

Paracetamol Poisoning



- Paracetamol may cause severe liver damage if $>150\text{mg}$ paracetamol/kg body weight are taken.
- Severe toxicity is unlikely if $<75\text{mg/kg}$ has been ingested. In obese patients ($>110\text{kg}$), calculate the toxic dose in mg/kg , and the dose of acetylcysteine using a weight of 110kg , rather than the patient's actual weight.



- A metabolite of paracetamol (*N*-acetyl-*p*-benzoquinone imine, NAPQI) binds glutathione in the liver and causes hepatic necrosis when stores of glutathione are exhausted.
- Renal failure from acute tubular necrosis occurs occasionally, but renal failure without liver failure is rare.



Risk factors

Previously, some patients were deemed to be at i risk of liver damage (eg alcoholics and patients on enzyme-inducing drugs) and were treated differently.

However, this is of historical interest only, as all patients are now treated as if 'high risk', with a low threshold for acetylcysteine use.



Clinical features

- Nausea, vomiting, and abdominal discomfort are common within a few hours.
- In untreated patients developing liver damage, vomiting continues beyond 12hr and there is pain and tenderness over the liver (from 24hr), jaundice (at 2–4 days), and sometimes coma from hypoglycaemia (at 1–3 days) and hepatic encephalopathy (onset at 3–5 days).
- Loin pain, haematuria, and proteinuria suggest incipient renal failure.
- Hepatic failure causes bleeding from coagulation abnormalities and hyperventilation from metabolic acidosis.



Clinical features

- In fatal cases, cerebral oedema, septicaemia, and DIC are common. However, many patients survive severe liver damage and recover completely.
- *LFTs* are normal until >18hr after the overdose. The most sensitive lab evidence of liver damage is often a prolonged INR (from 24hr after overdose).
- Liver enzymes (ALT and AST) may reach >10,000U/L at 3–4 days.
- Bilirubin rises more slowly (max at about 5 days).



Staggered overdose

- If paracetamol has been taken in excess ($\geq 75\text{mg/kg}$) over $>1\text{hr}$, consider this to be a 'staggered overdose'. Do not use the graph to guide treatment for patients with staggered overdoses.
- If the patient has symptoms of toxicity or the amount taken was $>75\text{mg/kg}$, take blood for INR, LFTs, U&E, and paracetamol level (which may confirm that some was taken), and treat with acetylcysteine.
- If in doubt, start treatment and get expert advice.



Management within 4 hours of ingestion

- Consider activated charcoal if 150mg/ kg paracetamol has been taken in the previous 1hr.
- Take blood at 4hr from ingestion and use the treatment graph to assess the risk of liver damage; if the result is above the treatment line, give IV acetylcysteine



Management at 4-8 hours of ingestion

- Measure paracetamol level, and use the graph to assess the risk of liver damage. If above the treatment line, or only just below it, give IV acetylcysteine.
- Treatment is most effective if started before 8hr—start it at once if the paracetamol level is not available by this time and $>150\text{mg/kg}$ has been taken.
- Patients treated with acetylcysteine within 8hr of an overdose should be medically fit for discharge at the end of the treatment course.



Management at 8-24 hours of ingestion

- Urgent action is needed—start treatment with IV acetylcysteine immediately if $>150\text{mg/kg}$ paracetamol has been taken. Measure plasma paracetamol level (plus creatinine, LFTs, and INR), and use the treatment graph to assess the risk of liver damage.
- If the paracetamol level is well below the line and the patient is asymptomatic, stop acetylcysteine treatment.



Management at 8-24 hours of ingestion

- Continue acetylcysteine if the level is above the treatment line, if there is doubt about the time of ingestion, or if the patient has nausea or vomiting.
- After 12–15hr, the graph is less reliable, and some laboratories may have a higher limit of detection than the treatment line. If there is any doubt, treat with acetylcysteine, especially if ALT is \uparrow , even if the level is below the treatment line.



Management at >24 hours of ingestion

- Measure paracetamol level, LFTs, U&E, creatinine, INR, and ABG.
- Start treatment with IV acetylcysteine if the patient is clinically jaundiced or has hepatic tenderness.
- Otherwise, wait for investigation results—treat with acetylcysteine if abnormal and seek advice from NPIS or a liver unit.
- If asymptomatic, with non-detectable paracetamol level and normal bloods, treatment is not required.



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