

# Paracetamol dosing for children in primary care

## KEY MESSAGES:

- Errors in paracetamol dosing is the leading cause of paediatric acute liver failure in New Zealand
- Paracetamol is dosed in milligrams per kilogram of body weight, rather than by age; the dose should be calculated in children using actual body weight, without exceeding the adult dose
- Children who are malnourished are more susceptible to paracetamol toxicity
- Advise caregivers to record each dose of paracetamol they administer and to use a syringe to measure dose volume

## Children aged under five years are at greatest risk of paracetamol toxicity

Paracetamol can be prescribed to infants from birth. However, paracetamol has a narrow therapeutic index and infants and children are at increased risk of overdose. Children aged under five years who are acutely unwell are particularly vulnerable to paracetamol toxicity, which can lead to liver failure and death.<sup>1</sup> From 2002–2012, there were 14 cases of acute paediatric liver failure in New Zealand and Australian attributed to paracetamol use.<sup>1</sup> Reasons for medicine errors with paracetamol included:<sup>1</sup>

- Exceeding recommended doses
- Too frequent dosing
- Prolonged dosing (up to 24 days in one case)

## What is the appropriate dose of paracetamol for pain management in children?


The analgesic effect of paracetamol is dependent on the plasma concentration of the medicine being high enough to cross the blood brain barrier in sufficient quantity, therefore appropriate dosing is required (see: “The pharmacology of paracetamol”). Due to the wide range of body weights across children of different ages, and because the overall rate of paracetamol

metabolism per kilogram of body weight does not vary with age, paracetamol is dosed in milligrams per kilogram of body weight, rather than by age.<sup>2</sup> The same milligram per kilogram of body weight method for paracetamol dose calculation is recommended for obese children. However, caution is needed to never exceed the adult dose, which can occur if weight-based dosing is applied to children weighing over 65 kg (see example).

Adverse effects are relatively uncommon when paracetamol is used at recommended doses,<sup>3</sup> although rarely malaise, and skin reactions, e.g. Stevens-Johnson syndrome, have been reported in children and adults.<sup>4</sup> Paracetamol is contraindicated in children with severe liver dysfunction.<sup>4</sup>

The oral dose of paracetamol for children aged 1 month to 18 years is:

- 15 mg/kg per dose, to a maximum of 1 g per dose, every four to six hours, with a maximum of 60 mg/kg daily, without exceeding 4 g daily

 For further information on paracetamol dosing, refer to the New Zealand Formulary for Children: [www.nzfchildren.org.nz/nzf\\_2439](http://www.nzfchildren.org.nz/nzf_2439)

The paracetamol dose should be prescribed as accurately as possible, however, in practice increments of 0.5 mL are often used. Caregivers should be strongly encouraged to use a syringe to measure the dose. Measuring cups are suitable for dose volumes over 10 mL.

Caregivers should be advised that as children grow, the volume of paracetamol will need to be increased in order to ensure that dosing is adequate; remind caregivers that they can also check the dose with their community pharmacist. The importance of not sharing a prescribed dose with another child should also be discussed, e.g. a smaller child may inadvertently be given a higher dose intended for their larger sibling.

#### **Example of calculating a paracetamol dose:**

*A boy, aged 10 years, weighing 67 kg presents with myalgia of a suspected viral cause. You prescribe paracetamol for management at home. The calculation for paracetamol dosing is 15 mg × 67 kg = 1005 mg, however, you round this down to the maximum adult dose of 1 g, which is prescribed as 20 mL of a 250 mg/5 mL formulation, every four to six hours with no more than four doses every 24 hours.*

#### **Caution is recommended when considering paracetamol in under-weight children**

Paracetamol should be prescribed cautiously to children who are significantly under-weight or malnourished, e.g. those failing to thrive. Children who are in a poor nutritional state are more susceptible to paracetamol toxicity due to a reduction in the levels of the detoxifying glutathione enzyme.<sup>5</sup> Reduced

paracetamol dosing, e.g. 10 mg/kg, or longer periods between dosing may be appropriate in these children.


#### **Use actual body weight to dose paracetamol in children**


The calculation of the paracetamol dose should be based on the child's actual body weight, without exceeding the adult dose. There is little evidence supporting the use of weight adjustments in paediatric paracetamol dosing (unless the child is malnourished) and accumulating evidence suggests that methods other than actual weight-based dosing may result in sub-therapeutic treatment.<sup>6,7</sup>

#### **Dosing errors are the greatest concern when prescribing paracetamol**

Clear communication about dosing and documentation of doses is important as the risk of medicine errors with paracetamol is increased in children who have multiple caregivers, e.g. mother, father and day care or school.<sup>9</sup> Health professionals can reduce paracetamol-induced harm by asking the child's caregiver to:<sup>9</sup>

