

C A S E R E P O R T

Early treatment with N-acetylcysteine reduces hepatotoxicity in acute acetaminophen poisoning

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Abstract. During the COVID19 outbreak measures taken to contain the spread of the virus have influenced the mental well-being of adults and adolescents. Acetaminophen overdose is the major cause of drug intoxication among children and adolescents. We reported a case of a 15-year-old girl referred to our Emergency Department 3 hours after ingestion of 10 g of paracetamol for suicidal purposes. She promptly started the administration of intravenous N-acetylcysteine (NAC) and the patient was discharged after 5 days of hospitalization in good clinical condition and with neuropsychiatric follow-up. Our case shows that the timing of the intravenous NAC administration is considered the most important factor in the prevention of acetaminophen-induced hepatic failure, despite high serum levels after acetaminophen ingestion. (www.actabiomedica.it)

Key words: Adolescents, acetaminophen; acute poisoning, N-acetylcysteine, suicide attempt

Introduction

During the COVID19 outbreak, measures taken to contain the spread of the virus have markedly influenced the mental well-being of adults and adolescents (1). Indeed, the lockdown increased rates of anxiety and depression for everyone and this could influence self-injurious and suicidal behaviors (2). Worldwide, acetaminophen overdose is the leading cause of drug intoxication among children and adolescents; in children, the event is mostly accidental while in adolescents often represents a suicide attempt (3). Paracetamol is the most popular analgesic and antipyretic drug used in pediatric age and its easy availability makes it one of the most frequent causes of attempted suicide among adolescents (3). In most cases the serum level of paracetamol after its ingestion is less to the toxic dose (150 mg/kg or 7.5 g in 24 hours in adult) and no treatment is required, but if the ingested dose is higher there is a high risk of hepatotoxicity. Timely

administration of N-acetylcysteine (NAC) may reduce the risk of hepatotoxicity and limit liver damage if this has already occurred (4).

Case report

We reported a case of a 15-year-old girl (56 kg) referred to our Emergency Department (ED) three hours after ingestion of 10 one-gram paracetamol tablets for suicidal purposes (10 g in total). The girl was already suffering from depressive disorder and was undergoing psychotherapy. On clinical examination she was alert and oriented, showing nausea and abdominal pain but no vomiting. Hemodynamic parameters were normal with heart rate of 110 bpm, respiratory rate of 28/m, blood pressure 140/90 mmHg and temperature 36 °C. Right after the admission to the ED, the girl underwent gastric lavage in sedation and decontamination with activated charcoal. The

serum acetaminophen level at 3 hours post-ingestion and after the gastric lavage was 178 $\mu\text{g/ml}$, above the paracetamol treatment line reported in the Rumack-Matthew nomogram (5), while alanine aminotransferase (ALT), bilirubin, creatinine, international normalized ratio (INR) and aPTT resulted in normal range. Afterwards, according to European Protocol (6), she started the administration of intravenous N-acetylcysteine (NAC, Hidonac, Zambon Italia Srl) as follow: 150 mg/kg over 4 hours, followed by repeated doses of 50 mg/kg in 4 hours for 20 hours total. Blood examination, carried out in the following hours, showed normal liver function with good clinical conditions. Informed consent was obtained from the parents to measure serum acetaminophen concentrations. Its level at 8 hours post-ingestion and at 3 hours after NAC treatment was 74.9 $\mu\text{g/ml}$, while decreased dramatically (<1.2 $\mu\text{g/ml}$) at 12 hours post ingestion and at 8 hours post-treatment (Figure 1). The girl was then discharged after 5 days of hospitalization in good clinical condition and with neuropsychiatric follow-up.

Discussion

Acetaminophen poisoning can lead to serious and irreversible hepatic damage and even death in acute overdose. Gastric lavage is quickly required to avoid hepatic failure but its usefulness is limited if administered 2 hours after ingestion, due to the rapid absorption of acetaminophen. In our case the patient referred late to ED, but the gastric lavage was performed anyway. After the gastric lavage, NAC infusion was promptly started, pending plasma level of acetaminophen.

