



## Paracetamol: use in children



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### Summary

It is sensible to use paracetamol to reduce the discomfort caused by minor acute infections, surgical procedures and triple antigen. It is also sensible to use paracetamol to reduce fever in patients with cardiac or respiratory failure. However, there is little evidence to support the use of paracetamol to treat fever in patients without heart or lung disease, or to prevent febrile convulsions. Paracetamol may prolong infection and reduce the antibody response in mild disease, and increase morbidity and mortality in severe infection. The dose in children is 10-15 mg/kg 4 hourly, to a maximum of 100mg/kg/day, and no patient should receive more than 4 g/day.

Key words: fever, pain, analgesia, antipyretic

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Despite the widespread use of paracetamol, there is still confusion about when it should be used and the correct dose.<sup>1</sup>

### Indications for paracetamol

#### *Fever*

In patients with cardiac or respiratory failure who are febrile, it can be helpful to give paracetamol to reduce oxygen consumption, carbon dioxide production and cardiac output. However, in patients without heart or lung disease, fever is harmful only at temperatures over 41°C. Such high temperatures are usually caused by heat stroke or brain injury<sup>2</sup>, and, if so, they do not respond to paracetamol or aspirin.

#### *Febrile convulsions*

There is no evidence that antipyretics prevent febrile convulsions; this is probably because the convulsion is caused by the rapid rise in temperature that usually occurs at the beginning of an illness.<sup>2</sup> There are no controlled

trials comparing an antipyretic to placebo for febrile convulsions, but one study comparing phenobarbitone plus antipyretic to placebo plus antipyretic found a high risk of febrile convulsions in the placebo plus antipyretic group, suggesting that antipyretic therapy did not protect against convulsions.<sup>3</sup> In a recent controlled trial in children who had had a febrile convulsion<sup>4</sup>, children given paracetamol 15-20 mg/kg every 4 hours were just as likely to have another convulsion as children given paracetamol only when their rectal temperature exceeded 37.9°C.

### *Discomfort*

It is sensible to give paracetamol to reduce the unpleasant symptoms caused by mild acute infections. However, paracetamol does not have a dramatic effect: a recent controlled trial<sup>5</sup> found that paracetamol caused only a modest improvement in activity and alertness in children with acute infection, and that there was no significant improvement in mood, comfort, appetite or fluid intake. Because many patients with infection have fever and discomfort, it is often assumed that fever causes discomfort but strenuous exercise causes temperatures up to 40°C without causing discomfort.

### *Triple antigen reactions*

Two studies<sup>6,7</sup> have shown that paracetamol reduces fever and abnormal behaviour in children who have had triple antigen injection. A third study<sup>8</sup> found that paracetamol had no significant effect, but only one dose of 10 mg/kg of paracetamol was given 4 hours after immunisation. A reduction in adverse reactions to triple antigen is likely to improve immunisation rates.

### *Postoperative pain*

There has been little systematic study of the use of paracetamol for postoperative pain, but controlled trials of nonsteroidal antiinflammatory drugs<sup>9</sup> and experience with paracetamol suggest that paracetamol provides adequate analgesia for minor surgery, and allows a reduced dose of opiates after major surgery. Paracetamol should probably be given *before* surgery, rather than waiting for pain to develop after surgery.<sup>9</sup>

### **The dose of paracetamol**

While a single dose of 5 mg/kg of paracetamol results in some reduction in the temperature of febrile children, there is a much larger fall with 10 mg/kg and an even larger and more prolonged fall with 20 mg/kg.<sup>10</sup>

The maintenance dose of paracetamol in children is 10-15 mg/kg 4 hourly<sup>10</sup>, to a maximum of 100 mg/kg/day, and no patient should receive more than 4 g/day. An initial dose of 20 mg/kg can be given if it is felt that maximum effect is needed quickly. A dose of 30 mg/kg 8 hourly gives levels in the therapeutic range.<sup>10</sup> A single dose of 30 mg/kg of paracetamol at bedtime can increase the amount of sleep for the whole family when a child has mild acute infection, but the danger of repeating this dose has to be emphasised.

