

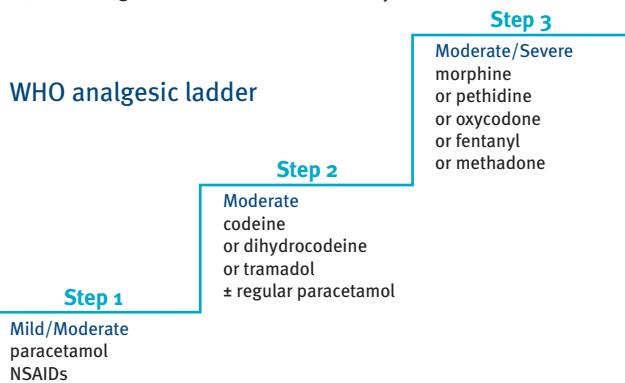
# Pharmacological Pain Management Following Injury

» A distillation of best practice reflecting ACC's current position

» DECEMBER 2006

- The World Health Organisation analgesic ladder is useful to treat all types of pain including pain following injury.
- In pain following injury the ladder will usually be descended, especially if pain is initially moderate/severe.
- Assessment of pain severity is important and determines the starting point on the ladder:
  - moderate/severe pain **Step 3 'strong' opioids**
  - moderate pain **Step 2 'weak' opioids**
  - mild/moderate pain **Step 1 non-opioids**
- Combinations of drugs from step 1 with steps 2 or 3 may be useful.
- The choice of drug from within each step of the ladder is determined by how well the drug is likely to suit the individual patient.

The World Health Organisation (WHO) analgesic ladder can be applied to any clinical situation that involves pain, including that following injury. Originally established for the control of cancer pain, the analgesic ladder is now over 20 years old.<sup>1,2</sup>



Following injury, as healing occurs and pain lessens, the ladder will usually be descended. Pain severity will determine the starting point on the ladder so thorough assessment is important. As pain is often underestimated and undertreated,<sup>3</sup> the key to success is adequate monitoring. This involves listening to patient descriptors and may include the use of pain scales.<sup>2</sup>

### Moderate to severe pain

The following drugs are short-term measures for post-injury pain and may be combined with step 1 analgesics. Where there are high risk factors for chronicity, please contact an ACC case manager for a Comprehensive Pain Assessment.

#### Morphine

Morphine, the first-line opioid analgesic, may be given intravenously, subcutaneously, intramuscularly, orally, or rectally. It has a short half-life of 2 to 3 hours and is usually given every 4 to 6 hours. Effects may be prolonged and dosing intervals increased to 12 hourly with the use of sustained release preparations.

The adverse effects of opioids (and morphine), include constipation, nausea and vomiting, drowsiness, confusion, and hallucinations. Laxatives should generally be prescribed in combination with opioids if not for short-term usage. Prokinetic anti-emetics e.g. metoclopramide, may also be required initially. Tolerance to the other effects listed usually develops over several days. The extent of the adverse effects varies with the opioid.

Although morphine is extensively metabolised by glucuronidation, an active metabolite morphine-6-glucuronide is excreted renally and may accumulate in patients with renal dysfunction. Dose adjustment may be necessary.

#### Pethidine

An opioid agonist, pethidine is used as an analgesic, particularly in obstetrics. However, as it may cause seizures and other neurotoxicities it should generally be avoided in those with moderate to severe post-injury pain.<sup>3</sup>

Pethidine has a half-life of 3 to 4 hours and is metabolised by demethylation to norpethidine. Norpethidine is a central nervous system stimulant with a half-life of 25 hours. Pethidine is particularly serotonergic and may interact with other serotonergic agents e.g. fluoxetine.

#### Oxycodone

Oxycodone, available in oral form, is an opioid analgesic with similar actions, half-life and adverse effects to morphine. It is predominately metabolised by CYP3A and 2D6 and so may be subject to more drug interactions than morphine.<sup>4</sup>

#### Fentanyl\*

A synthetic opioid agonist, injectable fentanyl may be useful where morphine is not appropriate. Although patches are available, their slow-release mechanism (over 72 hours) makes titration to acute pain difficult.

Fentanyl has a short half-life of 3 to 4 hours (iv). It is metabolised by CYP3A4 and is subject to interactions with drugs that are CYP3A4 inducers and inhibitors. It is safer than morphine in patients with renal impairment.

#### Methadone

Methadone is an opioid agonist that also acts as an N-methyl-D-aspartate (NMDA) antagonist. NMDA receptor antagonism decreases the risk of developing opioid tolerance.

Methadone use as an analgesic is relatively recent, and its usefulness in post-injury pain has not been established. It has a long and variable half-life ranging from 13 to 80 hours. Accumulation is a major concern, so patients should be frequently assessed for signs of toxicity. Methadone has no renal elimination, is metabolised by CYP3A4 and is subject to CYP3A4 interactions.

#### Moderate pain

The following may be combined with step 1 analgesics.

#### Codeine

Codeine is an opioid analgesic, approximately 10% of which is metabolised by CYP2D6 to morphine. Drug interactions with CYP2D6 inhibitors may result in a lack of analgesic effect. Effects and adverse effects are as expected for a low dose of morphine.

#### Dihydrocodeine

Dihydrocodeine, available as a slow-release tablet, is similar in effect and adverse effects to codeine. It is converted by CYP2D6 to dihydromorphine but unlike codeine, analgesia appears to be unaffected by CYP2D6 inhibitors.

#### Tramadol\*

Tramadol is mainly an opioid agonist, but it also increases both serotonin and noradrenaline spinal cord concentrations by re-uptake inhibition, thereby augmenting descending inhibitory pain pathways. There are therefore interactions with other serotonergic agents. Tramadol has a half-life of 5 to 6 hours. In moderate acute pain, it may be as, or less, effective than codeine plus paracetamol.

#### Mild pain

The final phase in descending the ladder: patients may move from a combination of step 1 analgesics down to paracetamol only, then down to none.

#### Paracetamol

Paracetamol is an effective analgesic when prescribed regularly, either alone or in combination with opioids or NSAIDs. Doses of greater than 4 g in 24 hours may result in hepatic toxicity. Lower maximums should be used in hepatic disease and in the elderly.

#### Non-Steroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs, usually administered orally, are particularly useful when inflammation is present. Blocking the production of inflammatory mediators, the effect develops slowly with regular dosage over a period of time. Long term use has been associated with gastric and duodenal mucosal, renal and cardiovascular toxicity. Diclofenac is also available as a suppository, and as an intramuscular injection, but this has been associated with sterile abscesses.

A further Review will discuss a multidisciplinary approach to pain management.

#### References

1. Cancer Pain Relief. WHO; 1986.
  2. Cancer Pain Relief 2nd edition. WHO; 1996.
  3. Therapeutic Guidelines. Analgesics. Therapeutic Guidelines Ltd; 2002.
  4. Lalovic B, et al. Quantitative contribution of CYP2D6 and CYP3A to oxycodone metabolism in human liver and intestinal microsomes. *Drug Metabolism and Disposition*; 2004; 32(4): 447-54.
- \* Prescribers should request ACC funding prior to prescribing these items. Forms (ACC1171) for this are available on [www.acc.co.nz/forproviders](http://www.acc.co.nz/forproviders)