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# Acetaminophen Poisoning – A Case Report.

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## Abstarct

Acetaminophen is a widely used analgesic agent, but at the same time, overdosing with acetaminophen is one of the leading causes of hospital admission. The administration of the specific antidote, N-acetylcysteine, should be initiated but renal replacement therapy, therapeutic plasmapheresis or even liver transplantation may be necessary.

We present a case of severe metabolic lactic acidosis and coma after massive intake of acetaminophen. The patient was treated with *N*-acetylcysteine at a higher dose and received hemodialysis. He presented with severe liver failure, and despite optimal treatment, except liver transplantation, he died 70 hours after hospitalization.

We describe the treatment of massive acetaminophen overdose and discuss the literature about the need for higher doses of *N*-acetylcysteine in these situations and the need for increasing doses, when co-administering hemodialysis.

**Keywords:** Acetaminophen. Overdose; N-acetylcystein; Extra Corporeal Treatment

## Introduction

Acetaminophen is a common analgesic agent [1-3]. It is available without prescription and it is effective and safe when consumed in therapeutic doses. However, overdosing with acetaminophen is one of the leading causes of hospital admission for hepatotoxicity, acute liver failure and renal damage [1-2]. The toxicity results from the formation of *N*-acetyl *p*-benzoquinonneimine (NAPQI). Toxic dose is defined as an intake of more than 10-15 g in adults and 150 mg/kg in children [4]. It is suspected that even repeated therapeutic doses can be hepatotoxic in some individuals, such as alcoholics or patients in malnutrition. These patients may not be able to detoxify the reactive metabolites and may increase risk for hepatotoxicity [5-7]. Patients may present with no symptoms within the first few hours, but within 24 hours develop vomiting, nausea, and abdominal pain. During the next days, it will, if untreated, develop into liver failure, coma, renal failure, and ultimately death [1,5]. Rapid recognition and specific treatment of acute acetaminophen overdose is important, since it is a potential treatable illness [1,5-7].

There is no standard definition of massive acetaminophen overdose. A review has defined a massive ingestion as greater than 32 g or an acetaminophen concentration above 300 mcg/mL [4]. Massive ingestions present rapidly with metabolic acidosis, elevated lactate concentrations and altered mental status prior to the onset of severe liver injury. The management include specific antidote, N-acetylcysteine (NAC), stabilization and, in some hospitals, decontamination by gastric lavage or activated charcoal, within the first 4 hours to prevent liver failure and death [4]. The main role of NAC is to supply cysteine for the production of glutathione which directly binds to N-acetyl p-benzoquinoneimine and produces a non-toxic metabolite [4]. NAC should be initiated within 8 to 10 hours after the overdose [5-6,8]. In severe cases with multi-organ failure, renal replacement therapies, therapeutic plasmapheresis or even liver transplantation may be considered [1,5,8]. Patients with severe poisoning may develop indications for ECTR (Extra Corporeal Treatment) [3].

We present a case with massive intake of acetaminophen, presenting with severe metabolic acidosis, coma and death.

## Case report

Written informed consent was obtained from the patient's wife for publication of this case report. A 59-year-old man was admitted to the emergency room at the Hospital of Southwest Jutland in Esbjerg, Denmark. He was in a comatose position, Glasgow Coma Scale of four. He was seen alive 36 hours before. He was known to have an intermittent abuse of alcohol but otherwise healthy. He was hyperventilating, hypotensive and tachycardic. Blood glucose was 15.2 mmol/L, his pupils were equal in size and normally responded to light. Temperature was 35.2°C. Blood tests revealed a pH 7.0, $pCO_2$ < 2.0 kPa, $pO_2$ 17 kPa, $HCO_3$ 6 mmol/L, BE -27 mmol/L and hyperlactatemia (26 mmol/L). The concentration of ethanol in the blood was low. The first serum acetaminophen level was > 2.5 mmol/L (>283 µg/mL). The liver and the kidney numbers on the blood tests were normal (alanine aminotransferase 56 IU/L; creatinine 50 µmol/L). No acute findings were noted on CT. His wife reported 270 tablets, each containing 500 mg of acetaminophen, missing.

In the emergency department, treatment with NAC-infusion at standard bolus (200 mg/kg, which was 4000 mg/h during 4 hours) was initiated. He was admitted to the intensive care unit. He was given NAC-infusion at a higher dose (300 mg/kg) due to the massive intake of acetaminophen. The second serum acetaminophen level was 1.8 mmol/L (204 µg/mL). He received tracheal intubation, treatment with vasopressors and antibiotics. Hemodialysis (Continuous Renal Replacement Therapy with blood flow 100 mL/min and dialysate of 1000 mL/h) was initiated to correct disturbance in the acid/base status by reducing lactate. Lactate decreased to 3 mmol/L within the first hours after hemodialysis, but the alanine aminotransferase (ALT) increased to 530 IU/L. With continuously NAC-infusion and hemodialysis, he was transferred to a larger specialty center and plasmapheresis was tried (8000 ml on daily basis). Despite this, his condition worsened with multi-organ failure and ALT increased to 6080 IU/L. He died 70 hours after hospitalization.

## Discussion

We have presented a case, in which the patient was treated with a higher dose of NAC, hemodialysis and plasmapheresis due to massive intake of acetaminophen.

Some authors have suggested a higher dose of N-acetylcysteine in case of large overdoses. However, there are no controlled studies demonstrating the effect on liver failure prevention following massive intake [5]. The patients, who require additional NAC, may be difficult to identify. A study suggests the need for higher doses in cases with concentrations of acetaminophen above 300-line (= 300 µg/mL) and 450-line due to the increased risk of hepatotoxicity and liver failure. Others have also recommended additional therapies including hemodialysis [3-4]. During hemodialysis, a supplemental acetylcysteine dose should be considered, eventually oral acetylcysteine concurrent with the intravenous acetylcysteine using a standard oral acetylcysteine dosing regimen [8]. Hemodialysis removes NAC as well as acetaminophen. Therefore, it may be necessary to double the standard dose in these circumstances [5,8]. However, hemodialysis is not considered as standard management or as an alternative to acetaminophen poisoning when N-acetylcysteine is available. Hemodialysis may be necessary when acute renal failure is presented or when acid/base status need to be corrected [3,5,8]. This is in accordance with the EXTRIP group, which recommends hemodialysis if acetaminophen concentration is above the 900-line, if there are signs of hyperlactatemia or acidemia or for patients with suspected severe acetaminophen poisoning [3]. Extracorporeal treatment (ECTR) in acetaminophen poisoning may be considered, and reserved for rare situations, e.g., when the NAC is insufficient and only in patients with excessively large overdoses and mitochondrial dysfunction. This is reflected by early development of altered mental status and severe metabolic acidosis prior to the onset of hepatic failure [3].
ECTR seems to be a beneficial adjunct to NAC treatment in these cases [3].

## Conclusion

Since there is no standard definition of massive acetaminophen overdose, the need of rapid recognition is very important, and according to the serum acetaminophen level, the clinician may consider treatment with a higher dose of the specific antidote. It is also important to be familiar with the possibility of renal replacement therapies, plasmapheresis and ECTR in patients with severe acetaminophen toxicity. ECTR should be reserved for rare situations.

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**Conflict of interest:**

The authors have no conflicts of interest.

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