

15 June 2017

## Options for pain relief (analgesic) medication after surgery

**DISCLAIMER:** The information presented here is NOT intended on being a comprehensive source of drug information. For each drug, a minimum of information is provided, with the MAJORITY of known facts on the drug being OMITTED. For instance, contra-indications, precautions, side-effects/adverse-reactions, breast-feeding and pregnancy information, interactions, and toxicity are not consistently detailed. Treatment recommendations for patients with significant illness (eg. kidney, liver, respiratory, cardiac, or neurological disease) are not detailed. This is simply intended on being an extension or reminder of the information discussed around the time of hospital admission, and further clarification should be sought prior to making a therapeutic decision. Please check website for latest version.

### Paracetamol (eg. **Panadol**<sup>®</sup>)

#### Dosing in children over 6 months to adults

- 15mg/kg/dose administered 4 to 6 hourly as required up to a maximum of 60mg/kg/day (ie. a maximum of 4 doses/day). Note:
  - No single dose should ever exceed 1g
  - Never exceed 4g per 24hours
- Adults and children over 12 years of age are most commonly given 0.5-1.0g every 4 to 6 hours, as long as the above mg/kg per dose and daily instructions are followed

#### Practice points

- In overweight children, the 'ideal weight' rather than the child's actual weight, is used for calculating the dose of paracetamol. This is to prevent inadvertent over-dosage. Alternatively, an age-based dosing guideline can be used, such as that used by **Children's Panadol**<sup>®</sup>. Please seek clarification if unsure
- Onset of pain relief is approximately 30minutes after oral administration
- Paracetamol decreases the amount of other stronger pain relievers required by 20-30%
- Paracetamol can be used at the same time as non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen (eg. **Nurofen**<sup>®</sup>)
- Paracetamol is generally considered safe for short-term use in pregnancy and whilst breast-feeding
- Please be aware that many over-the-counter products and prescription medications (eg. **Panadeine Forte**<sup>®</sup>) contain paracetamol, and the total daily dose of paracetamol taken must include all sources. The daily maximum dose of paracetamol must never be exceeded
- Reduce the frequency of taking paracetamol, and cease administration altogether, as soon as is practicable. Poor oral intake or a poor nutritional state can increase the danger of irreversible liver damage from ongoing paracetamol use. This damage can occur even with the recommended doses. After 2-3days of continuous use at maximal doses, temporarily cease use for 24hours and use alternative pain relievers during this time. Contact me for advice if you still need to use paracetamol at maximal doses at this time

## Paracetamol and Codeine combination products for use by adults (eg. **Panadeine Forte®**)

### Dosing

- Paracetamol dosing is detailed above. In adults over 60kg, the dosing is 30-60mg administered every 4 to 6 hours as required to a daily maximum of 240mg
- **Panadeine Forte®** contains 500mg paracetamol and 30mg codeine per tablet. The normal dose for adults is 1-2tablets every 4 to 6 hours if needed, up to a maximum of 8tablets daily, as long as the above per dose and daily instructions for paracetamol are followed

### Practice points

- Remember that these combination products contain paracetamol, the maximum single and daily doses of which should never exceed the recommended amounts (see above paracetamol entry for further details)
- Codeine's analgesic action depends on metabolism of about 10% of a given dose to morphine. A proportion of the population, known as "ultrapid metabolisers", produce significantly higher levels of morphine after the same dose of codeine. Therefore:
  - Patients who are ultrapid metabolisers may attain high peak morphine levels and are at risk of sedation and respiratory depression. Therefore, the initial dose should be the lowest applicable for the patient's age or weight
  - Breastfeeding women should be aware of the risk of respiratory depression (ie. stopping breathing) in the breast-fed baby should the mother be an ultrapid metaboliser of codeine. The safest recommendation is to express and discard breast-milk whilst taking codeine-containing medications, ie. do not take codeine if breast-feeding
- The use of codeine in children has come under increased scrutiny in recent times. For more information, please refer to the Australian Government's Therapeutic Goods Administration ([tga.gov.au](http://tga.gov.au)), the National Prescribing Service ([nps.org.au](http://nps.org.au)), or to international sources such as the USA's FDA ([fda.gov](http://fda.gov)). Essentially, I follow the Australian guidelines published by the NPS, an independent body funded by the Australian Government's Department of Health. These guidelines recommend codeine:
  - Should not be used in children under 12yrs for any reason
  - Should not be used in children under 18yrs following tonsillectomy and/or adenoidectomy
  - This means that I advise against administering medicines containing codeine to children. Such products include **Painstop for Children Day-Time Pain Reliever Syrup®** and **Painstop Night-Time Pain Reliever Syrup®**
  - If codeine is nonetheless administered against my advice, parents or carers must monitor for signs of overdose, such as unusual sleepiness, difficulty being aroused or awakened, shallow, difficult or noisy breathing (whilst simultaneously confirming the child is breathing normally), confusion, small pupils, nausea or vomiting, or lack of appetite, and to seek immediate medical attention if these occur
- Short-term use of **Panadeine Forte®** in pregnancy appears safe
- Opiates such as codeine can produce troublesome constipation – it is wise to have some laxatives available. Consider regular laxative treatment whilst taking codeine
- Be careful when you stand up as codeine can make you feel dizzy if you stand up too quickly
- Codeine may make you feel drowsy and may increase the effects of alcohol. If you are affected, do not drive or operate machinery. If you are very sleepy or have trouble staying awake, stop taking the medication and seek medical assistance urgently

## Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), including Ibuprofen (eg. **Nurofen**<sup>®</sup>) and Diclofenac (eg. **Voltaren**<sup>®</sup>)

### Dosing for oral administration of Ibuprofen

- Adults: 200-400mg administered 6 to 8 hourly as required, maximum 1200mg/day, taken with or shortly after food
- Children over 3 months of age: 5-10mg/kg/dose to a maximum of 400mg, administered 6 to 8 hourly as required, maximum 30mg/kg/day upto 1200mg/day, taken with or shortly after food

### Dosing for oral administration of Diclofenac

- Adults: 25-50mg administered 8 hourly as required, maximum 150mg/day, taken with or shortly before food
- Children over 6 months of age: 1mg/kg/dose to a maximum of 50mg, administered 8 hourly as required, maximum 3mg/kg/day upto 150mg/day, taken with or shortly before food

### Practice points

- NSAIDs such as ibuprofen can be used at the same time as paracetamol, tramadol, and opioids (including codeine and oxycodone), but should not be taken with coxibs such as celecoxib (eg. **Celebrex**<sup>®</sup>)
- Most NSAID use in children is with ibuprofen because of the variety of formulations available. Diclofenac use in children is normally via the use of suppositories because there are no oral liquid formulations enabling oral administration of smaller doses
- NSAID use decreases the amount of other stronger pain relievers required
- Initial dose should be the lowest recommended dose, and only increase if pain relief is inadequate
- After 3days for children, and 5days for adults, of continuous use at maximal doses, temporarily cease use for 24hours and use alternative pain relievers during this time. Contact me for advice if you still need to use NSAIDs at maximal doses at this time
- Most concern regarding NSAIDs in the perioperative period, and the reason why they are generally avoided in the elderly, involves:
  - Peptic ulceration – increased risk when taking higher doses, with >5days use, in the elderly, and in those with a history of the disease. I suggest taking a type of antacid treatment whilst taking NSAIDs regularly if at increased risk, or if symptoms of ‘heartburn’ occur, such as ranitidine (available in supermarkets as **Zantac**<sup>®</sup>) or rabeprazole (prescription only, eg. **Pariet**<sup>®</sup>). Ibuprofen and diclofenac appear to have the lowest risk of gastro-intestinal complications
  - Renal impairment - decreased kidney function. It is particularly important to ensure that your intake of oral fluids is adequate whilst taking NSAIDs post-operatively. If you find that you are vomiting post-operatively, you should avoid taking NSAIDs. Also, NSAIDs and coxibs should not be taken with some medications used to treat high blood pressure or heart failure, as the risk of kidney damage or an exacerbation of heart failure is increased
  - Interference with blood clotting:
    - Concerns with short-term use around the time of surgery focus on increased bleeding due to impaired platelet function (think of a relative taking aspirin for the prevention of heart disease)
    - Guidelines advise that ibuprofen can be used safely for pain control after tonsillectomy. Despite concerns that use of NSAIDs increases the risk of bleeding after tonsillectomy, a recent Cochrane Review showed that there was no evidence for withholding ibuprofen after this procedure. NSAIDs do not increase clinically significant bleeding after tonsillectomy but reduce nausea and vomiting compared with placebo or other analgesics

- Increased cardiovascular risk (eg. increased risk of heart attacks) with long term-treatment of chronic conditions (ie. this is not the situation with short-term use after an operation). In patients at risk, other types of pain relievers are preferred. Nonetheless, if NSAIDs are to be taken, naproxen would be the best option, and diclofenac the worst
  - Bronchospasm (exacerbation of asthma symptoms) in patients at risk, which can include patients with nasal polyps or chronic sinusitis
  - Wound and bone healing
- The latest TGA advice (Sep 2016) on NSAID use in pregnancy is not to use if likely to become pregnant (they may impair fertility by preventing or delaying ovulation), during the first 6 months of pregnancy unless on medical advice (associated with increased risk of miscarriage), and not to use at all during the last three months of pregnancy (risk of specific foetal complications)
- Of all the NSAIDs, ibuprofen has the best safety profile for use in the breast-feeding mother, and dosing should be as for the non-lactating adult. Short-term or occasional use of diclofenac whilst breast-feeding is considered reasonable
- Aspirin specifically should not be given to children or breast-feeding mothers

