3.26 PARACETAMOL OVERDOSE

A. DEFINITION

Taking more than the licenced dose of paracetamol. Sheffield Children’s local trust guidance allows short term use of paracetamol at 80mg/kg/day for acute pain therefore this dose has been used throughout this guideline. Toxbase and BNF advice maximum paracetamol dose to be 75mg/kg/day.

Definition of a staggered overdose is where the ingestion of an overdose of paracetamol has taken place over a period greater than one hour.

B. BACKGROUND

Paracetamol is the most common drug overdose in the UK, with both accidental and deliberate overdoses being seen. After overdose the normal metabolism of paracetamol becomes saturated leading to increased formation of the metabolite, N-acetyl-p-benzoquinone (NAPQI). This toxic metabolite is detoxified by Glutathione, but in excess it binds to hepatocytes and leads to cell death. Acetylcysteine (NAC) is a highly effective antidote which replenishes glutathione preventing hepatocyte injury. Death or acute liver failure is extremely rare when this is started within 8 hours of overdose.

In children under 6, where there is absolute certainty that the amount ingested is under 150 mg/kg, blood testing can be reasonably considered unnecessary, and the child discharged.

In children 6 years of age and over, where there is absolute certainty that the amount ingested is under 80mg/kg, blood testing can reasonably be considered unnecessary, and the child discharged. If there exists any doubt about how much they have ingested, such as cases of deliberate overdose when it can never be considered absolutely certain, they should have blood tests.

The need for treatment with acetylcysteine is determined by plotting the measured plasma paracetamol concentration against the time since ingestion on the treatment nomogram. The normogram is unreliable if the timing of ingestion is uncertain. If there is any uncertainty about whether the patient’s paracetamol concentration is above or below the nomogram line, the patient should be treated with acetylcysteine.

If there is any doubt over time of ingestion, patients should be managed as per the staggered paracetamol overdose advice.
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Any patient who has taken a deliberate overdose of any quantity must be admitted to the medical team for referral to STAR team/ CAMHS as part of their management.

Accidental ingestions should be highlighted to Paediatric Liaison and the health visitor using Medway forms.

C. EARLY MANAGEMENT

Take an accurate history, as the quantity and timing of the overdose are crucial. Clinical judgement is important, as the history may be inaccurate. If in doubt when blood levels are available and close to the appropriate treatment line, err on the side of safety and treat.

Follow the management steps on TOXBASE. Any unusual cases can be discussed with the poison information service 0344 892 0111.

Presentation less than 1 hour post ingestion:

Consider activated charcoal if the patient presents within 1 hour of ingesting more than 150 mg/kg of paracetamol. However, many children, especially younger ones, will not take activated charcoal. Do not fight with the child if administration is difficult.

- Neonate and Child: 1g/kg (maximum 50g)
- Child (12-17years): 50g

Continue management as for presentation 1-4 hours post ingestion.

Presentation 1 - 4 hours post ingestion:

Check paracetamol levels at 4 hours post ingestion. Not before this, as absorption continues, therefore paracetamol levels before 4 hours unreliable. See below for full investigation list. Treat with acetylcysteine if on or above appropriate treatment line.

Presentation 4 - 8 hours post ingestion:

Check paracetamol levels. They need to be processed urgently if presentation is close to 8 hours. See below for full investigation list. Treat with acetylcysteine if on or above appropriate treatment line for time of blood test.

Note - There is normally no indication to start acetylcysteine without a paracetamol blood concentration provided the result can be obtained and acted upon within 8 hours of ingestion. If there is going to be undue delay in obtaining the paracetamol concentration, treatment should be started if more than 150 mg/kg paracetamol has been ingested.

Presentation 8 - 24 hours post ingestion:

Urgent action is needed because efficacy of acetylcysteine declines after 8 hours post ingestion. Give acetylcysteine immediately to all patients if it is thought that more than 150 mg/kg body weight paracetamol has been ingested as an acute overdose (i.e. all doses taken within one hour). If the patient has ingested less than 150 mg/kg, wait for blood results before considering treatment with acetylcysteine.
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Only discontinue acetylcysteine if paracetamol level is below treatment line, PT, LFT’s and U&E’s are normal, the patient is asymptomatic and there is no doubt over the timing of the overdose.

If the patient has biochemical tests suggesting acute liver injury, (e.g. ALT above the upper limit of normal), consider use of acetylcysteine even if the plasma paracetamol concentration is below the line on the nomogram, (in cases of severe poisoning the ALT rises rapidly and is commonly abnormal at first presentation to hospital). A raised ALT may also indicate that the overdose was taken earlier than suggested by the history.

**Presentation over 24 hours post ingestion:**

Measure plasma paracetamol prior to commencing acetylcysteine if possible. Measure glucose in addition to standard investigations listed below.

