

## Paracetamol Overdose in the Postoperative Postpartum Period

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### ABSTRACT

Paracetamol is the most commonly used medication for pain and fever worldwide and is readily available over the counter. The recommended maximum daily dose for an adult is three to four-gram. Paracetamol poisoning is the foremost cause of acute liver failure in the Western world and accounts for the highest percentage of drug overdose worldwide. Paracetamol administered in therapeutic doses is mainly conjugated with sulfate and glucuronide to form non-toxic metabolites via phase II metabolism. A small portion is metabolized to N-acetyl-p-benzoquinoneimine (NAPQI), a toxic metabolite. NAPQI is conjugated with glutathione and detoxified to form cysteine and mercapturic acid conjugates in normal circumstances. However, under certain conditions, NAPQI is not effectively detoxified due to depleting glutathione, causing hepatocellular necrosis and subsequently, liver failure. We present a case involving paracetamol overdose in a 35-year-old female who self-medicated on a large number of paracetamol pills daily for two weeks because of postoperative pain. This resulted in deranged liver enzymes. N-acetylcysteine was administered and led to clinical improvement and normalized LFTs. The case highlights patients' ignorance of the dangers of paracetamol overdose and the importance of N-acetylcysteine in its management.

**Keywords:** Paracetamol overdose; N-acetyl-p-benzoquinone mine; N-acetylcysteine

### INTRODUCTION

Paracetamol is widely available and self-medicated, hence its potential toxicity is commonly underestimated. Its ubiquity may make patients feel it is harmless despite ingestion of increased doses. Today, Paracetamol remains a significant cause of overdose and overdose-related liver failure and death [1].

Symptoms for the first 24-48 hours of paracetamol intoxication are usually absent or nonspecific. They may include fatigue, abdominal pain, nausea, and vomiting. This is generally followed by jaundice, altered sensorium, coagulopathy, metabolic acidosis, acute liver failure [2], and ultimately death when untreated. Treatment options include activated charcoal (if the patient presents within 1hour of ingestion), and N-acetylcysteine (NAC), which acts by increasing the synthesis of glutathione in the liver [3], or liver transplant if severe liver damage results. Here is a case of paracetamol overdose in a 35-year-old female who presented with abdominal distension and pain and was managed for Paracetamol poisoning.

### CASE PRESENTATION

A 35-year-old female presented to the clinic two weeks after undergoing an elective cesarean section for fetal macrosomia, complaining of abdominal swelling and pain for two days. The surgery and her immediate postpartum period preceding discharge were uneventful.

On examination, the patient had generalized abdominal swelling with no tenderness. The surgical site was clean and had no swelling, erythema, or discharge. The patient was afebrile (temperature of 36.6°C), blood pressure of 130/80mmhg, pulse 94 beats per minute, and respiratory rate of 19 cycles per minute. She had no jaundice, no pallor, no nausea or vomiting, and reported no changes in mental status.

An urgent abdominopelvic ultrasound scan showed mild hepatomegaly with moderate ascites. No mass or internal hemorrhage was found. She was started on painkillers (Oral Diclofenac 100mg BD).

On further questioning, the patient admitted that she took around 12-24 pills of Paracetamol, with each pill being 500mg, during the day to help with her pain. She took them daily for the past two weeks. In light of the new information, a diagnosis of paracetamol overdose was made, and the patient was admitted.

She was kept on nil-per-oral, and further tests assessing her liver function tests, shown in Table 1, were also sent. Due to the unavailability of serum paracetamol measurement facilities in our hospital, her serum paracetamol levels could not be ascertained. The patient was negative for hepatitis B and hepatitis C.

**TABLE 1:** Liver function test on presentation

Liver function test parameters	Normal values	Patient's values
Total bilirubin	2-10 mg/dL	0.437 mg/dL
Direct bilirubin	0.1-1 mg/dL	0.339 mg/dL
AST	< 46 U/L	49.491
ALT	< 49 U/L	55.362 U/L
Albumin	3.5 - 5.5 g/dL	1.77g/dL

In the table above, showing LFT on presentation, AST and ALT are elevated; an evidence of liver damage.

She was started on N-acetylcysteine (NAC) at a 19.5g (an initial loading dose of 200mg/kg/dose in normal saline over 4hrs, followed by a maintenance dose of 100mg/kg/dose over 16hrs).

The patient was discharged on day seven, and her liver function tests shown in Table 2 were done prior to discharge.

