Paracetamol ingestion - Emergency management in children

Purpose

This document provides clinical guidance for all staff involved in the care and management of a child presenting to an Emergency Department (ED) in Queensland following a paracetamol ingestion.

This guideline has been developed by senior ED clinicians and Paediatricians across Queensland, with input from Queensland Poisons Information Centre, Clinical Toxicology, Princess Alexandra Hospital and Pharmacy, Gastroenterology and PICU, Queensland Children’s Hospital, Brisbane. It has been endorsed for use statewide by the Queensland Emergency Care of Children Working Group in partnership with the Queensland Emergency Department Strategic Advisory Panel and the Healthcare Improvement Unit, Clinical Excellence Queensland.

Key points

- Toxic paracetamol ingestions require prompt treatment with Acetylcysteine infusion to avoid serious hepatic injury and death.
- The need for acetylcysteine is guided by serum paracetamol concentration levels using a treatment nomogram.
- Administer acetylcysteine immediately if paracetamol concentration levels are not likely to be available within eight hours of a potentially toxic ingestion (due to delay in presentation to ED or time for testing or uncertain time of ingestion) or patient has symptoms of hepatic injury.
- Careful attention is required to avoid acetylcysteine dosing errors. Fluid adjustment is required for children.
- Seek urgent toxicological advice from Poisons Information (Ph: 131126) for IV or very large overdoses (50 g or 1 g/kg), or if evidence of hepatotoxicity (ALT greater than 1,000 IU/L). Critical care may be required.

Introduction

Paracetamol is a widely used analgesic that is readily available in many different preparations. Accidental or deliberate overdose can cause hepatic failure and death. This can be prevented by the early administration of acetylcysteine.1

This guideline is based on the recommendations made in 2020 by a group of Australasian Clinical Toxicologists consulting to the Poisons Information Centre.1 2

While there are certain groups who are at higher risk of hepatotoxicity (such as those with malnutrition, eating disorders, cystic fibrosis or acute viral infections) the recommended management is conservative and so remains unchanged.
Pharmacokinetics

Paracetamol is rapidly absorbed in the small intestine and reaches peak concentrations within 30 minutes for liquid preparations and one to two hours for standard tablet preparations. Distribution then occurs within two hours for liquid preparations and four hours for standard tablet preparations.¹ Hepatic biotransformation results in 90% of paracetamol being metabolised to Acetylcysteine sulphate and glucuronide conjugates which are then excreted by the kidneys. The remaining 10% requires cytochrome p450 to make an intermediary compound of N-Acetyl-p-benzoquinone imine (NAPQI) which then in turn binds to intracellular glutathione for renal excretion. Depletion of glutathione occurs with higher production of NAPQI which subsequently binds to other proteins and thus damages hepatocytes. Clinical or biochemical evidence of this damage may take up to 24 hours post overdose to become apparent.¹ ³ ACETYLCYSTEINE is an effective antidote to paracetamol toxicity by increasing the synthesis and availability of glutathione and directly binding to NAPQI. Appropriate treatment commencing within eight hours of the overdose will prevent almost all serious hepatic injury.

Assessment

The aim of the initial assessment is to determine the risk of hepatic injury following paracetamol ingestion.

History

History-taking should include information on:
- number, quantity and timing of ingestions
- symptoms of hepatic injury (such as abdominal pain, nausea or vomiting, anorexia)

Examination

Full examination focussing on eliciting any toxidromes to suggest co-ingestion, neurological status for co-ingestion risk and hepatic encephalopathy, and serial abdominal examinations which can elicit right upper quadrant tenderness.

Calculation of ingested dose

Use the available information to calculate the dose per kilogram of paracetamol ingested. When in doubt of the quantity, use the maximum possible ingested dose to determine the potential for hepatic injury.

