**PARACETAMOL** = Acetaminophen (USAN) [WEB COMMENTARY]

## Use

Paracetamol is a valuable analgesic also sometimes used to control fever. An IV formulation is now available.

## Pharmacology

Paracetamol, which has analgesic and anti-pyretic but no anti-inflammatory properties, was first marketed as an alternative to phenacetin in 1953. Now that aspirin (q.v.) is no longer recommended for children under 16 (except as an antithrombotic and in Kawasaki disease) because of its link to Reye's syndrome, paracetamol has become the most widely used analgesic for children (although dosage is often suboptimal). Intermittent (p.r.n.) administration in response to perceived pain seldom provides optimal relief and, while anticipatory use (treatment started 1–2 hours before surgery) certainly helps to control post-operative pain, visceral pain often needs opiate analgesia. Clearance is slightly slower in babies with visible jaundice. Tolerance does not develop with repeated use (as it does with opioid drugs), and respiratory depression is not a problem, but there is an analgesic ceiling that cannot be overcome by using a higher dose.

Paracetamol is rapidly absorbed by mouth, widely distributed in the body ($V_D$ ~1 l/kg), and mostly conjugated in the liver before excretion in the urine. Optimum pain relief only occurs an hour after the blood level peaks. The main metabolite changes during childhood, but elimination in babies over 3 months old (half life ~3 hours) is as rapid as in adults. It is a little slower in term babies at birth (4 hours), and is initially 8 hours in babies born more than 8 weeks early. Rectal absorption is rapid but incomplete, and influenced by the volume given. Luckily, although the manufacturer has not yet endorsed its use in the preterm baby, the development of an IV formulation (see web commentary) is set to render rectal administration unnecessary. Toxicity is uncommon in infancy, possibly because reduced cytochrome P-450 activity limits toxic arene metabolite production, but an overdose could still cause late lethal liver failure if not treated promptly. Paracetamol seems the analgesic of choice in pregnancy, and the breastfed baby is only exposed to 5% of the weight-related maternal dose.

## Management of fever

While paracetamol can give symptomatic relief to a child who is feverish (just as an adult will sometimes take two aspirins and retire to bed!), its use to control fever *per se* is usually uncalled for. One oral 30 mg/kg dose often suffices. Prophylactic use for febrile convulsions is of no proven value, and these are only of concern if they are focal, last more than 15 minutes, or recur during the same febrile illness. Most children just need to be unwrapped. Forced cooling does not work. Ibuprofen (q.v.) may be preferable for babies over 3 months old because asthma seems commoner later on in children who experienced early paracetamol exposure.

## Treatment in the neonate

***Oral pain relief:*** Give a 24 mg/kg loading dose (1 ml/kg of the 24 mg/ml oral elixir) and a maintenance dose of 12 mg/kg every 4 hours (every 8 hours in babies of less than 32 weeks postconceptional age).

***IV administration:*** Give a 20 mg/kg loading dose over about 15 minutes. Then give further maintenance doses once every 6 hours as follows: 10 mg/kg to babies of less than 30 weeks postmenstrual age, 12·5 mg/kg to babies of 31–36 weeks postmenstrual age, and 15 mg/kg to term babies.

***Rectal administration:*** Give term babies a 36 mg/kg loading dose and then 24 mg/kg once every 8 hours

***Sustained use:*** These doses are higher than those suggested by the manufacturer, so it is wise to check the trough blood level before giving high dose treatment by *any* route for more than 36 hours to a baby less than 3 months old (sooner in the jaundiced or very preterm baby) to check safety and also optimise pain relief.

## Treatment in babies over 3 months old

***Oral pain relief:*** Give a 24 mg/kg loading dose and then 18 mg/kg once every four hours.

***IV pain relief:*** Give a 20 mg/kg loading dose and then 15 mg/kg once every 4 hours.

## Toxicity

Lethal liver damage can occur in adults if the plasma level exceeds 150 mg/l four or more hours after ingestion (1 mg/l = 6·62 mmol/l). The safe threshold after repeated use is much less certain. Give 150 mg/kg of IV acetylcysteine *promptly* over 30 minutes, in a little 5% dextrose, if there is concern. Then give 12 mg/kg per hour for 4 hours, followed by 4 mg/kg per hour for 48 hours. Later doses can be given orally.

## Blood levels

Collect at least 50 µl of plasma, and aim to sustain a trough level of 10 mg/l. Patients can be asymptomatic despite toxic blood levels, but relief of pain almost certainly requires a peak plasma level of over 20 mg/l.

## Supply

100 ml of the 24 mg/ml sugar-free elixir costs 41p. Parents can get this for a baby over 3 months old without a prescription. Using this elixir rectally (instead of a suppository) speeds absorption. 50 ml (10 mg/ml) IV vials cost £1·50. Use within an hour of dilution. 10 ml ampoules of acetylcysteine (200 mg/ml) cost £2·50.

## References

See also the relevant Cochrane reviews ©


Jacqz-Aigrain E, Anderson BJ. Pain control: non-steroidal anti-inflammatory agents. *Sem Fetal Neonatal Med* 2006;**11**:251–9.

Palmer GM, Atkins M, Anderson BJ, *et al.* IV acetaminophen pharmacokinetics in neonates after multiple doses. *Br J Anaesth* 2008;**101**:523–30.

Anderson BJ, Allegaert K. Intravenous neonatal paracetamol dosing: the magic 10 days. [Editorial] *Pediatr Anesth* 2009;**19**:289–95.

Duggan ST, Scott LJ. Intravenous paracetamol (acetaminophen). *Drugs* 2009;**69**:101–13.


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