**TABLE 2:** Liver function test on day seven of admission

Liver function test parameters	Normal values	Patient's values
Total Bilirubin	2 -10 mg/dL	1.41 mg/dL
Direct Bilirubin	0.1 - 1 mg/dL	0.47 mg/dL
AST	<46 U/L	37.5 U/L
ALT	<49 U/L	42.8 U/L
Albumin	3.5 - 5.5 g/L	2.5 g/L

The table above shows LFT on day seven of admission; days after administration of N Acetyl cysteine. It shows an improvement in the LFT values as AST and ALT are now within reference range.

Repeat liver function test, seen in Table 3, done a week after discharge showed a further improvement in liver function and resolution of abdominal swelling.

**TABLE 3:** Repeat liver function test a week after discharge of patient

Liver function test parameters	Normal values	Patient's values
Total bilirubin	2 - 10 mg/dL	0.94 mg/dL
Direct bilirubin	0.1 - 1 mg/dL	0.43 mg/dL
AST	<46 U/L	28.08 U/L
ALT	<49 U/L	34.53 U/L
Albumin	3.5 - 5.5 g/dL	3.05 g/dL

The table above shows LFT a week after the patient was discharged. It shows a further improvement in liver function, evidenced by a further drop in AST, ALT and an increase in serum albumin levels in comparison to previous values.

## DISCUSSION

The maximum recommended therapeutic dose of Paracetamol in adults is about 4g/day [4] and would require about 7.5 g/day to 10 g/day to produce clinical symptoms of toxicity [5]. The report describes a well-educated woman in the puerperal period who indiscriminately consumed about 6-12g of paracetamol a day for two weeks. Unintentional chronic paracetamol poisoning in the early post-partum period is poorly described. But there exist reports of chronic paracetamol toxicity in pregnancy. One such case is that of a 22-year pregnant female who presented with abdominal pain and hepatotoxicity after taking approximately 8-9 grams of Paracetamol per day for 10-14 days for dental pain resulting in fulminant hepatitis requiring liver transplantation [6]. The patient in this case report has no identifiable risk factors for liver disease, similar to the patient in our report who also had no identifiable risk factors for liver disease such as chronic alcohol consumption, viral hepatitis, or preeclampsia.

This highlights that predictors of severe disease after chronic paracetamol poisoning still have to be further investigated.

Although physiologic changes in pregnancy, such as a significantly reduced serum albumin seen in most women in the third trimester and the early postpartum period, may have contributed to the patient's presentation [7]. The patient in our report presented with serum albumin of 1.77mg/dl, serum albumin levels below 2.5mg/dl in early postpartum are abnormal [7].

Hepatotoxicity is the most prominent concern regarding acute or chronic paracetamol poisoning. ALT is a sensitive marker of hepatotoxicity [8], and this patient presented a mildly elevated serum ALT level which does not suggest hepatotoxicity. Rises in liver enzymes can be expected with long-term paracetamol intake even at therapeutic levels(<4g/day) [4,9]. Despite no apparent biochemical features of hepatotoxicity, the patient presented with moderate ascites, which a low plasma oncotic pressure could explain because of reduced serum albumin concentration. Low serum albumin level was most likely because of reduced production by the liver.

Our patient's diagnosis of chronic paracetamol poisoning was made by history and examination supported by a deficient serum albumin level. The unavailability of tests to assess serum paracetamol levels should not delay treatment. Conservative treatment with N-acetylcysteine (NAC), at a dose of 19.5g (an initial loading dose of 200mg/kg/dose in normal saline over 4hrs, followed by a maintenance dose of 100mg/kg/dose over 16hrs) to reduce the possibility of hepatotoxicity and serial monitoring of liver function was proven to be sufficient care as evidenced by a resolved ascites and positive response of serum albumin from a value of 1.77 to 2.5 mg/dl within seven days. However, this rapid recovery could also have been contributed to by postpartum changes, which work to bring pregnancy-related changes such as low serum albumin to pre-pregnancy levels.

Our report has also highlighted the importance of educating patients on all prescribed drugs. An apparent gap in communication can be identified in the cause of this presentation.

### CONCLUSION

With the insistence of acute paracetamol poisoning in the general population, measures towards imparting the public and imploring the clinicians and scientific expertise to curtail its impact on global health should be scaled up. These should include closer attention to dosing by pharmacists and more intervention from toxicologists. Vulnerable populations, such as individuals in the immediate post-operative period, postpartum, and those experiencing chronic pain, should be mainly targeted for awareness of this danger.

### AUTHOR'S CONTRIBUTIONS

Each named author has substantially contributed to the underlying research and has approved the final manuscript.

### CONFLICT OF INTEREST

This manuscript has not been published and is not under consideration for publication elsewhere. We have no funding and none of the authors have any conflict of interest, financially or otherwise.

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