<table>
<thead>
<tr>
<th>Age</th>
<th>Acute single ingestion</th>
<th>Repeated supratherapeutic ingestion</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 6 years</td>
<td>Greater than 200 mg/kg &lt; than eight hours from ingestion time</td>
<td>Any of the following:</td>
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<tr>
<td></td>
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<td>• greater than 60 mg/kg per 24-hour period for greater than 48 hours (may have abdominal pain, nausea or vomiting)</td>
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<tr>
<td>Over 6 years</td>
<td>Greater than 200 mg/kg or 10g (whichever is lower) &lt; than eight hours from ingestion time</td>
<td>Any of the following:</td>
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<td></td>
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<td>• greater than 150 mg/kg or 6 g (whichever is lower) per 24-hour period for the preceding 48 hours</td>
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<td></td>
<td></td>
<td>• greater than 60 mg/kg or 4 g (whichever is lower) per 24-hour period for greater than 48 hours AND symptoms indicating possible liver injury (such as abdominal pain, nausea or vomiting)</td>
</tr>
</tbody>
</table>

*Use the ideal body weight for body weight calculations in obese children
Investigations

**ALERT** – Administer acetylcysteine immediately if paracetamol concentration levels are not likely to be available within eight hours of a potentially toxic ingestion (due to delay in presentation to ED or time for testing or uncertain time of ingestion) or patient has symptoms of hepatic injury (abdominal pain, nausea and anorexia). Do not delay for paracetamol concentration levels.

Serum paracetamol concentration testing is used to determine the need for acetylcysteine (by plotting on the treatment nomogram provided below). Testing is recommended for patients with a history of:

- ingesting a toxic dose (refer to table in Assessment section)
- deliberate self-poisoning regardless of the stated ingested dose
- accidental exposures if uncertain of ingested dose

**Investigations recommended for the management of paracetamol overdose**

| Children aged less than 6 years post-ingestion of liquid paracetamol | Serum paracetamol concentration at 2 hours post-ingestion. Concentrations less than 150 mg/L require no further treatment. Repeat at four hours post-ingestion if two-hour level is greater than or equal to 150 mg/L. |
|---|
| **Patients with single potentially toxic paracetamol ingestion** | **Time of presentation** | **Testing** |
| Within 8 hours of ingestion | Serum paracetamol concentration and ALT at 4-8 hours post-ingestion. Two hours before the end of acetylcysteine infusion repeat level and measure ALT. |
| 8-24 hours post-ingestion | Serum paracetamol concentration and ALT on presentation and commence acetylcysteine while awaiting level Measure ALT and paracetamol level two hours before end of acetylcysteine infusion. |
| Greater than 24 hours post-ingestion | Serum paracetamol concentration, transaminases (ALT/AST), INR/PT, creatinine, urea, glucose and arterial or venous blood gas on presentation and commence acetylcysteine while awaiting level. Follow up as clinically indicated. |
| Unknown | Serum paracetamol concentration, ALT and INR on presentation and commence acetylcysteine while awaiting level. Seek toxicologist advice for further testing. |
| **Patients post-ingestion of sustained release paracetamol** (e.g. Panadol Osteo® and Osteomol®) | Serum paracetamol concentration minimum of four hours post-ingestion. ALT and repeat serum paracetamol concentration four hours after initial testing to capture the delayed release. Repeat paracetamol levels and ALT again two hours prior to cessation of the infusion. |
Investigations recommended for the management of paracetamol overdose

| Patients with potentially toxic repeated supratherapeutic ingestions | Serum paracetamol concentration and ALT on presentation. Repeat at eight hours after initial measurement if either serum paracetamol concentration greater than 20 mg/L or ALT greater than 50 U/L. Check ALT every twelve hours if ALT greater than 50 U/L or paracetamol concentration is greater than 10 mg/L. |

Paracetamol treatment nomogram


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Management

Refer to Appendix 1 for a summary of the emergency management for a child following a paracetamol ingestion.