Acetaminophen is metabolized in the liver into non-toxic glucuronide (52-57%), and sulphate conjugates (30-44%), and a small part (5%), by cytochrome P450, into the reactive metabolite N-acetyl-p-benzoquinoneimine (NAPQI). In case of acute overdose, the rapid production of the toxic intermediate NAPQI reduces glutathione reserves and leads to various biochemical processes, resulting in cellular damage and liver necrosis (7). NAC increases the synthesis of glutathione and can mimic

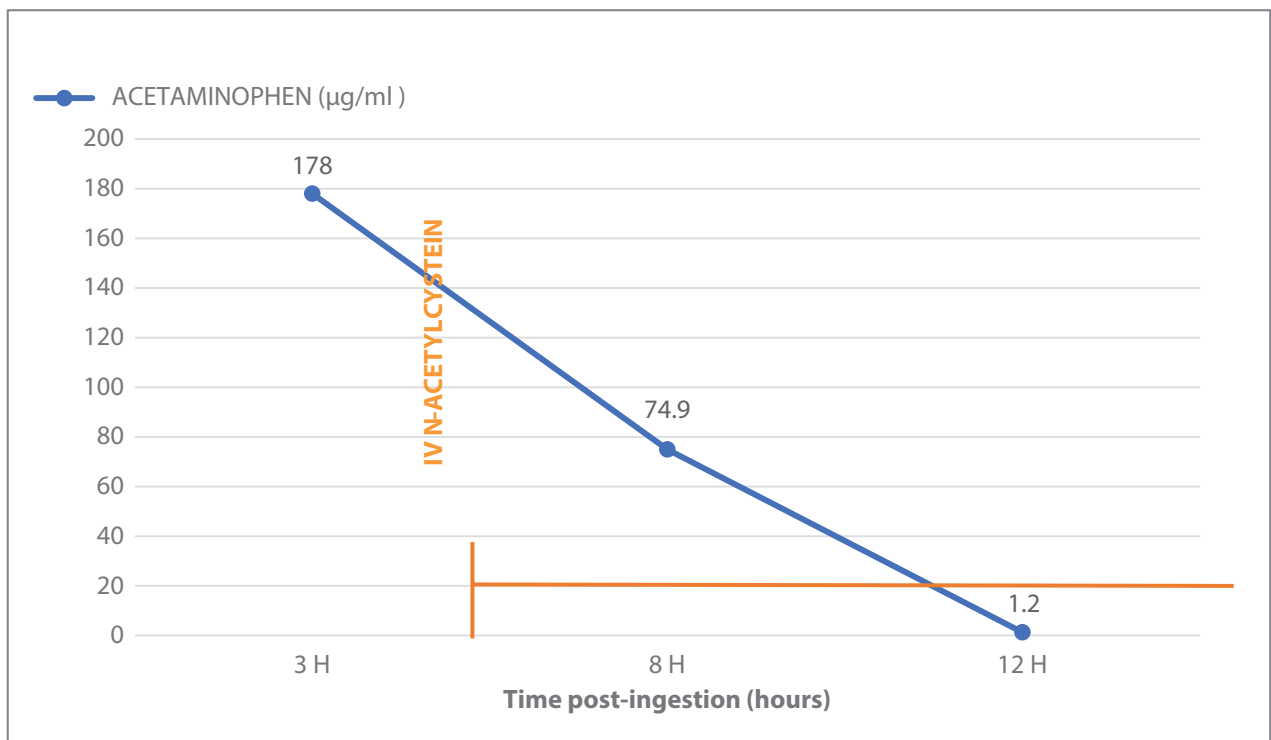


Figure 1. Acetaminophen serum concentration versus time post-ingestion.

glutathione effects by directly binding and detoxifying NAPQI, so increasing non-toxic metabolites (3). The timing of the intravenous NAC administration is considered the most important factor in the prevention of acetaminophen-induced hepatic failure (8, 9). We highlight the efficacy of early intravenous NAC treatment to prevent acute hepatic damage, despite high serum levels after acetaminophen ingestion.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Consent Form for Case Reports: Written informed consent was obtained from the patient concerned.

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Received: 20 September 2022

Accepted: 14 October 2022

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