EMERGENCY CASEBOOK

Death from paracetamol overdose despite appropriate treatment with N-acetylcysteine

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A case of death from severe paracetamol poisoning which presented early and received appropriate treatment according to evidence-based guidelines is presented here. It is very rare for patients to die from paracetamol poisoning when they receive N-acetylcysteine (NAC) within 8 h of ingestion. The patient had a marked lactic acidosis on presentation to hospital. This case demonstrates that a patient can die from paracetamol poisoning despite early and appropriate treatment, and raises the question whether lactic acidosis in a patient following paracetamol overdose should prompt the initiation of NAC treatment while awaiting paracetamol levels.

Paracetamol is the most common drug taken in overdose in the UK. Management of paracetamol overdose presented to hospital within a few hours of ingestion is often thought of as straightforward. We present a fatal case of paracetamol overdose that presented early and received appropriate treatment according to available evidence.

CASE HISTORY

A previously well 55-year-old man presented to the emergency department 2 h after taking 50 g of paracetamol, 3.15 g of aspirin and 1.125 g of cinnarizine. His 4 h paracetamol level was 534 mg/l. He was not identified as at high risk for paracetamol poisoning for the purposes of the N-acetylcysteine (NAC) nomogram.

The notable blood results on admission were creatinine 109 µmol/l, alanine aminotransferase (ALT) 15 U/l, prothrombin time (PT) 9.8 s and lactate 15.54 mmol/l. Arterial blood gases at 8 h after ingestion showed a marked compensated lactic acidosis despite adequate fluid resuscitation, pH 7.35, partial pressure of carbon dioxide 22.2, partial pressure of oxygen 118.7, BE-13.5, bicarbonate 11.0, lactate 12.76 mmol/l and glucose 20.6 mmol/l. Salicylate levels were not significantly raised on immediate and later testing.

Infusion of NAC was commenced at 6 h after ingestion after obtaining the 4-h paracetamol level. This was in accordance with evidence-based guidelines for patients not at high risk for paracetamol poisoning.¹ At 8 h after ingestion, the patient developed signs of agitation, confusion and a falling conscious level. He was admitted to the intensive care unit, and was intubated and ventilated for airway protection.

Over the next 48 h, he developed non-oliguric acute renal failure with creatinine peaking at 283 µmol/l, and continuous renal replacement treatment was commenced at an early stage. Interestingly, his liver function tests did not become grossly abnormal. International normalised ratio at 48 h had risen to 2.0 and ALT was 138 U/l. The NAC infusion was continued.

In the 24 h that followed, his condition deteriorated rapidly. A vasodilatory state of shock developed, and he required high doses of vasopressors to maintain adequate mean arterial pressure guided by invasive cardiac output monitoring.

Oxygenation became problematic and chest x ray showed four-quadrant alveolar shadowing consistent with acute respiratory distress syndrome.

The international normalised ratio peaked at 2.5 at 72 h after ingestion, ALT remained only moderately increased at 145 U/l and bilirubin never rose above 25 µmol/l. The patient became hypoglycaemic, requiring a 50% dextrose infusion to maintain acceptable blood glucose levels. His cardiovascular status continued to deteriorate and he died at 84 h after ingestion. His condition was discussed at regular intervals with a tertiary liver unit, and they did not recommend transfer at any point.

A postmortem examination showed a normal-looking liver with no evidence of cirrhosis. Liver histology was not performed. Appearance of the lung was consistent with severe acute respiratory distress syndrome. Causes of death were recorded as multi-organ failure and paracetamol toxicity.

DISCUSSION

Deaths from paracetamol overdose are extremely rare when NAC is administered within 8 h of ingestion. A study by Prescott *et al*² identified only one case of liver damage among 62 patients treated with NAC within 10 h of ingestion and described optimal results from NAC if the infusion is commenced within 8 h.

This patient gave a history of massive paracetamol overdose 2 h before presenting to the emergency department, and was managed according to the guidelines for early presentation. An intravenous NAC infusion was commenced 4 h after presentation to hospital as soon as the result of the 4 h paracetamol level was obtained. The paracetamol level was extremely high, indicating that this was a substantial overdose.

It is unusual for death to occur after paracetamol poisoning without the patient showing obvious signs of liver damage that may indicate a poor prognosis. PT has been suggested as a reliable predictor of poor outcome.³ The peak PT on day 4 in our patient was 25 s, well below the levels associated with poor outcome. He never became jaundiced, and the rise in ALT was only moderate.

The very high initial lactate value in this case might have alerted us sooner to the severity of the overdose. Lactate values >3.5 mmol/l on presentation and >3.0 mmol/l after fluid resuscitation have been found to predict a poor outcome in paracetamol overdose.⁴ This case highlights the importance of measuring lactate levels on admission to hospital in cases where significant overdose of paracetamol is suspected, and raises the question of whether lactic acidosis in a patient following paracetamol overdose should prompt the initiation of NAC treatment while awaiting paracetamol levels. It is important to note that a patient can die from paracetamol poisoning despite early and appropriate treatment.

Abbreviations: ALT, alanine aminotransferase; NAC, N-acetylcysteine; PT, prothrombin time

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