Paracetamol

Paracetamol overdose is a common cause of hospital presentation and admission.

Previous guidelines for the management of paracetamol overdose **DID NOT**

- provide uniformity in a treatment nomogram in Australasia
- deal with extended-release paracetamol
- reflect current clinical toxicology practice or poison centre recommendations.

In 2006 a panel of Australian and New Zealand toxicologists met to draft new consensus guidelines. Revised guidelines were released in 2007. A consensus statement was published in the Medical Journal of Australia in 2008 and summarized in a one page document prepared by industry.

The one page document (see page 2) provides information about treatment of paracetamol overdose including:

- administration of N-acetylcysteine
- a paracetamol treatment nomogram *(enlarged on page 3)*
- management of acute single ingestions
- what to do when the nomogram does not apply.

**Further Reading**

*Daly FFS, Fountain JS, Murray L, Graudins A, Buckley NA. Guidelines for the management of paracetamol poisoning in Australia and New Zealand – explanation and elaboration. MJA 2008;188:296–301.*  

Guidelines for the management of paracetamol overdose

Paracetamol Use PD2006_004

**Recommended action by Area Health Services**

- Forward to appropriate areas for information.
Guidelines for the management of paracetamol overdose

General Information
1. Paracetamol overdose is a significant cause of hospital admission, but severe liver injury is rare and even when it does occur the prognosis is usually good.
2. Signs consistent with paracetamol poisoning include repeated vomiting, abdominal tenderness in the right upper quadrant or mental status changes.
3. Hypoprolactinaemia on presentation is very rare, but is important to consider in late presentations if fever has occurred.
4. Any patient should be considered to be at risk of severe liver injury if they have ingested paracetamol above the thresholds below (See Table 1).
   - Children <20 kg body weight: If the dose ingested is estimated to be more than 200mg/kg, manage as per the 200mg/kg dose threshold.
   - Children >20 kg body weight: Following acute overdose, the most important factor that determines prognosis is the time (beyond 8 hours) following overdose.
2. Signs consistent with paracetamol poisoning include repeated vomiting, abdominal tenderness in the right upper quadrant or mental status changes.
3. Hypoprolactinaemia on presentation is very rare, but is important to consider in late presentations if fever has occurred.
4. Any patient should be considered to be at risk of severe liver injury if they have ingested paracetamol above the thresholds below (See Table 1).
   - Children <20 kg body weight: If the dose ingested is estimated to be more than 200mg/kg, manage as per the 200mg/kg dose threshold.
   - Children >20 kg body weight: Following acute overdose, the most important factor that determines prognosis is the time (beyond 8 hours) following overdose.

Paracetamol Treatment Nomogram
- Treat all patients with serum paracetamol levels above the nomogram treatment line.
  1. Potential to misread estimate of time of ingestion.
  2. Increased safety for all patients with potential risk factors.

TABLE 1: Thresholds: Potentially Hepatotoxic Paracetamol Overdoses

<table>
<thead>
<tr>
<th>BODY WEIGHT (kg)</th>
<th>Thresholds</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>150 mg/kg</td>
</tr>
<tr>
<td>15–30</td>
<td>100 mg/kg</td>
</tr>
<tr>
<td>30–60</td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>60–110</td>
<td>25 mg/kg</td>
</tr>
<tr>
<td>&gt; 110</td>
<td>20 mg/kg</td>
</tr>
</tbody>
</table>

Adapted from Knezevic and the New Zealand Clinical Toxicology Network.

What To Do When The Nomogram Does Not Apply
Unknown Time Of Paracetamol Ingestion
- If there is a detectable paracetamol level with an unknown time of ingestion, commence NAC and treat the patient as per the 12-18 hours scenario (i.e. a) on the Acute Ingestion Management Flow-Chart.

Staggered Overdose
- A staggered overdose comprises several ingestions over a period of less than 24 hours.
- If the patient has taken an overdose of paracetamol at two time intervals within the 8-12 hours, instead of 12-24 hour interval, the levels at the first and second overdose are treated as separate ingestions for the 12-24 hour scenarios in the Acute Ingestion Management Flow-Chart.

Sustained-Release Paracetamol Preparations
- If more than 310mg or 200mg/kg (whichever is less) has been ingested combine NAC.
- Measure serum paracetamol level at 4 or more hours post-ingestion, then again 4 hours later if the first level is below the nomogram line.
- If both levels are below the nomogram line NAC may be discontinued.
- If level is above the nomogram line NAC should be continued and managed followed according to the Acute Ingestion Management Flow-Chart.

Repeated Supratherapeutic Ingestion in Adults and Children
- If the patient has ingested sufficient doses to suggest risk of developing hepatic injury (Refer to Table 1), manage as for the Repeated Supratherapeutic Ingestion Management Flow-Chart.