Commence acetylcysteine if clearly jaundiced or hepatic tenderness, otherwise waiting for blood results is appropriate. Consult TOXBASE regarding treatment advice.

**Staggered overdose**

These patients require careful assessment. Risk assessment is based on the history of staggered dose and timing of paracetamol ingestion, the presence or absence of clinical features suggestive of paracetamol toxicity, and the results of blood tests. For all patients who have taken a staggered overdose, (i.e. over more than one hour), the recommendations are that treatment with acetylcysteine should be given. See TOXBASE for further guidance.

**Therapeutic Excess**

Patients ingesting a dose greater than the licensed daily dose (as per BNFc) AND more than 80mg/kg/24 hours for the treatment of pain or fever without self-harm intent is common. Please consult TOXBASE for details of management.

**D. INVESTIGATIONS**

Complete initial investigations as per TOXBASE, if starting infusion further investigations will be required at, or just before the end of the acetylcysteine infusion.

Wait until 4 hours from paracetamol ingestion to check paracetamol levels, if presenting over 4 hours post ingestion, levels can be checked at this time. Other initial investigations include U&E, creatinine, bicarbonate, LFTs, PT/INR and FBC.

Plot paracetamol level on paracetamol normogram, which is available below.
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Paracetamol Normogram (Plasma concentration-time graph)

E. TREATMENT

Acetylcysteine is used as an antidote to paracetamol overdose. Children are treated with the same doses and regimen as adults. However, the quantity of intravenous fluid used has been modified to take into account age and weight, as fluid overload is a potential danger.

Calculating doses in obese children: NPIS advises that the child’s actual weight should be used for calculating both the toxic dose and acetylcysteine dose, up to a maximum of 110kg.

Calculating doses in pregnant patients: NPIS advises that for pregnant patients the toxic dose should be calculated using the patient’s pre-pregnancy weight and the acetylcysteine dose should be calculated using the patient’s actual pregnant weight.

Adverse reactions to acetylcysteine are relatively common, previous allergic reactions are no longer a contraindication. TOXBASE offers advice on management for patients experiencing an adverse reaction as well as prophylactic management for those patients with previous anaphylactoid reactions to acetylcysteine.
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N-Acetylcyesteine (NAC) Preparation and Infusion regimes

Use TOXBASE for infusion and dosing regimes for the child’s weight. The table included below summarises this information.

The recently developed Scottish and Newcastle Acetylcysteine Protocol (SNAP) regimen has now been adopted for use in Sheffield Children’s hospital. TOXBASE recommends this regime as equivalent to the standard 21 hour treatment. This reduces the standard infusion time from 21 hours to 12 hours and has been shown to be an equally effective treatment at preventing liver injury, while also reducing anaphylactoid reactions. TOXBASE has detailed advice on both dosing regimens but we recommend using the 12 hour (SNAP) regime detailed below.

StoppingTreatment

TOXBASE has detailed recommendations regarding blood tests required and how to interpret their results. All patients will require bloods taken at, or just before the end of the second infusion. These include plasma paracetamol concentration, PT/INR, Creatinine, venous pH or plasma bicarbonate and ALT.

Discharging Patients

If patients are discharged with abnormal LFT’s they should be advised to avoid paracetamol for 2 weeks, at which time their liver function would be expected to have normalised.

TOXBASE patient information leaflet:

https://www.toxbase.org/Chemical-incidents/Miscellaneous/Paracetamol-Patient-Information-Sheets/

Modified 12 Hour Regime (SNAP) for patients under 40kg

First Infusion

- Prepare a 50 mg/mL solution by diluting each 10 mL ampoule of acetylcysteine (200 mg/mL) with 30 mL glucose 5% or sodium chloride 0.9% to give a total volume of 40 mL stock solution.

- Prepare the appropriate volume for the weight of the child.

- (e.g. 2 x 10 mL acetylcysteine plus 60 mL diluent = 80 mL stock solution. 54 mL stock solution required for a 25 kg child. See table below for infusion volumes and rates).

- The dose is infused over 2 hours at the infusion rate stated in the table.

Second Infusion

- Prepare a 10 mg/mL solution by diluting each 10 mL ampoule of acetylcysteine (200 mg/mL) with 190 mL glucose 5% or sodium chloride 0.9% to give a total volume of 200 mL stock solution.

- Prepare the appropriate volume for the weight of the child.
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- (e.g. 3 x 10 mL acetylcysteine plus 570 mL diluent = 600 mL stock solution. 540 mL stock solution required for a 25 kg child. See table below for infusion volumes and rates).

- The dose is infused over 10 hours at the infusion rate stated in the table.

For example for a child weighing 12 kg, the first infusion would be 24mL infused at 12 mL/h over 2 hours, the second infusion would be 240mL infused at 24mL/h over 10 hours.

Note: Actual dose in mg must be prescribed in addition to ml/hr. Actual dose in mg is calculated on the weight in the middle of each band.

