Paediatric Medication Guideline

N-Acetylcysteine (Intravenous) for Paracetamol Poisoning

Purpose

The purpose of this guideline is to provide clinical advice around the use of intravenous N-Acetylcysteine in paediatric patients at the Lady Cilento Children’s Hospital (LCCH).

Scope

This guideline is intended to assist all clinical staff to prescribe and administer intravenous N-acetylcysteine appropriately to patients at LCCH. It is not intended to be a substitute for specific professional or clinical advice, or to replace consultation with senior staff, which should always be sought if clinically relevant. The CHQ Guideline: Paracetamol overdose guideline – Emergency management in children and Guidelines for the Management of Paracetamol Poisoning in Australia and New Zealand contain important information that should be viewed in combination with this document.

This material is published by Queensland Health with the intention of providing a guideline for use at Lady Cilento Children’s Hospital. Anyone wishing to use this guideline outside LCCH should refer to their local Medicines Committee before using.

Related documents

Policy and standard(s)

- Australian Commission on Safety and Quality in Healthcare
Procedures, Guidelines, Protocols

- Guidelines for the management of paracetamol poisoning in Australia and New Zealand.¹
- CHQ Guideline: Paracetamol overdose guideline – Emergency management in children
- CHQ Procedure 01001: Medication - Prescribing
- CHQ Procedure 01039: Medication - Administration
- CHQ Procedure 01017: Adverse Drug Reaction (ADR) Monitoring

Forms and templates

- Clinical forms for N-Acetylcysteine chart –
  - N-Acetylcysteine order form (<20kg)
  - N-Acetylcysteine order form (20-50kg)
  - N-Acetylcysteine order form >50kg

Description and Indications for Use

N-Acetylcysteine (NAC, acetylcysteine) is used as an antidote in paracetamol poisoning.

---

**ALERT**

Refer to the CHQ Guideline: Paracetamol overdose guideline – Emergency management in children for important information regarding risk assessment and indications for N-Acetylcysteine use.

---

Paracetamol is rapidly absorbed in the small intestine and reaches peak concentrations within half an hour for liquid preparations and 1-2 hours for standard tablet preparations. Distribution then occurs within 2 hours for liquid preparations and 4 hours for standard tablet preparations.² Hepatic biotransformation results in 90% of paracetamol metabolised to inactive 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.²³ Treatment commencing within 8 hours of the overdose will prevent serious hepatic injury in almost all patients.

N-Acetylcysteine is an effective antidote to paracetamol overdose by increasing the synthesis and availability of glutathione and also directly binding to NAPQI.

N-Acetylcysteine reduces mortality even if commenced in patients presenting with established paracetamol-induced fulminant hepatic failure. The mechanisms of action in this period may be different.
N-Acetylcysteine (Acetadote®, DBL®, Link®) is available as a 2000mg/10mL solution for injection.

**Prescribing Instructions**

N-Acetylcysteine treatment consists of staged infusions that are given sequentially over a period of 21 hours. Care must be taken in dose calculation and administration instructions. Dosage of N-Acetylcysteine is based on actual bodyweight with a ceiling weight of 110kg.\(^1\) Doses are written in milligrams. The entire treatment course must be written at the time of initial prescribing to ensure there is no delay in receiving the antidote.

---

**ALERT**

For safety and prescription clarity, N-Acetylcysteine should be prescribed on the Paediatric Intravascular and Subcutaneous Fluid Order Form or N-Acetylcysteine order form if available. Final solution volume and rate of infusion must be clearly prescribed.

---

**N-Acetylcysteine dosing:**

**For infants and children weighing less than or equal to 20kg (total fluid volumes have been standardised to reduce calculation errors):**

Infusion 1: N-Acetylcysteine 150mg/kg diluted to a total volume of 100mL with glucose 5%. Infuse over 60 minutes, immediately followed by:

Infusion 2: N-Acetylcysteine 50mg/kg diluted to a total volume of 100mL with glucose 5%. Infuse over 4 hours, immediately followed by:

Infusion 3: N-Acetylcysteine 100mg/kg diluted to a total volume of 250mL with glucose 5%. Infuse over 16 hours

**For children weighing more than 20kg and less than 50kg:**

Infusion 1: N-Acetylcysteine 150mg/kg diluted to a total volume of 100mL with glucose 5%. Infuse over 60 minutes, immediately followed by:

Infusion 2: N-Acetylcysteine 50mg/kg diluted to a total volume of 250mL with glucose 5%. Infuse over 4 hours, immediately followed by:

Infusion 3: N-Acetylcysteine 100mg/kg diluted to a total volume of 500mL with glucose 5%. Infuse over 16 hours

**For children and adolescents weighing more than or equal to 50kg:**

Infusion 1: N-Acetylcysteine 150mg/kg diluted to a total volume of 200mL with glucose 5%. Infuse over 60 minutes, immediately followed by:

Infusion 2: N-Acetylcysteine 50mg/kg diluted to a total volume of 500mL with glucose 5%. Infuse over 4 hours, immediately followed by:

Infusion 3: N-Acetylcysteine 100mg/kg diluted to a total volume of 1000mL with glucose 5%. Infuse over 16 hours
Different rates of initial infusions (using the same total dose) are increasingly being used. Some toxicology units use 200mg/kg over the first 4 hours (50mg/kg/hour), and a similarly adjusted regimen has been trialled in the UK. These have demonstrated advantage of lower rates of N-acetylcysteine non-IgE mediated anaphylactoid reactions. Efficacy data to date is similar but this has not been clearly established in large studies.¹ These regimes are currently being used in a number of Queensland hospitals, however no paediatric studies have been performed. These regimens are not currently recommended for use in CHQ.

