral)

- immediate release** 4 to 6 hourly
- slow release** 12 hourly

(For differences in dosing see below)

### The Differences

#### Dosing

##### Converting from immediate to slow release oral preparations

- morphine** - the last dose of immediate release is usually given with the first dose of slow release
- oxycodone** - the last dose of immediate release is **not** usually given with the first dose of slow release because the slow release formulation has an immediate release component

##### 'Breakthrough' analgesia

Many patients prescribed slow release opioids are also prescribed some immediate release tablets or liquids to be taken for 'breakthrough' pain (pain that occurs during the 12 hour dosing interval).

- morphine** - the dose of immediate release is usually  $1/5^{\text{th}}$  to  $1/6^{\text{th}}$  of the 24 hour dose of slow release, given four to six hourly
- oxycodone** - the dose of immediate release is initially  $1/10^{\text{th}}$  to  $1/12^{\text{th}}$  (may increase to  $1/5^{\text{th}}$  to  $1/6^{\text{th}}$ ) of the 24 hour dose of slow release, given four to six hourly

#### Pharmacokinetics

	morphine	oxycodone
<b>oral availability</b>	20 to 40%	70 to 80%
<b>half-life</b>	2 to 3 hours	3 to 4 hours
<b>metabolism</b>	glucuronidation	CYP2D6, 3A4

The lower oral availability of morphine is due to high first-pass metabolism. Both opioids are metabolised to active metabolites. Morphine to morphine-6-glucuronide and oxycodone to noroxycodone and oxymorphone. These are all excreted to differing extents renally. Morphine-6-glucuronide and oxymorphone have fractions excreted unchanged in the urine of 0.9 and 0.5, respectively. All active metabolites may accumulate in patients with renal dysfunction and dose adjustment may be necessary.

#### Place(s) in Therapy

- morphine** - first line opioid in most patients except in those with moderate to severe renal impairment
- oxycodone** - alternative to morphine
  - in patients with severe adverse effects from morphine
  - in patients who have developed tolerance to morphine
  - in patients with renal impairment - **may** get less toxicity than with morphine but may still be at risk

#### Costs

	immediate release oral	slow release oral	injection
<b>10mg morphine</b>	\$0.11-\$0.29	\$0.23	\$1.00
<b>5mg oxycodone</b>	\$0.15-\$0.24	\$0.39	\$3.02* <sub>(10mg)</sub>

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

### Converting from morphine to oxycodone

- 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 e.g. clinical pharmacists, Drug Information, Palliative Care, Anaesthesia

Conversion between opioids is always difficult and there is little agreement internationally on equivalent doses in both acute and chronic settings. As the oral availability of oxycodone is about twice that of morphine and the half-life is similar, giving oral oxycodone at half the dose of oral morphine is pharmacologically robust. As oxycodone is metabolised by CYP2D6 and 3A4, patients who are taking CYP inducers or inhibitors or who have a slow CYP2D6 metaboliser genotype should be monitored closely.

### Summary

While morphine and oxycodone have similar efficacy and toxicity, there are significant differences between them. These should be considered when choosing which opioid to use.