Contact a Clinical Toxicologist via Poisons Information Centre (ph.: 131126) urgently for:
- overdoses of 50 g or 1 g/kg (always use lower threshold)
- tested paracetamol concentration is double the nomogram line
- IV overdoses
- evidence of hepatotoxicity (ALT greater than 1,000 IU/L)

Higher concentrations of acetylcysteine may be required. Contact paediatric critical care specialist (onsite or via Retrieval Services Queensland (RSQ)) as advised by Poisons Information Centre/Clinical Toxicologist

Refer patients with a deliberate overdose for a psychiatric assessment as per local practices

Activated charcoal

Activated charcoal is not a life-saving treatment but may prevent or reduce the need for treatment with acetylcysteine if used appropriately. Activated charcoal is only routinely recommended for cooperative patients aged greater than six years if able to be administered one to two hours post-ingestion. It may be given up to four hours post-ingestion for very large overdoses, or beyond this time frame for large overdoses of sustained release paracetamol preparations on advice from Poisons Information Centre/Clinical Toxicologist. It is not recommended in liquid preparation overdose due to the fast absorption time.

Acetylcysteine

Acetylcysteine following single toxic paracetamol ingestion

The need for acetylcysteine is guided by serum paracetamol concentration levels using a treatment nomogram (see Assessment section).

**Alert** – Additional management is required for sustained release paracetamol ingestions. Refer to section below.

<table>
<thead>
<tr>
<th>Time from ingestion</th>
<th>Indications for acetylcysteine</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 hours</td>
<td>acetylcysteine will not be required for children aged less than 6 years with serum paracetamol concentration less than 150 mg/L at two hours post-ingestion of liquid paracetamol. If greater than or equal to 150 mg/L do not commence acetylcysteine but repeat level at four hours.</td>
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<tr>
<td>4-8 hours</td>
<td>Commence acetylcysteine if:</td>
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<td>• serum paracetamol concentration levels taken at 4 hours post-ingestion are greater than or equal to 150 mg/L or</td>
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<tr>
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<td>• serum paracetamol concentration levels taken 4-8 hours post-ingestion are above the nomogram treatment line.</td>
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</table>
• sustained release dosing is greater than 10g or 200mg/kg regardless of paracetamol levels. A full course of acetylcysteine is required.

Await serum levels if results are expected within 8 hours of ingestion. If results are not expected within 8 hours, commence acetylcysteine and review serum levels when available. Continue acetylcysteine if levels taken within 4-8 hours of ingestion are above the nomogram treatment line. Otherwise cease infusion.

Greater than 8 hours

Commence acetylcysteine immediately if present 8 -24 hours post-ingestion. If present greater than 24 hours post-ingestion, collect bloods for further testing prior to commencing acetylcysteine (refer to Investigations).

Continue acetylcysteine if serum paracetamol concentration levels above the nomogram treatment line or ALT greater than 50 U/L.

Unknown

Commence acetylcysteine immediately. Continue acetylcysteine if paracetamol concentration is greater than 10 mg/L or ALT is greater than 50 U/L.

Sustained release paracetamol preparations (such as Panadol Osteo® and Osteomol® both with 665mg paracetamol/tablet) result in potentially delayed peak concentrations above the nomogram treatment line. A single measurement of paracetamol level is not adequate to make decisions around acetylcysteine administration if an unknown quantity or a potentially toxic quantity has been ingested.

Acetylcysteine following sustained release paracetamol ingestions

Acetylcysteine administration following sustained release paracetamol ingestions

In addition to the management previously described for single toxic ingestions, repeat serum level four hours after initial testing and commence acetylcysteine if either level is above the treatment line.

For all patients requiring acetylcysteine:
• If the dose ingested is greater then 30g or 500mg/kg, or either 4 hour apart paracetamol level is double the treatment line then double the second bag of acetylcysteine and seek toxicology advice
• measure paracetamol concentration levels and ALT two hours before completion of the acetylcysteine E infusion.
• continue the acetylcysteine infusion and seek toxicology advice if ALT is greater than 50 U/L or paracetamol concentration is greater than 10 mg/L

Acetylcysteine following repeated supratherapeutic ingestions*

Acetylcysteine administration following repeated supratherapeutic ingestions*

Commence acetylcysteine E if either serum paracetamol concentration greater than 20 mg/L or ALT greater than 50 U/L.