In Australia, paracetamol is sold in preparations containing 60mg in 0.6 mL (or 100 mg/mL), 100 mg/mL, 50 mg/

mL, 120 mg in 5 mL (or 24 mg/mL) and 240 mg in 5 mL (or 48 mg/mL). It is difficult to calculate a dose of 15 mg/kg from these formulations. Parents often give a very low dose of paracetamol because they use the infant dropper, designed for 100 mg/mL preparations, to measure a dose of the more dilute preparations designed for use in older children.<sup>10</sup>

### Cost

Liquid preparations of paracetamol are expensive, with the MIMS price varying from \$1.11 to \$5.39 per g of paracetamol (mean \$2.52 per g). In contrast, the MIMS price of 500 mg tablets of paracetamol is 10c to 45c per g. Tablets are a much cheaper form of paracetamol than liquid preparations, and some brands of paracetamol tablets are very much cheaper than others (the brands listed in the Schedule of Pharmaceutical Benefits tend to be less expensive).

## Antipyretics may be harmful

### *Immunity*

Too many parents and health workers think that infection is bad, infection causes fever, and that therefore fever is bad. In fact, fever is often a beneficial host response to infection, and moderate fever improves immunity.<sup>11</sup> Therefore, it may not be a good idea to give drugs that reduce temperature to patients with severe infection. I have recently reviewed the results of 9 controlled trials in mammals of the effect of paracetamol or aspirin on mortality or virus excretion. Four trials found that aspirin increased mortality in bacterial or viral infection. Viral shedding was increased by paracetamol or aspirin in 3 studies, possibly increased in one, and not affected in two (one used only pharyngeal washings, and one had only 9 subjects in the aspirin and placebo groups). One study found that antibody production was impaired by both paracetamol and aspirin, but no effect on antibody production was detected in the study with only 9 subjects in the aspirin and placebo groups. This evidence suggests that aspirin and paracetamol increase mortality in severe infection, and that they may prolong the infection and reduce the antibody response in mild disease.

### *Direct toxicity*

Despite the millions of children treated with paracetamol, very little serious toxicity has been recognised (but note that the association between aspirin and Reye's syndrome was not recognised for many years). Penna and Buchanan<sup>12</sup> reviewed reports of 7 deaths and 11 cases of hepatotoxicity associated with paracetamol in children. The children who died had had more than 300 mg/kg/day of paracetamol for 1-6 days, except for one child where the plasma level suggested that the actual dose may have been much higher than the reported dose. The children who had hepatotoxicity but survived had all had 150 mg/kg/day for 2-8 days, except for two children where there was a discrepancy between the low reported doses and the high plasma levels of paracetamol (which was probably due to miscalculation of the dose or deliberate poisoning). Presumably, other cases of paracetamol toxicity in children have occurred and have gone unrecognised or unreported, but the evidence suggests that toxicity from paracetamol is rare with doses less than 150mg/kg/day. The dose of paracetamol should not exceed 100mg/kg/

day in children, and no patient should receive more than 4 g/day.

In acute poisoning from paracetamol, treatment with acetylcysteine should be started within 10 hours if possible. If the delay in starting acetylcysteine is more than 10 hours or if there is established liver failure, a longer course of acetylcysteine should be given.<sup>13,14</sup> The best regimen has not been determined; I suggest giving 150 mg/kg of acetylcysteine in 5% dextrose intravenously over 15 minutes; then 12mg/kg/hour (200 microgram/kg/minute) for 4 hours; then 6mg/kg/hour (100 microgram/kg/minute) for at least 16 hours if the delay in starting was less than 10 hours, for at least 28 hours if the delay was 10-16 hours and at least 68 hours if the delay was more than 16 hours. Acetylcysteine should be continued as long as the patient has encephalopathy, abnormal liver function tests or paracetamol detected in the serum.

## Conclusion

The antipyretic action of paracetamol is useful in febrile patients with cardiac or respiratory failure. The analgesic action is useful in minor acute infection, for postoperative pain and after vaccination with triple antigen.

There is little evidence to support the use of paracetamol to treat fever in patients without heart or lung disease, or to prevent febrile convulsions. Indeed, paracetamol may decrease the antibody response to infection, and increase morbidity and mortality in severe infection. It should be explained to parents that fever is usually a helpful response to infection, and that paracetamol should be used to reduce discomfort, but not to treat fever.

Although an initial dose of 20 mg/kg of paracetamol can be given, this is rarely necessary. The maintenance dose in children is 10-15 mg/kg 4 hourly. Hepatotoxicity has been reported with doses of 150 mg/kg/day, and no patient should be given more than 100 mg/kg/day (up to a maximum of 4 g/day).

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## Self-test questions

The following statements are either true or false ([click here for the answers](#))

1. Paracetamol should not be used to relieve the adverse effects of triple antigen as it may reduce the immune response.
2. A gram of liquid paracetamol is approximately 10 times more expensive than the paracetamol contained in tablets.

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