---

**ALERT**

In case of large/massive paracetamol overdose with a serum paracetamol concentration more than double the nomogram line, infusion 3 should be replaced with:

N-Acetylcysteine 200mg/kg diluted to an appropriate volume of glucose 5%. Infuse over 16 hours

---

**Reconstitution/Dilution**

N-Acetylcysteine must be diluted before infusion preferably with glucose 5% but can also be diluted with sodium chloride 0.9% if necessary. Beware of the risk of hyponatremia and hypoglycaemia in the choice of diluting fluid.

Before adding the N-Acetylcysteine to the infusion bag, an equal volume should first be withdrawn from the bag.

Ensure that N-Acetylcysteine is thoroughly mixed after dilution.

Once diluted, the solution should be used immediately. However, the diluted solution is stable for up to 24 hours when refrigerated between 2 and 8°C.

Patients who are fluid restricted may need the fluid volume reduced. Contact the prescriber and pharmacy if required.

---

**Route and Method of Administration**

N-Acetylcysteine is administered by intravenous infusion using dose error reduction software (DERS).

N-Acetylcysteine is generally not compatible with other medications and should not be diluted or infused with other drugs. Contact pharmacy for advice if required.

---

**Contraindications/Precautions**

Patients can be moved to the Short Stay Unit in the Emergency Department (ED) once the first infusion has been completed due to a reduced risk of anaphylactoid reaction after the first bag. Administration of N-acetylcysteine is not restricted to the ED providing adequate monitoring can be performed.

- Monitoring requirements:
  - Baseline: Heart rate, blood pressure, oxygen saturation, temperature, respiration rate and before the infusion is commenced.
During infusion: Heart rate, blood pressure, oxygen saturation, temperature, respiration rate every 30 minutes for the first 2 hours, then every hour until the end of the infusion.

Telemetry monitoring is not routinely required but could be considered in cases of polypharmacy overdose with drugs that would require cardiac monitoring.

- Clinical effects associated with NAC administration:
  
  | Nausea, vomiting | Rash, flushing, itchiness |
  | Shortness of breath, wheeze | Hypotension |

In case of mild adverse effects: Notify medical officer. Infusion can be paused briefly and recommenced at a slower rate (half the current infusion rate) for a short period of time then increased back to target infusion rate. An antiemetic and antihistamine may be given if required.

**ALERT**

In case of severe anaphylactoid reaction including widespread or generalised rash, urticaria, flushing, or hypotension and/or bronchospasm, stop infusion immediately and notify medical officer.

If severe anaphylactoid reaction occurs, stop N-Acetylcysteine for one hour and treat complications. All attempts should be made to recommence and continue the infusion rather than stopping it permanently.

Previous adverse events (including anaphylactoid reactions) do not preclude the future use of N-Acetylcysteine.

**Clinical Considerations**

Additional monitoring including serum paracetamol concentration, ALT, blood sugar level, INR, urea, electrolytes, serum creatinine and VBG may be required. Refer to the CHQ Guideline: Paracetamol overdose guideline – Emergency management in children for more information.

Additional N-Acetylcysteine infusions may be required based on ALT and serum paracetamol concentration.

**ALERT**

It is strongly recommended to seek further advice from Poisons Information Centre in the following situations where the risk of hepatotoxicity may be greater and optimum advice is potentially changing:

- Very large overdoses:
  - Immediate release or modified release paracetamol overdoses of greater than 50gram or 1gram/kg (whichever is lower)
  - A very high paracetamol concentration, more than double the nomogram line
- Intravenous paracetamol errors or overdoses
- Patients with hepatotoxicity (eg. ALT > 1000 IU/L).
Additional Information

Refer to the CHQ Guideline: Paracetamol overdose guideline – Emergency management in children or the Guidelines for the management of paracetamol poisoning in Australia and New Zealand\(^1\) for additional information including optimal use of activated charcoal.

Consultation

Key stakeholders who reviewed this version:
- Pharmacist Critical Care
- Pharmacist Team Leader – Critical Care
- Senior Medical Officer, Department of Emergency Medicine
- Medical Director, Queensland Poisons Information Centre
- Manager, Queensland Poisons Information Centre

Definition of terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT</td>
<td>Alanine transaminase</td>
<td></td>
</tr>
<tr>
<td>INR</td>
<td>International normalised ratio</td>
<td></td>
</tr>
<tr>
<td>NAC</td>
<td>N-Acetylcysteine</td>
<td></td>
</tr>
<tr>
<td>VBG</td>
<td>Venous blood gas</td>
<td></td>
</tr>
</tbody>
</table>

References and suggested reading


## Guideline revision and approval history

<table>
<thead>
<tr>
<th>Version No.</th>
<th>Modified by</th>
<th>Amendments authorised by</th>
<th>Approved by</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>Pharmacist Team Leader – Critical Care</td>
<td>Medicines Advisory Committee</td>
<td>General Manager Operations</td>
</tr>
</tbody>
</table>

### Keywords

Paracetamol, NAC, N-Acetylcysteine, 01230

### Accreditation references

NSQHS Standards (1-10): 4 – Medication Safety