For example a child weighing 12kg will have a dose of 1200mg (12 x 100) for the first infusion and a dose of 2400mg (12 x 200) for the second infusion. Any child weighing 10-14kg will have the same exact dose.

### Modified 12 Hour Regime (SNAP) for patients equal to or over 40kg

#### First Infusion

- Add the appropriate volume of acetylcysteine (100 mg/kg body weight, maximum 11g) to 200 mL 5% glucose or 0.9% sodium chloride, infused over 2 hours.
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- Note that the 200 mL bags of 5% glucose or sodium chloride 0.9% required for the first infusion are not currently commercially available. For this infusion, the excess amount of fluid should be removed from a larger bag using a syringe and discarded, before adding the acetylcysteine, e.g. by removing and discarding 50 mL from a 250 mL infusion bag.

Second Infusion

- Add the appropriate volume of acetylcysteine (200 mg/kg body weight, maximum 22g) to 1000 mL 5% glucose or 0.9% sodium chloride and infuse over the next 10 hours. In this trust we stock 500ml bags, therefore infusion will be delivered in two 500ml bags.

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**Acetylcysteine prescription for adults and children weighing 40 kg or more**

<table>
<thead>
<tr>
<th>12-hour Regimen</th>
<th>First Infusion</th>
<th>Second Infusion</th>
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</thead>
<tbody>
<tr>
<td>Infusion fluid</td>
<td>200 mL 5% glucose or 0.9% sodium chloride</td>
<td>1000 mL 5% glucose or 0.9% sodium chloride</td>
</tr>
<tr>
<td>Duration of infusion</td>
<td>2 hours</td>
<td>10 hours</td>
</tr>
<tr>
<td>Drug dose</td>
<td>100 mg/kg acetylcysteine</td>
<td>200 mg/kg acetylcysteine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Weight</th>
<th>Ampoule volume</th>
<th>Infusion Rate</th>
<th>Ampoule volume</th>
<th>Infusion Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>kg</td>
<td>mL</td>
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<td>mL/h</td>
</tr>
<tr>
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<td>55</td>
<td>128</td>
<td>110</td>
<td>111</td>
</tr>
</tbody>
</table>

1. Dose calculations are based on the weight in the middle of each band. If the patient weighs less than 40 kg use the paediatric dose table.
2. Ampoule volume has been rounded up to the nearest whole number.

For example, for a child weighing 55 kg, the first infusion would be 228mL (200ml bag + 28ml volume of drug) infused at 114 mL/h over 2 hours. The second infusion would be 1055ml total. (2x 500ml bags + 27.5ml volume of drug in each) infused at 106mL/h over 10 hours (5 hours for each 500ml bag).

Note: Actual dose in mg must be prescribed in addition to mL/hr. Actual dose in mg is calculated on the weight in the middle of each band.

For example a child weighing 55kg will have a dose of 5500mg (55 x 200) for the first infusion and a dose of 11000mg (55 x 200) for the second infusion, (5500mg in each 500ml bag). Any child weighing 50-59kg will have the same exact dose.

F. References

1. National Poisons Information Service / TOXBASE- checked 16.6.21
2. British National Formulary (Children)
### 3.26 PARACETAMOL OVERDOSE

#### Paracetamol overdose – Flowchart

**Document** Amount in mg/kg
(Use actual weight if <110kg) and time taken

**Was overdose taken over a period of >1 hour?**

- **If <75mg/kg – LOW risk** of toxicity - Can be safely discharged
- **If >150mg/kg – HIGH risk**
- **If in doubt about dose err on side of safety**

**IN SELF-HARM – ASSUME HIGH RISK UNLESS AMOUNT TAKEN WITNESSED/CONFIRMED**

**If yes – Staggered Overdose**
- Take blood tests and commence on NAC immediately

1. **<1 hour ago?**
   - Prescribe activated charcoal (1g/kg PO/NG)

2. **<4 hours ago**
   - Take bloods at 4 hours following overdose and chase results, commence treatment if:
     - Paracetamol over treatment line
     - Derangement to LFT/INR

3. **4-8 hours ago**
   - Take bloods immediately and chase results
     - If High risk results not expected to be back before 8 hours then commence NAC

4. **8-24 hours**
   - Take bloods immediately
     - If High risk Commence NAC while awaiting results

5. **>24 hours**
   - Take bloods + glucose
     - Commence on NAC if clinically unwell, jaundiced or RUQ tenderness

**Bloods include**
- FBC, U&E, LFT, Clotting screen, VBG, Paracetamol and salicylate levels
- + cannula for treatment

**Ensure NAC is started in time to prevent any potential damage, can be discontinued if not required**

- See SNAP protocol = 2 hour infusion followed by 10 hour infusion
- See Toxbase or ED handbook for further information of NAC prescription