Cyclo-oxygenase-2 selective inhibitors ('coxibs'), including celecoxib (eg. **Celebrex**<sup>®</sup>) and Meloxicam (eg. **Mobic**<sup>®</sup>)

Dosing for **Celebrex**<sup>®</sup> capsules in adults  $\geq 18$  yrs of age

- 100-200mg administered every 12 hours if needed - maximum 5 days continuous treatment at short-term doses
- Maximum 400mg/day for short-term treatment. 200mg/day is the long-term treatment maximum
- First dose should be 100mg, and only increase to 200mg if pain relief is inadequate

Dosing for **Mobic**<sup>®</sup> tablets and capsules in adults  $\geq 18$  yrs of age

- 7.5–15mg administered once daily if needed taken with food - maximum 5 days continuous treatment
- First dose should be 7.5mg, and only increase to 15mg if pain relief is inadequate

Practice points

- Coxibs such as celecoxib and meloxicam can be used at the same time as paracetamol, tramadol, and opioids (including codeine and oxycodone), but should not be taken with NSAIDs like ibuprofen (eg. **Nurofen**<sup>®</sup>)
- Coxib use decreases the amount of other stronger pain relievers required
- Compared to NSAIDs:
  - Coxibs are safer and the preferred option in patients at risk of peptic ulceration/gastro-intestinal upset, although other types of pain relievers are preferred. Nonetheless, if Coxibs are to be taken, concurrent use of antacids, such as ranitidine (available in supermarkets as **Zantac**<sup>®</sup>) or rabeprazole (prescription only, eg. **Pariet**<sup>®</sup>), should be considered
  - Coxibs have no effect on platelet function, so there is no risk of increased bleeding peri-operatively
  - Coxibs are unlikely to produce bronchospasm in patients that normally suffer from NSAID-exacerbated respiratory symptoms
- Most concern regarding coxibs in the perioperative period, and the reason why they are generally avoided in the elderly, involves:

- Renal impairment - decreased kidney function. It is particularly important to ensure that your intake of oral fluids is adequate whilst taking NSAIDs post-operatively. If you find that you are vomiting post-operatively, you should avoid taking NSAIDs. Also, NSAIDs and coxibs should not be taken with some medications used to treat high blood pressure or heart failure, as the risk of kidney damage or an exacerbation of heart failure is increased
- Increased cardiovascular risk (eg. increased risk of heart attacks) with long term-treatment of chronic conditions (ie. this is not the situation with short-term use after an operation). In patients at risk, other types of pain relievers are preferred. Nonetheless, if coxibs are to be taken, celecoxib would be the best option
- Coxibs should be avoided in pregnancy, and whilst the use of celecoxib appears safe for the breast-feeding mother to use, there is limited data, and avoidance would be the most prudent recommendation
- Celecoxib should be avoided by those allergic to sulfonamides
- For elderly patients with a bodyweight of less than 50 kg treatment with celecoxib should be initiated at the lowest recommended dose

### Tramadol (eg. **Tramal Capsules**<sup>®</sup>)

#### Dosing

- 50-100mg administered 4 to 6 hourly as required, maximum 8mg/kg/day upto 400mg/day for adults and children >12yrs of age

#### Practice points

- Analgesia starts within 1 hour of oral administration and peaks at 2–4 hours
- Tramadol is possibly less likely to produce respiratory depression (ie. stopping breathing) than other opioids at equivalent doses (eg. morphine, codeine, or oxycodone)
- The Society for Paediatric Anaesthesia in NZ and Australia in May 2017 warned of tramadol's use in children under 18yrs for post-tonsillectomy pain, with greater concern for those children who are obese, or those with obstructive sleep apnoea (OSA) – the concern relates to serious, potentially fatal, breathing problems. If prescribed in these cases, the suggested dosing is 0.5mg/kg/dose administered 6 to 8 hourly as required, maximum 2mg/kg/day
- Nausea and vomiting are side-effects of tramadol, as they are with other opioids (eg. morphine, codeine, or oxycodone), whilst tramadol produces less constipation and itching than other opioids (ie. strong pain relievers)
- Tramadol alone does not increase the incidence of seizures compared with other pain relievers, as long as prescribed doses are not exceeded
- Tramadol should be avoided in patients taking most anti-depressant, anti-psychotic, anti-smoking and weight-loss medications, to avoid the risk of seizures and serotonin toxicity
- Dosing is decreased in patients over 75yrs of age to a maximum of 300mg/day, and use is avoided in patients with kidney disease
- Avoid whilst pregnant or breast-feeding – safety data lacking

