Case Report

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Acetaminophen Ingestion Turns Toxic

Bhumika Rajpal[1], Manas Mitra[2], Arun Kaushik[3], Kishalay Datta[4]

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Abstract

Acetaminophen, commonly called "Paracetamol" is an over the counter medication available in all the pharmacies in the Indian subcontinent. The emergency and critical care department is commonly involved in the diagnosis and treatment of acetaminophen poisoning patients. The treatment guidelines are ages old but in recent times, the presentation for acetaminophen poisoning has been varied. In this case report, we will discuss the diagnosis and management of acetaminophen poisoning in a child, along with review of literature.

Keywords: Acetaminophen; Paracetamol poisoning; N-acetyl cysteine; Rumack Matthew nomogram.

INTRODUCTION

Acetaminophen is widely available over the counter antipyretic and analgesic worldwide, especially in the Southeast subcontinent. Paracetamol can be used as an intentional or accidental cause for self poisoning owing to its easy availability.[1,2] Paracetamol poisoning can turn fatal due to its hepatotoxicity and nephrotoxicity.[3] Acute paracetamol poisoning is considered massive when the intake is more than 30 grams.[4] Treatment is generally supportive in most of the cases with the use of N-acetyl cysteine as an antidote for acetaminophen poisoning. In this case report, we will discuss how an antipyretic overuse leads to acute paracetamol poisoning in a 6 year old child, leading to severe hepatic failure, the diagnosis and management along with review of literature for paracetamol poisoning.

Author's Affiliation: [1]Emergency Medicine Resident, [2]Resident, [3]Associate Consultant, [4]Director and HOD, Department of Emergency Medicine, Max Hospital, Shalimar Bagh 110088, New Delhi, India.

Corresponding Author: Bhumika Rajpal, Emergency Medicine Resident, Department of Emergency Medicine, Max Hospital, Shalimar Bagh 110088, New Delhi, India.

E-mail: bhumikarajpal99@gmail.com

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CASE

A 6 year old child was brought to the Emergency Room by her mother with complaints of lethargy and increased sleepiness. On physical examination, the child was weighing around 20kg, the patient was found to have raised body temperature with elevated heart rate, capillary refill time was normal. The patient was found to have icterus with tender hepatomegaly. The patient was having travel history 1 week back, where she consumed outside food and water. The patient was having fever

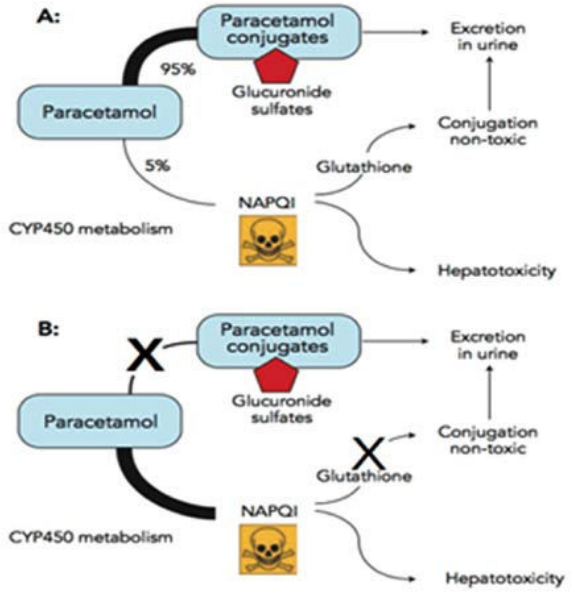
spikes for the last 5 days for which her mother was giving her paracetamol syrup. For the last 2 days, she noticed her child developing an icterus. An initial diagnosis of viral hepatitis was made, but her blood reports for viral hepatitis (hepatitis A, B, C, hepatitis E) were negative with a deranged liver profile (raised serum bilirubin, SGOT, SGPT, ALP). Further digging of the history revealed that the mother has increased the quantity of paracetamol more than the prescribed amount by her local physician because her child was having fever spikes. Now she was giving her 5ml paracetamol syrup 6-8 times a day for the last 2 days (image showing paracetamol syrup with quantity - each 5 ml has 250mg paracetamol content). The patient was immediately shifted to Paediatric Intensive care unit (PICU) and serum paracetamol levels were sent alongwith coagulation and urine examination. She received the initial dose of N-acetyl cysteine

(150 mg/kg) in 500ml dextrose over 30 minutes, followed by 50 mg/kg over 4 hours then 100 mg/kg over 16 hours (21 hours protocol, all dilutions in dextrose normal saline).[4] She also received other supportive measures like injection vitamin K, injection L-ornithine-L-aspartate during her stay in the PICU. The N-acetyl cysteine infusion was continued alongwith the supportive care.

From the 5th day onwards, the liver parameters started improving. On the 7th day of admission, the patient was well and blood parameters were normal. The patient was discharged healthy on the 9th day with proper parental counseling for medicine administration. The post discharge follow up was satisfactory and child growth was well.

