Paracetamol Overdose Management

<table>
<thead>
<tr>
<th>CATEGORY:</th>
<th>Clinical Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLASSIFICATION:</td>
<td>Clinical</td>
</tr>
<tr>
<td>Controlled Document Number:</td>
<td>CG163</td>
</tr>
<tr>
<td>Version Number:</td>
<td>1</td>
</tr>
<tr>
<td>Controlled Document Sponsor:</td>
<td>Clinical Guidelines Group</td>
</tr>
<tr>
<td>Controlled Document Lead (Author):</td>
<td>Consultant Emergency Department JSD</td>
</tr>
<tr>
<td>Approved By:</td>
<td>Clinical Guidelines Group</td>
</tr>
<tr>
<td>On:</td>
<td>January 2015</td>
</tr>
<tr>
<td>Review Date:</td>
<td>January 2018</td>
</tr>
</tbody>
</table>
PARACETAMOL OVERDOSE

Please note that EVERY patient with a DELIBERATE overdose needs RAID referral and an assessment before discharge

RECOGNITION AND ASSESSMENT

Symptoms and signs

- Usually none
- Extremely common: nausea and vomiting (occur within a few hours of ingestion of a hepatotoxic dose)
- Very rarely: coma and severe metabolic acidosis in patients who have extremely high plasma paracetamol concentrations (usually greater than 800 mg/L). Drowsiness in the first 1-2 days after a single paracetamol overdose is unlikely to be due to liver failure, so consider other causes.
- In those presenting late, loin pain, haematuria and proteinuria after 24 hours suggest incipient renal failure, whereas right subcostal pain and tenderness with recurrent nausea, vomiting and jaundice after 2 to 3 days are features of hepatic necrosis.
- Later features in severe cases (12-36 hours): abdominal pain.

Investigations – to be perform in ALL patients

- Patient's weight – this should be recorded clearly in patient’s notes as this would guide further assessment and treatment.
- Plasma paracetamol 4 hours after ingestion (but not before).
- Compare plasma paracetamol levels with treatment graph (figure 1)
- Baseline:
  - FBC, INR
  - U&E, LFTs (ALT - most sensitive marker for liver injury), phosphate
  - Acid-base (venous sample) and venous blood lactate, bicarbonate, glucose.

IMMEDIATE TREATMENT

When using body weight to estimate dose ingested or antidote dose, allow maximum body weight 110 kg even in very obese patients weighing > 110 kg.

In pregnant patients the toxic dose should be calculated using the patient’s pre-pregnancy weight and the antidote dose should be calculated using the patient’s actual pregnant weight (to a max 110kg).
Activated Charcoal

If patient is thought to have taken >12g or 150 mg/kg and presents within 1 hour of ingestion, give activated charcoal 50 g (1 g/kg for children) orally or via nasogastric tube.

Acetylcysteine (standard regimen) - Adults

Acetylcysteine should be administered by intravenous infusion preferably using Glucose 5% as the infusion fluid. Sodium Chloride 0.9% solution may be used if Glucose 5% is not suitable.

- The full course of treatment comprises of 3 consecutive intravenous infusions. Doses should be administered sequentially with no break between the infusions. The patient should receive a total dose of 300 mg/kg body weight over a 21 hour period. As per shown in Table 1.
- If <8 hours from ingestion the use of acetylcysteine should be avoiding until plasma paracetamol concentrations are known.
- Acetylcysteine efficacy declines rapidly after 8 hours so treatment shouldn’t be delayed during this period.
- However, in patients who present more than 24 hours after the overdose, there is no evidence that treating with acetylcysteine before blood test are available confers benefit or that delaying treatment for a short period while waiting for blood results worsen prognosis.
- Staggered overdose treatment should be started within one hour of the patient arriving to the department.

Adverse reaction to acetylcysteine & management

- Can occur in up to 15% of patients, usually within first 30 minutes of administration when large amounts are given rapidly.
- Nausea, vomiting, flushing, urticarial rash, angioedema, tachycardia, bronchospasm are relatively common. Hypotension and collapse are rare. Very rarely, in severe cases, respiratory depression, renal failure and DIC.