- Confirm they know which strength of paracetamol they are using, i.e. 120 mg/5mL or 250 mg/5mL, the correct volume to administer, and the daily dose not to exceed
- Record the volume and time of administration, preferably in a place where the medicine is stored so it is not missed
- Store medicines out of sight and reach of children, preferably in a locked cupboard
- Ensure there is a childproof lid on liquid formulations when they are dispensed from the pharmacy
- Use a syringe with appropriate increments to measure dose volume (a syringe may need to be provided); ensure they can use the syringe confidently and know not to use a household spoon for measuring

 A parent guide for paediatric paracetamol dose calculations and record keeping is available from: [www.saferx.co.nz/paracetamol-for-children\\_leaflet.pdf](http://www.saferx.co.nz/paracetamol-for-children_leaflet.pdf)

 Further information on pain management in children is available from: [bpac.org.nz/BPJ/2014/March/pain.aspx](http://bpac.org.nz/BPJ/2014/March/pain.aspx)

## +/- The pharmacology of paracetamol

Paracetamol is highly lipid-soluble and has a relatively short half life of 2–2.5 hours.<sup>2</sup> Following oral administration, paracetamol is rapidly absorbed across the mucosa of the duodenum and into the bloodstream where it is mainly metabolised by the liver.<sup>2</sup> Paracetamol is predominantly metabolised by glucuronidation and sulphation, with a minor pathway involving the CYP2E1 enzyme being responsible for hepatotoxicity.<sup>7</sup> The glucuronidation and sulphation pathways are present in children, however, the contributions that they make to paracetamol metabolism are variable until the glucuronidation pathway matures, which occurs by age two years.<sup>2</sup>

The analgesic effects of paracetamol are determined by its concentration in the brain.<sup>2</sup> Plasma levels of paracetamol therefore need to be high enough to allow the medicine to cross the blood brain barrier and accumulate in neuronal tissue at levels sufficient to exert a therapeutic effect.<sup>2</sup> At least 15 mg/kg is required orally

for paracetamol to produce effective analgesia, with four-hour dosing quickly achieving steady-state therapeutic concentrations.<sup>2</sup> Where rapid onset of analgesia is required, a single loading dose of paracetamol, e.g. 30 mg/kg, will shift the pharmacokinetics towards the desired steady-state.<sup>2</sup>

The same mg/kg method of paracetamol dosing is recommended for obese children, with care being taken never to exceed the adult dose. This is because lipid-soluble paracetamol is evenly distributed throughout the body. If dose reductions are made for children who weigh more than their ideal body weight there is the risk that they will be under-dosed and will not receive adequate pain relief.<sup>6</sup> Furthermore, data from adults shows that morbid obesity is associated with a lower exposure to paracetamol due to increases in the rate of metabolism for all three metabolic pathways for paracetamol.<sup>7</sup>

## References

1. Rajanayagam J, Bishop JR, Lewindon PJ, et al. Paracetamol-associated acute liver failure in Australian and New Zealand children: high rate of medication errors. *Arch Dis Child* 2015;100:77–80. doi:10.1136/archdischild-2013-304902
2. de Martino M, Chiarugi A. Recent Advances in Pediatric Use of Oral Paracetamol in Fever and Pain Management. *Pain Ther* 2015;4:149–68. doi:10.1007/s40122-015-0040-z
3. Working Group of the Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. Acute pain management: scientific evidence. 2015. Available from: [http://fpm.anzca.edu.au/documents/apmse4\\_2015\\_final](http://fpm.anzca.edu.au/documents/apmse4_2015_final) (Accessed Dec, 2017)
4. New Zealand Formulary for Children. NZFC v67. 2018. Available from: [www.nzfchildren.org.nz/](http://www.nzfchildren.org.nz/) (Accessed Feb, 2017).
5. World Health Organization (WHO). WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses. 2012. Available from: [http://apps.who.int/iris/bitstream/10665/44540/1/9789241548120\\_Guidelines.pdf](http://apps.who.int/iris/bitstream/10665/44540/1/9789241548120_Guidelines.pdf) (Accessed Jan, 2018)
6. Chidambaran V, Tewari A, Mahmoud M. Anesthetic and pharmacologic considerations in perioperative care of obese children. *J Clin Anesth* 2017;45:39–50. doi:10.1016/j.jclinane.2017.12.016
7. van Rongen A, Väilitalo PAJ, Peeters MYM, et al. Morbidly Obese Patients Exhibit Increased CYP2E1-Mediated Oxidation of Acetaminophen. *Clin Pharmacokinet* 2016;55:833–47. doi:10.1007/s40262-015-0357-0
8. Carasco CF, Fletcher P, Maconochie I. Review of commonly used age-based weight estimates for paediatric drug dosing in relation to the pharmacokinetic properties of resuscitation drugs. *Br J Clin Pharmacol* 2016;81:849–56. doi:10.1111/bcp.12876
9. Waitemata DHB. Paracetamol - safe prescribing - mind that child! 2016. Available from: [www.saferx.co.nz/full/paracetamol-for-children.pdf](http://www.saferx.co.nz/full/paracetamol-for-children.pdf) (Accessed Jan, 2018)



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