DISCUSSION

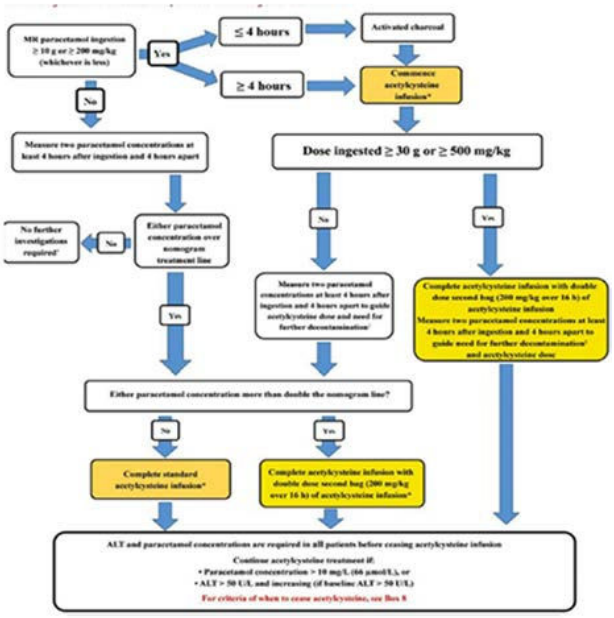
The child was diagnosed with acetaminophen (a.k. a Paracetamol/Crocin) poisoning. This was a case of delayed presentation of acute acetaminophen poisoning. Acetaminophen is widely accepted antipyretic and analgesic worldwide. The therapeutic level of paracetamol in adults is 4g/day and 50mg/kg/day in children. An over dose can induce life threatening conditions like acute hepatic failure.[5] In normal conditions, the majority (90%) of paracetamol is metabolized in the liver to form sulfate and glucuronide as end products. These metabolites are non toxic and readily excreted by the kidneys. A small fraction (5%–10%) of paracetamol is metabolized by enzyme CYP450 into a toxic and highly reactive metabolite, N-acetyl-p-benzoquinoneimine (NAPQI). This compound is detoxified in the liver by conjugation with glutathione. When a very large dose of paracetamol is administered, the detoxification capacity of the liver is saturated. Therefore, more NAPQI is freely available in the liver, causing hepatic necrosis and acute tubular necrosis.[5]



A: In a healthy individual, about 95% of paracetamol is conjugated with glucuronide and excreted in the urine. Most of the remainder is conjugated with glutathione. B: In starvation, impaired conjugation and depletion of glutathione result in accumulation of hepatotoxic N-acetyl-p-benzoquinone imine (NAPQI).

Paracetamol poisoning has various clinical manifestations (box).[5] Massive overdose can lead to hepatic failure and central nervous depression.[6] Serum acetaminophen levels must be established and should be plotted on Rummack Matthew nomogram for the useful consideration to start intravenous N-acetylcysteine.

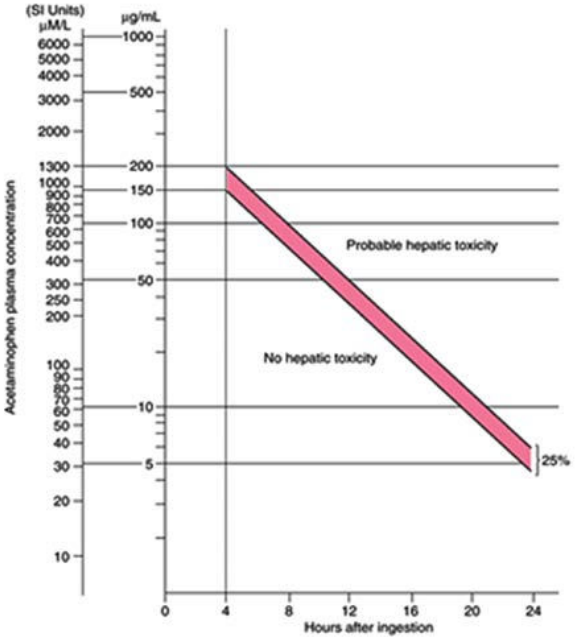
Clinical manifestations of acetaminophen hepatotoxicity	
Stage I (first 24 h)	Nausea, vomiting, malaise, lethargy, diaphoresis (some patients remain asymptomatic) AST/ALT are typically normal (AST/ALT may begin to rise at 8–12 h after massive overdose)
Stage II (24–72 h)	Stage I symptoms usually improve or resolve (so-called latent period) Subclinical AST/ALT elevation In severe cases, RUQ pain, tender hepatomegaly, jaundice, and prolonged PT may be seen Nephrotoxicity (elevated creatinine and oliguria) may become evident
Stage III (72–96 h)	Systemic symptoms of stage I reappear AST/ALT elevation, typically peak at 72–96 h after ingestion (often >3000 IU/L) Jaundice, encephalopathy, prolonged PT, and lactic acidosis may develop ARF (10%–50%) and acute pancreatitis (0.3%–5%) may develop Death often in this stage, usually from multiorgan system failure
Stage IV (96 h–2 wk)	Survivors of stage III enter recovery phase, which often lasts 1–2 wk, but may take several weeks in severe cases Histologic recovery occurs slower than clinical recovery and may take up to 3 mo When recovery occurs, it is complete; chronic hepatitis has not been reported



Intravenous N-acetylcysteine is the antidote for acetaminophen poisoning and is very effective when used early in the course of treatment.[7] The routinely used treatment protocol is the "21 hours IV protocol" which uses 3 bags of N-acetylcysteine.[7,8] A newer regime which is a simplified 2 bag N-acetylcysteine regimen (200 mg/kg over 4 h, then 100 mg/kg over 16 h) which has similar efficacy and lower side effects when compared to standard therapy.

CONCLUSION

Acetaminophen (paracetamol, crocin) is widely available, cost-effective over the counter medications in the Indian subcontinent. There exists little knowledge about the therapeutic and toxic dose of paracetamol and over dose may have severe lethal complications. Intravenous N-acetylcysteine is the antidote of choice in acetaminophen



poisoning, along with other supportive measures to protect the liver and kidneys from damage. Proper knowledge about the therapeutic levels must be given to the public by campaigns and other media to prevent lethal effects of paracetamol.

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