1. Stop the infusion (usually this is all that is required).
2. Give an H1 antihistamine if necessary (e.g. chlorphenamine 10 mg IV).
3. Give nebulised salbutamol if bronchospasm is significant.
4. Other measures as indicated by the patient's clinical condition (e.g. hydrocortisone 100mg IV if the reaction is severe).
5. Restart treatment when the reaction has settled.
Previous reaction to acetylcysteine

- Is NOT a contraindication for a further treatment course.
- Acetylcysteine is more likely to cause adverse effects if paracetamol concentrations are low or absent. Adverse effects are also more likely in women, asthmatics and in patients with a family history of allergy.
- **Prophylactic treatment** with H1 and H2 antihistamines should be considered (e.g. chlorphenamine 10 mg IV and ranitidine 50 mg diluted to 20 mL and given intravenously over at least 2 minutes).
- Pretreatment with nebulised salbutamol may be considered in those patients with a history of bronchospasm following acetylcysteine.
- Consider giving the first bag more slowly than normal, e.g. over 2 hours, if the patient has had a previous severe reaction to NAC.
MANAGEMENT

<table>
<thead>
<tr>
<th>Time from OD (hours)</th>
<th>Management</th>
<th>Discharge policy and subsequent management</th>
</tr>
</thead>
</table>
| **0 - 8** | • Consider activated charcoal if presentation within 1 hour from ingestion.  
• **Take bloods 4 hours after ingestion and await plasma paracetamol levels.**  
• Treat if above, on, or slightly below the appropriate treatment line (figure 1). | If the paracetamol concentration is below the treatment line; the INR and ALT are normal⁶; the patient is asymptomatic and has a normal serum creatinine s/he can be discharged with advice to return to hospital if vomiting or abdominal pain occurs. |
| **8 - 24** | • Take bloods  
• If >150 mg/kg give acetylcysteine immediately.  
• If < 150 mg/kg, wait for blood results before considering treatment. |  
If 24-hours after overdose or after antidote treatment complete:  
➢ Paracetamol concentration is not detectable  
➢ INR ≤ 1.3  
➢ ALT < X2 the upper limit of normal  
➢ Asymptomatic.  
➢ Creatinine is normal.  
The patient is not considered to be at risk of liver damage and does not need treatment. If treatment has been started it can be discontinued.  
The patient can be discharged with advice to return if vomiting or abdominal pain occurs. |
| **> 24** | • Take bloods  
• If patient is jaundiced or has hepatic tenderness treat with acetylcysteine.  
• Otherwise wait for blood results before commencing treatment. |  
Treat if:  
➢ Paracetamol detected.  
➢ INR >1.3  
➢ ALT > X2 times the upper limit of normal. |

**Staggered Overdose** (doses taken over >1 hour)  

<table>
<thead>
<tr>
<th>Time from OD</th>
<th>Management</th>
<th>Discharge policy and subsequent management</th>
</tr>
</thead>
</table>
| **> 24** | • Take bloods  
• Treat with acetylcysteine | |

**Therapeutic excess** (>than a licensed dose for that individual or >75 mg/kg in any 24-hour period).  

<table>
<thead>
<tr>
<th>Time from OD</th>
<th>Management</th>
<th>Discharge policy and subsequent management</th>
</tr>
</thead>
</table>
| **> 24** | • Take bloods  
• **Treat if:**  
➢ Jaundice or hepatic tenderness  
➢ There is any uncertainty (dose or timing).  
➢ Ingested >150mg/kg in any 24 hours.  
➢ Abnormal ALT, INR or detectable paracetamol concentration more |  
If after treatment blood results are abnormal:  
➢ the ALT has more than doubled since the admission measurement, OR  
➢ the ALT is ≥ X2 the upper limit of normal, OR  
➢ the INR ≥ 1.3 (in the absence of another cause, e.g. warfarin)  
Continue acetylcysteine at |

⁶ If biochemical tests suggest acute liver injury (e.g. ALT above the upper limit of normal) consider acetylcysteine even if the plasma paracetamol is below the treatment line as in cases of severe poisoning the ALT rises rapidly and is commonly abnormal at first presentation to hospital.
than 24 hours after the last dose.