Repeat levels at 8 hours after initial testing. Discontinue acetylcysteine if ALT is less than 50 U/L or static AND paracetamol concentration is less than 10 mg/L. Otherwise continue acetylcysteine and recheck ALT every twelve hours.
**Acetylcysteine administration**

**ALERT** – Careful attention is required when ordering fluids. Fluid adjustment orders are required for smaller children due to risk of hyponatremia if using the total adult fluid volume (1500mls). Secondary seizures have resulted when using 5% glucose.4,5,6

Refer to the acetylcysteine guideline and use the appropriate order form (based on child’s weight) or the electronic ordering system.

The total acetylcysteine dosing is 300 mg/kg administered over 20 hours in two sequential IV infusions and is compatible with any glucose and/or sodium-based fluids. Dosing is calculated on actual body weight up to 110 kg (with dosing based on 110 kg weight for children over 110 kg). Acetylcysteine is packaged in 10 mL ampoules each containing 2,000 mg (20%). Doses are written in mg.

Where a two bag regime is available on smart pumps, use these profiles. If not available, confirm if the general acetylcysteine profile will allow the infusion to run. If not, revert to the mL/hour functionality (if programmed). Due to differences in doses and durations, it is not suitable to use the superseded three bag regime profile to run the two bag regime.

Prescribe the entire treatment course at the time of the initial presentation to avoid administration delays.

**Adverse drug reactions**

Anaphylactoid reactions including rash, pruritus, angioedema, bronchospasm and rarely hypotension may occur following acetylcysteine administration with females and asthmatics at higher risk. Progression to a more clinically significant reaction is rare.

If drug reactions occur, slow the infusion or temporarily cease the infusion, treat with antihistamines or bronchodilators and restart once the reaction settles.

**Ongoing liver impairment**

Seek specialist advice (Toxicology/Gastroenterology/Critical Care) for patients with ongoing evidence of liver impairment.

For patients with ongoing liver impairment, continue acetylcysteine and 12-hourly-blood-testing until clinically improving, ALT is reducing, INR is improving and less than 2.0 and the paracetamol level is less than 10 mg/L.

**Indications for referral to a liver transplant unit**

- INR greater than 3.0 at any time
- oliguria or creatinine greater than 200 μmol/L
- persistent acidosis pH less than 7.3
- systolic hypotension despite resuscitation
- hypoglycaemia
- severe thrombocytopenia
- encephalopathy not otherwise explained 2

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Escalation and advice outside of ED

Clinicians can contact the services below if escalation of care outside of senior clinicians within the ED is needed, as per local practices. Transfer is recommended if the child requires a higher level of care.

Critical care is unlikely to be required following a paracetamol overdose in isolation but may be required if co-ingestions have occurred. Seek critical care advice (onsite or via RSQ) if advised by toxicologist or child is critically unwell.

**Toxicology advice is required for the following:**
- overdoses of more than total of 50 g or 1 g/kg (always use lower threshold)
- tested paracetamol concentration is double the nomogram line
- IV overdoses
- evidence of hepatotoxicity (ALT greater than 1,000 IU/L)

**Reason for contact | Who to contact**

| Advice (including management, disposition or follow-up of all children requiring a ACETYLCYSTEINE infusion) | Follow local practices. Options:
- Poisons Information Centre 13 11 26 (24-hour service)
- onsite/local paediatric service
- Queensland Children’s Hospital experts via Children’s Advice and Transport Coordination Hub (CATCH) on 13 CATCH (13 22 82) (24-hour service)
- local and regional paediatric videoconference support via Telehealth Emergency Management Support Unit TEMSU (access via QH intranet) on 1800 11 44 14 (24-hour service) |
| Referral | First point of call is the onsite/local paediatric service |

**Inter-hospital transfers**

| Do I need a critical transfer? | • discuss with onsite/local paediatric service
• view Queensland Paediatric Transport Triage Tool |
| Request a non-critical inter-hospital transfer | • contact onsite/local paediatric service
• contact RSQ on 1300 799 127 for aeromedical transfers
• contact Children’s Advice and Transport Coordination Hub (CATCH) on 13 CATCH (13 22 82) for transfers to Queensland Children’s Hospital |
| Non-critical transfer forms | • QH Inter-hospital transfer request form (access via QH intranet)
• aeromedical stepdown (access via QH intranet)
• commercial aeromedical transfers:
  - Qantas
  - Virgin
  - Jetstar |
When to consider discharge from ED

Consider discharge for the following patients:

- Acetylcysteine infusion not required (based on assessment of serum paracetamol concentration levels or clear history of quantity of accidental ingestion)

AND

- if ingestion deliberate, a psychiatric assessment has been conducted as appropriate.

