Paracetamol is well known for its capacity to cause serious patient harm. It is the most common medicine involved in childhood poisonings and the leading cause of paediatric acute liver failure in New Zealand. In the 10 years from 2002-2012, 14 children presented with acute liver failure in Australia and New Zealand with paracetamol attributed as the underlying cause. Of those, 3 children required liver transplantation and 2 died. Risk factors for paracetamol-induced hepatotoxicity include chronic malnutrition, prolonged fasting and dehydration. The most common errors with paracetamol dosing are increased frequency of dosing, exceeding recommended doses, and prolonged duration of therapy (>48 hours). These errors coupled with an already sick child can be a fatal combination. Parents and carers have expressed difficulty reading and understanding labelled instructions, and using measuring devices. Clearly explain the dosing instructions and emphasise the risk of toxicity particularly for children less than 5 years who are most at risk.

EDUCATE CAREGIVERS TO STORE ALL MEDICINES OUT OF REACH AND OUT OF SIGHT OF CHILDREN

Many childhood overdoses of paracetamol are attributed to unsupervised ingestion. Use every opportunity to remind families and caregivers to store all medicines and poisons well out of reach, and out of sight of children, ideally in a locked cupboard. National initiatives to reduce poisonings have centred on discouraging the unsafe behaviour of storing liquid paracetamol in the fridge, with good effect.

Child resistant closures must be placed on dispensed oral liquid formulations of paracetamol. Before these closures were introduced, the Poison Information Centre received 90 enquiries over a three month period concerning childhood poisoning with liquid paracetamol; this reduced to 20 enquiries in three months after the introduction of the closures.

ENCOURAGE PARACETAMOL TO BE USED FOR APPROVED CONDITIONS ONLY

Paracetamol is generally considered to be a safe analgesic option, and is indicated for mild to moderate pain, or pyrexia with discomfort. Health professionals should encourage caregivers to avoid unnecessary use and to reserve it for children in discomfort or with known painful conditions.

Pyrexia alone does not require treatment and is not known to endanger an otherwise healthy child; analgesia is only recommended if the child is distressed or in pain. There is no evidence that anti-pyretic therapy decreases the recurrence of febrile seizures. There is some evidence to suggest that fever may increase the metabolism of paracetamol to the toxic metabolite. This, coupled with vomiting, diarrhoea and poor oral intake can further increase the risk of hepatic injury.

The primary goal should be to improve the child’s comfort rather than focusing on the normalisation of body temperature. The use of prophylactic paracetamol during paediatric immunisations (including the influenza vaccine) is not recommended because it may affect the antibody response.

Note: Although evidence from a large international study shows a dose-dependent association between paracetamol use in infancy and asthma symptoms in children aged 6-7 years, there still appears to be no conclusive evidence of a link between paracetamol and asthma.
USE INDIVIDUALISED DOSES; SUPPLY SMALLER VOLUMES

Medsafe recommends giving the lowest dose of paracetamol that is necessary for the shortest time possible. Health professionals can promote the safe and effective use of paracetamol in many ways:

- Restrict volume to 200mL per dispensing
- Prescribe for each child rather than an entire family
- Individualise doses with volumes that are easy to measure
- Avoid combined therapy [eg with ibuprofen] which may confuse the dosing regimen
- Recommend giving for no more than 48 hours
- Provide clear verbal and written information
- Check that caregivers understand the directions on the label

Paracetamol dose for infants and children over 1 month of age

<table>
<thead>
<tr>
<th>Dose and frequency</th>
<th>15 mg/kg/dose, every four hours, up to four times a day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum doses</td>
<td>60mg/kg/day, up to 1000mg/dose or 4000mg/day</td>
</tr>
</tbody>
</table>

Pharmacy dispensing software has a dosing label with weight-based dosing information that can be printed and attached to dispensed bottles of paracetamol.

CHECK THAT CAREGIVERS AND FAMILIES KNOW HOW TO MEASURE EACH DOSE

Ask caregivers if they have appropriate measuring devices and they understand how to use them correctly. A survey of 200 parents revealed that over 60% had administered incorrect doses of paracetamol to their children. Ensure that all caregivers are aware of which strength they are using [120mg/5ml or 250mg/5ml], and which volume to give. It may be safer to encourage families to use only one strength [eg use 120mg/5ml for children under 5yrs]; this approach may reduce poisonings requiring hospitalisation.

Children (and adults) must not be given more than four doses of paracetamol in any 24-hour period. One of the most commonly reported scenarios of caregiver-related overdose has involved too frequent administration [intervals of less than four hours]. Cases of liver failure requiring transplantation have occurred from this cause. There is a greater risk of this happening if there are multiple caregivers; encourage clear communication between caregivers, and documentation of doses.

A study involving 60 caregivers revealed that 17% admitted the dosage instructions for children were difficult to understand. It is important that dosing information is clear and has been understood. More than one form of information, such as written and verbal, is recommended. Even if caregivers can read the information provided, they cannot always apply this information to dosage requirements for their children.

If parents or caregivers suspect that their child has received too much paracetamol, it is important that they receive immediate medical attention. Nausea and vomiting are the only early features of poisoning, and may be attributed to the condition being treated.

Hepatic damage may not be apparent for 4-6 days. Patients at high risk of liver damage, including those who are malnourished, can develop toxicity with 75mg/kg paracetamol. Acetylcysteine protects the liver if infused within 24 hours of ingestion, and is most effective if given within 8 hours.

Note: Recently there has been a reported association with paracetamol and serious skin reactions. Patients should be advised to consult their doctor at the first appearance of a skin rash, peeling or mouth ulcers. The FDA has issued a drug safety warning that paracetamol has been associated with severe cutaneous adverse reactions [SCARs] which include Stevens Johnson Syndrome.

VISIT WWW.SAFERX.CO.NZ FOR USEFUL PATIENT RESOURCES

A leaflet about giving paracetamol safely to babies and children is available in English, Chinese and Korean on www.saferx.co.nz. Either print directly from the site, or contact feedback@saferx.co.nz for printed versions. Several practices provide this leaflet to caregivers during the 6-week immunisation appointment.
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REFERENCES