- If 75-150 mg/kg in any 24-hour period clinical judgement* should be used in determining the need for treatment. Discuss with senior.

  - The underlying clinical reason for the chronic excess dosage should be considered.

<table>
<thead>
<tr>
<th>Uncertain time of ingestion</th>
<th>Take bloods and <strong>treat immediately if jaundice or hepatic tenderness.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>And the dose &gt;75 mg/kg.</td>
<td><strong>If within the last 24 hours</strong></td>
</tr>
<tr>
<td></td>
<td>- Take bloods</td>
</tr>
<tr>
<td></td>
<td>- Treat immediately if ≥150mg/kg.</td>
</tr>
<tr>
<td></td>
<td>- If 75-150mg/kg clinical judgement should be used. Discuss with senior.</td>
</tr>
<tr>
<td></td>
<td><strong>If between 24-72 hours</strong></td>
</tr>
<tr>
<td></td>
<td>- Take bloods</td>
</tr>
<tr>
<td></td>
<td>- Treat immediately if ≥150 mg/kg in any 24 hour period within the last 72 hours.</td>
</tr>
<tr>
<td></td>
<td>- If between 75 - 150 mg/kg in any 24 hour period within the last 72 hours, clinical judgement should be used. Discuss with senior.</td>
</tr>
<tr>
<td></td>
<td><strong>If &gt;72 hours ago</strong></td>
</tr>
<tr>
<td></td>
<td>- Take bloods</td>
</tr>
<tr>
<td></td>
<td><strong>If &gt;7 days</strong></td>
</tr>
<tr>
<td></td>
<td>Asymptomatic patients, who have had no new symptoms since the time of ingestion, and who have no history of chronic kidney or liver disease, will not normally require further assessment, providing the timing of ingestion is certain.</td>
</tr>
<tr>
<td></td>
<td><strong>Other measures</strong> as indicated by patient's clinical condition.</td>
</tr>
</tbody>
</table>

Patients should **be advised on discharge to seek medical attention if symptoms subsequently develop.**

* Clinical judgement should take into account the magnitude of the exposure, its duration, intent insofar as it relates to the reliability of the history, and any other relevant factors.
In case of uncertainty discuss with National Poisons Information Service
0844 892 0111
ALL ingestions of >75mg/kg are consider significant

LIFE-THREATENING FEATURES

A poor prognosis is indicated by:

- INR > 3.0
- Plasma creatinine > 200 micromol/L
- Blood pH < 7.3
- Signs of encephalopathy (mental confusion, drowsiness, spatial disorientation, asterixis)

If any of these features are present after overdose, seek advice from a consultant gastroenterologist

- Patients with incipient or established hepatic failure may be candidates for liver transplantation. Please seek advice from liver team.
- Hypophosphataemia usually occurs after paracetamol poisoning and correlates well with the degree of hepatic damage.
- Treat haemorrhage with fresh frozen plasma.

Please note that EVERY patient with a DELIBERATE overdose needs RAID referral and an assessment before discharge
Figure 1 - Treatment Nomogram
Table 1 – Adult dosage table

