

## Morphine and Oxycodone – Similarities and Differences

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 is in patients in whom morphine use is ineffective or has resulted in adverse effects or tolerance. There has been a national campaign around reducing the amount of oxycodone used in New Zealand both in hospital and in the community. This has been driven by concerns over misuse and safety issues in particular. At Christchurch hospital approximately \$32,000 was spent on oxycodone and \$112,000 on morphine in the 2012/2013 financial year.

### Things to consider with oxycodone

- it appears to have high abuse and addiction potential and has been suggested to be the 'Rolls Royce of opioids' in addiction literature – there is the potential of diversion of oxycodone when prescribed on discharge perhaps more so than morphine
- it is often confused with codeine with some prescribers believing codeine and oxycodone to be equivalent – codeine is considered to be a 'weak' opioid receptor agonist which is metabolised (approx 10%) to morphine while oxycodone is a 'strong' opioid receptor agonist
- the available strengths differ from morphine and this has safety implications if used by a prescriber unfamiliar with it
- there is confusion over trade names particularly with immediate vs slow release
- many prescribers think that morphine and oxycodone are orally equivalent

### Similarities between morphine and oxycodone

#### 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, similar efficacy

#### Adverse effects

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

NB. Tolerance develops over days to analgesic effects and the majority of adverse effects with the exception of constipation. Co-prescription of laxatives should always be considered on initiation. Anti-emetics may also be required initially.

#### Dosing (oral)

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

(For differences in dosing see below)

### Differences between morphine and oxycodone

#### Dosing

If **immediate release** alone (e.g. post-op) is being used dosing 4 to 6 hourly is appropriate. In some patients oxycodone 6 hourly may be sufficient. If the **slow release** is used it should be given 12 hourly with consideration of the following breakthrough doses of **immediate release**:

- morphine** - the dose is usually 1/5<sup>th</sup> to 1/6<sup>th</sup> of the 24 hour dose of slow release, given 4 to 6 hourly
- oxycodone** - the dose is initially 1/10<sup>th</sup> to 1/12<sup>th</sup> (may increase to 1/5<sup>th</sup> to 1/6<sup>th</sup>) of the 24 hour dose of slow release, given 4 to 6 hourly

### Pharmacokinetics

	<b>morphine</b>	<b>oxycodone</b>
<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. 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.

### Place(s) in therapy

- morphine** - first-line opioid except in those with moderate to severe renal impairment
- oxycodone** - alternative to morphine in patients with severe adverse effects from morphine or who have developed tolerance to morphine or who have renal impairment (**may** get less toxicity than with morphine but may still be at risk)
- use of either in combination with tramadol or codeine is not pharmacologically robust

### Costs

	immediate release oral	slow release oral	injection
<b>10mg morphine</b>	\$0.14-\$0.29	\$0.23	\$1.01
<b>5mg oxycodone</b>	\$0.15-\$0.24	\$0.39	\$2.12* <sub>(10mg)</sub>

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

### 'Equivalent' doses

There is little agreement internationally on equivalent doses. As the oral availability of oxycodone is twice that of morphine and the half-life is similar, giving oral oxycodone at half the dose of oral morphine is pharmacologically robust.

- oral morphine 10 mg = oral oxycodone 5 mg**
- morphine injection 10 mg = oxycodone injection 10 mg**
- BUT if converting between opioids seek specialist advice e.g. clinical pharmacists, Drug Information, Palliative Care, Anaesthesia

### Prescribing on discharge

- consider the appropriateness of use in the community
- always include a quantity on discharge scripts
- inform the GP about how long you expect it to continue

### Summary

While morphine and oxycodone have similar efficacy and toxicity, there are significant differences between them. Use morphine first-line and if oxycodone needs to be used, consider the differences in pharmacokinetics and formulations carefully both during hospital admission and on discharge.