### Oxycodone (eg. **Endone**<sup>®</sup>, **OxyNorm**<sup>®</sup> and **Targin**<sup>®</sup>) and Morphine (**Sevredol**<sup>®</sup>)

#### Dosing

- **Endone**<sup>®</sup> 5mg tablets should be taken after meals or with milk - 1tablet every 6hours as needed. **Endone**<sup>®</sup> must not be given to children
- **OxyNorm**<sup>®</sup> - a single 5mg capsule can be taken every 6hours as needed. **OxyNorm**<sup>®</sup> capsules must not be given to children, but **OxyNorm Liquid**<sup>®</sup> (1mg/ml) can be given to children >1year as prescribed

- **Targin®** differs from the **Endone®** and **OxyNorm®** as it a “controlled-release” formulation of oxycodone, which means that one tablet is taken every 12hours as needed. **Targin®** has the added benefit of an active ingredient to minimise constipation. Ensure the tablet is taken whole, not crushed or chewed. Either the 5mg/2.5mg or the 10mg/5mg strength tablets will be prescribed depending upon your clinical situation. Regardless of the form prescribed, the dose is a single tablet every 12hours as needed. **Targin®** cannot be used in children under 12yrs of age
- **Sevredol®** - a single 10mg tablet can be taken every 4hours as needed, and can be used in adults and children over 12yrs of age

#### Practice points

- This medicine is a strong morphine-like drug that can cause great harm through stopping the patient’s breathing. Specifically, if your child has undergone a *tonsillectomy*, the first 72hrs is the most likely time they will run into problems with their breathing due to residual anaesthetic effects, throat swelling due to the surgery, and changes in their sleep patterns. As such, *it is ideal if you can avoid giving your child OxyNorm Liquid® during this first 72hr period*. Note that the at-risk period can last greater than 7days. If you are desperate after paracetamol, ibuprofen, and non-drug methods to comfort your child have failed, then you can administer the **OxyNorm Liquid®** as prescribed, observing your child closely as detailed below for any breathing difficulties or excessive sleepiness
- It is very important to follow the prescribed dose exactly when dealing with **OxyNorm Liquid®**. This is of critical importance when giving **OxyNorm Liquid®** to children as a small error in dosing may have catastrophic consequences. Parents or carers must monitor children for signs of overdose, such as unusual sleepiness, difficulty being aroused or awakened, shallow, difficult or noisy breathing (whilst simultaneously confirming the child is breathing normally), confusion, small pupils, nausea or vomiting, or lack of appetite, and to seek immediate medical attention if these occur
- Opioids include drugs such as codeine, oxycodone, fentanyl, and morphine– they are very potent pain relievers but also strongly depress breathing. It is critical that only one type of opioid should ever be taken within 72hrs of another. Failure to follow these instructions could have fatal consequences
- Following oral administration of **Endone®** tablets, the analgesic effect occurs within 10-15minutes, reaches its maximum in 30-60minutes and persists for 3-6hours
- No other sedative medications, including sleeping aids (eg. benzodiazepines such as diazepam or **Valium®**) or sedating anti-histamines (eg. promethazine or **Phenergan®**) should be taken concurrently, as the risk of respiratory depression (ie. the patient’s breathing stopping) is significantly increased
- Opiates can produce troublesome constipation – it is wise to have some laxatives available (eg. docusate with senna). Consider regular laxative treatment whilst taking codeine. **Targin®** contains an active ingredient to combat the constipation that opioids can cause, but laxatives may still be required
- Be careful when you stand up as opiates can make you feel dizzy if you stand up too quickly
- Opiates may make you feel drowsy and may increase the effects of alcohol. If you are affected, do not drive or operate machinery. If you are very sleepy or have trouble staying awake, stop taking the medication and seek medical assistance urgently
- Overall, the short-term use of opioids to treat pain in pregnancy appears safe, although **Targin®** must not be used in the pregnant or breast-feeding woman
- Safe to use occasional doses whilst breast-feeding. Use repeated doses with caution, especially if infant is premature or <4 weeks old. The infant must always be monitored for sedation and adequacy of breathing or ventilation. As a component of multimodal analgesia (ie. used as rescue when paracetamol and NSAIDs are insufficient) in the first 72 hours after caesarean section, there may be minimal risk to breastfeeding infants as only a low volume of milk is

ingested during this period. Of all opioids, morphine is the preferred option if potent analgesia is required in breast-feeding mothers. **In other words**, the breast-feeding mother's safest option is to avoid taking opioids, and if opioid treatment was desired, then breast-feeding the infant should cease whilst regular opioid medication is taken (ie. express and discard breast-milk during treatment)

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