<table>
<thead>
<tr>
<th>Adult acetylcysteine prescription</th>
<th>Please circle appropriate weight and volume.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(each ampoule = 200mg/mL acetylcysteine)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regimen</th>
<th>First Infusion</th>
<th>Second Infusion</th>
<th>Third Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion fluid</td>
<td>200 mLs 5% glucose or sodium chloride 0.9%</td>
<td>500 mLs 5% glucose or sodium chloride 0.9%</td>
<td>1000 mLs 5% glucose or sodium chloride 0.9%</td>
</tr>
<tr>
<td>Duration of infusion</td>
<td>1 hour</td>
<td>4 hours</td>
<td>16 hours</td>
</tr>
<tr>
<td>Drug dose</td>
<td>150 mg/kg acetylcysteine</td>
<td>50 mg/kg acetylcysteine</td>
<td>100 mg/kg acetylcysteine</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Weight (kg)</th>
<th>Ampoule volume (mL)</th>
<th>Infusion Rate (mL/h)</th>
<th>Ampoule volume (mL)</th>
<th>Infusion Rate (mL/h)</th>
<th>Ampoule volume (mL)</th>
<th>Infusion Rate (mL/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>34</td>
<td>234</td>
<td>12</td>
<td>128</td>
<td>23</td>
<td>64</td>
</tr>
<tr>
<td>50-59</td>
<td>42</td>
<td>242</td>
<td>14</td>
<td>129</td>
<td>28</td>
<td>64</td>
</tr>
<tr>
<td>60-69</td>
<td>49</td>
<td>249</td>
<td>17</td>
<td>129</td>
<td>33</td>
<td>65</td>
</tr>
<tr>
<td>70-79</td>
<td>57</td>
<td>257</td>
<td>19</td>
<td>130</td>
<td>38</td>
<td>65</td>
</tr>
<tr>
<td>80-89</td>
<td>64</td>
<td>264</td>
<td>22</td>
<td>131</td>
<td>43</td>
<td>65</td>
</tr>
<tr>
<td>90-99</td>
<td>72</td>
<td>272</td>
<td>24</td>
<td>131</td>
<td>48</td>
<td>66</td>
</tr>
<tr>
<td>100-109</td>
<td>79</td>
<td>279</td>
<td>27</td>
<td>132</td>
<td>53</td>
<td>66</td>
</tr>
<tr>
<td>≥110</td>
<td>83</td>
<td>283</td>
<td>28</td>
<td>132</td>
<td>55</td>
<td>66</td>
</tr>
</tbody>
</table>

1 Dose calculations are based on the weight in the middle of each band. If the patient weighs less than 40kg use the paediatric dosage table.
2 Ampoule volume has been rounded up to the nearest whole number.
Please note that EVERY patient with a deliberate overdose needs RAID referral and an assessment before discharge.

**PARACETAMOL OD FLOWCHART**

- **Time of OD**
  - **Amount** mg
  - **Weight** kg
  - mg/kg

- **Staggered Doses taken over 1 hr**
  - <1 hr
  - 1-4 hrs
  - 4-8 hrs
  - 8-24 hrs
  - >24 hrs

- **Check bloods**
  - **Start NAC immediately**
  - **Paracetamol level**
    - Above line
      - **Start or continue treatment**
    - Below line
      - **Stop treatment**
  - **Check blood at**
    - **INR > 1.3**
      - ALT >2X
        - **Start treatment**
    - **INR < 1.3**
      - ALT < 2X
        - **No treatment**

- **Check bloods**
  - Taken at
    - FBC
    - U&E's
    - LFT's
    - INR
    - Phosphate
    - VBG

- **Paracetamol levels**

- **1st dose in ED at**
- **2nd dose in ED at**

- **ADMIT**
REFERENCES

http://www.toxbase.org/
http://www.collemergencymed.ac.uk/Shop-Floor/Clinical%20Guidelines/Clinical%20Guidelines/Paracetamol%20Overdose/
http://www.patient.co.uk/doctor/paracetamol-poisoning

AUDITABLE OUTCOMES

http://www.collemergencymed.ac.uk/Shop-Floor/Clinical%20Audit/Current%20Audits
http://www.collemergencymed.ac.uk/Shop-Floor/Clinical%20Standards

CEM STANDARDS

1. Plasma levels should not be measured earlier than 4 hours after the estimated ingestion time.
2. Staggered overdoses - treatment started within one hour of arrival.
3. Patients arriving < 8 hours after ingestion - treatment given as per the 2012 MHRA guideline.
4. Patients arriving 8 to 24 hours after ingestion - treatment started before blood results available if there is a clear history of > 6 g ingestion (or 75 mg/kg whichever is the smaller).
5. Patients presenting > 24 hours. INR, urea and electrolytes bicarbonate & LFTs performed and recorded in the notes.