Repeated Supratherapeutic Ingestion Management Flow-Chart

Does the patient meet the criteria for repeated supratherapeutic ingestion?
- Adults > 16 years
  - At least 10g or 2000mg (whichever is greater) over a single 24 hour period.
  - At least 40g or 4000mg (whichever is greater) over the preceding 48 hours.
- Children
  - 10g or 2000mg over a single 24 hour period.
  - 40g or 4000mg over the preceding 72 hours.

TABLE 2: Acute Ingestion Management Flow-Chart

<table>
<thead>
<tr>
<th>Management of Acute Single Ingestions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decontamination</strong></td>
</tr>
<tr>
<td>No decontamination if any kind is indicated in paediatric patients.</td>
</tr>
</tbody>
</table>

Specific Paediatric Considerations
- Paracetamol levels, LFTs or follow-up.

NAC Intravenous Infusion Dosage Guide

<table>
<thead>
<tr>
<th>BODY WEIGHT (kg)</th>
<th>NAC Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>30-45 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>15–30</td>
<td>20-30 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>30–60</td>
<td>15-20 mg/kg over 20 minutes</td>
</tr>
<tr>
<td>60–110</td>
<td>10-15 mg/kg over 20 minutes</td>
</tr>
</tbody>
</table>

If the patient has ingested sufficient doses to suggest risk of developing hepatic injury (Refer to Table 1), manage as for the Repeated Supratherapeutic Ingestion Management Flow-Chart.

Repeated Supratherapeutic Ingestion Management Flow-Chart

Does the patient meet the criteria for repeated supratherapeutic ingestion?
- Adults > 16 years
  - At least 10g or 2000mg (whichever is greater) over a single 24 hour period.
  - At least 40g or 4000mg (whichever is greater) over the preceding 48 hours.
- Children
  - 10g or 2000mg over a single 24 hour period.
  - 40g or 4000mg over the preceding 72 hours.

TABLE 2: NAC Intravenous Infusion Dosage Guide

<table>
<thead>
<tr>
<th>BODY WEIGHT (kg)</th>
<th>NAC Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>30-45 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>15–30</td>
<td>20-30 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>30–60</td>
<td>15-20 mg/kg over 20 minutes</td>
</tr>
<tr>
<td>60–110</td>
<td>10-15 mg/kg over 20 minutes</td>
</tr>
</tbody>
</table>

If the patient has ingested sufficient doses to suggest risk of developing hepatic injury (Refer to Table 1), manage as for the Repeated Supratherapeutic Ingestion Management Flow-Chart.

Repeated Supratherapeutic Ingestion Management Flow-Chart

Does the patient meet the criteria for repeated supratherapeutic ingestion?
- Adults > 16 years
  - At least 10g or 2000mg (whichever is greater) over a single 24 hour period.
  - At least 40g or 4000mg (whichever is greater) over the preceding 48 hours.
- Children
  - 10g or 2000mg over a single 24 hour period.
  - 40g or 4000mg over the preceding 72 hours.

TABLE 2: NAC Intravenous Infusion Dosage Guide

<table>
<thead>
<tr>
<th>BODY WEIGHT (kg)</th>
<th>NAC Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>30-45 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>15–30</td>
<td>20-30 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>30–60</td>
<td>15-20 mg/kg over 20 minutes</td>
</tr>
<tr>
<td>60–110</td>
<td>10-15 mg/kg over 20 minutes</td>
</tr>
</tbody>
</table>

If the patient has ingested sufficient doses to suggest risk of developing hepatic injury (Refer to Table 1), manage as for the Repeated Supratherapeutic Ingestion Management Flow-Chart.

Repeated Supratherapeutic Ingestion Management Flow-Chart

Does the patient meet the criteria for repeated supratherapeutic ingestion?
- Adults > 16 years
  - At least 10g or 2000mg (whichever is greater) over a single 24 hour period.
  - At least 40g or 4000mg (whichever is greater) over the preceding 48 hours.
- Children
  - 10g or 2000mg over a single 24 hour period.
  - 40g or 4000mg over the preceding 72 hours.

TABLE 2: NAC Intravenous Infusion Dosage Guide

<table>
<thead>
<tr>
<th>BODY WEIGHT (kg)</th>
<th>NAC Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>30-45 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>15–30</td>
<td>20-30 mg/kg over 15 minutes</td>
</tr>
<tr>
<td>30–60</td>
<td>15-20 mg/kg over 20 minutes</td>
</tr>
<tr>
<td>60–110</td>
<td>10-15 mg/kg over 20 minutes</td>
</tr>
</tbody>
</table>

If the patient has ingested sufficient doses to suggest risk of developing hepatic injury (Refer to Table 1), manage as for the Repeated Supratherapeutic Ingestion Management Flow-Chart.
Paracetamol Treatment Nomogram

- Treat ALL patients with serum paracetamol levels above the nomogram treatment line
- A single nomogram treatment line is recommended. This line has been lowered by 25% from standards lines to take into account:
  1. Potential for minor error estimating the time of ingestion
  2. Increased safety for all patients with potential risk factors
- Ensure that correct units are used (i.e. μmol/L or mg/L)