On discharge, educate the family regarding safe paracetamol administration and storage.

Follow-up

Not routinely required.

When to consider admission

Admission to an inpatient service or SSU is recommended for patients requiring ongoing ACETYLCYSTEINE infusion once serum paracetamol concentration and ALT levels are available.

Related documents

Guidelines

- Paediatric Medication Guideline Acetylcysteine (Intravenous)

Forms

- N- Acetylcysteine Order form- Child (less than 20kg)
- N- Acetylcysteine Order form- Child (20-50kg)
- N- Acetylcysteine Order form- Child (greater than 50kg)

References

Guideline approval

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<td>Queensland Emergency Care Children Working Group</td>
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Keywords
Paracetamol, overdose, ingestion, acetylcysteine, paediatric, emergency, guideline, children, 60018

Accreditation references
NSQHS Standards (1-8): 1, 4, 8

Disclaimer
This guideline is intended as a guide and provided for information purposes only. The information has been prepared using a multidisciplinary approach with reference to the best information and evidence available at the time of preparation. No assurance is given that the information is entirely complete, current, or accurate in every respect. We recommend hospitals follow their usual practice for endorsement locally including presenting it to their local Medicines Advisory Committee (or equivalent) prior to use.

The guideline is not a substitute for clinical judgement, knowledge and expertise, or medical advice. Variation from the guideline, taking into account individual circumstances may be appropriate.

This guideline does not address all elements of standard practice and accepts that individual clinicians are responsible for:
- Providing care within the context of locally available resources, expertise, and scope of practice
- Supporting consumer rights and informed decision making in partnership with healthcare practitioners including the right to decline intervention or ongoing management
- Advising consumers of their choices in an environment that is culturally appropriate and which enables comfortable and confidential discussion. This includes the use of interpreter services where necessary
- Ensuring informed consent is obtained prior to delivering care
- Meeting all legislative requirements and professional standards
- Applying standard precautions, and additional precautions as necessary, when delivering care
- Documenting all care in accordance with mandatory and local requirements

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Appendix 1

CHQ-GDL-60018 – Paracetamol Overdose – Emergency management in children
Box B: Criteria for toxicologist advice
Seek urgent toxicological advice via Poisons Information (ph.: 131126) for the following:
- IV overdoses
- very large overdoses (greater than 50 g or 1 g/kg) (always use lower threshold)
- evidence of hepatotoxicity (ALT greater than 1,000 IU/L)

Critical care may be required.
If unknown time of potentially toxic single ingestion, commence Acetylcysteine and seek advice re testing.

Box C: Acetylcysteine administration following sustained release paracetamol ingestions
Sustained release paracetamol preparations (such as Panadol Osteo and Osteomol) result in potentially delayed peak concentrations above the nomogram treatment line.
A single measurement of paracetamol level is not adequate to make decisions regarding acetylcysteine.
Consider activated charcoal use even if after 4 hours since ingestion in discussion with Poisons.
In addition to the management described for single toxic ingestions, repeat serum level 4 hours after initial testing and commence acetylcysteine if either level is above the treatment line.
- For all patients requiring acetylcysteine measure paracetamol concentration levels and ALT 2 hours before completion of the acetylcysteine infusion
- continue acetylcysteine infusion and seek toxicology advice if ALT is greater than 50 U/L or paracetamol concentration is greater than 10 mg/L

Box D: Acetylcysteine administration following liquid paracetamol ingestions in children aged <6 years
Acetylcysteine will not be required for children aged less than 6 years with serum paracetamol concentration less than 150 mg/L at 2 hours post-ingestion of liquid paracetamol.
If greater than or equal to 150 mg/L do not commence Acetylcysteine but repeat level at 4 hours.

Box E: Repeated supratherapeutic paracetamol ingestion that may be toxic
<table>
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