# CASE REPORT

# Plasmapheresis as an Emergency Therapy for Acetaminophen-Related Acute Hepatic Failure: Case Series

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***ABSTRACT***

**Background:** Paracetamol (acetaminophen) overdose is one of the most common causes of drug-induced acute liver injury worldwide. Early administration of N-acetylcysteine (NAC) is highly effective in preventing hepatotoxicity. However, some patients develop progressive liver injury despite appropriate NAC therapy and may clinically deteriorate without fulfilling criteria for liver transplantation. Therapeutic plasma exchange (TPE) has emerged as a potential supportive therapy in severe drug-induced liver injury.

**Case Series:** We report three cases of acute high-dose paracetamol poisoning presenting with markedly elevated serum transaminases. All patients received standard treatment with the intravenous NAC 21-hour protocol followed by a 72-hour regimen along with supportive therapy including glutathione and vitamin despite treatment, patients demonstrated persistent elevation of SGOT and SGPT with progressive clinical deterioration and severe metabolic acidosis requiring mechanical ventilation. Serum paracetamol levels were approximately 30 µg/mL. None of the patients met King's College criteria for liver transplantation. Therapeutic plasma exchange was initiated using albumin, fresh frozen plasma, and normal saline as replacement fluids. After five sessions of TPE, there was a significant decline in liver enzyme levels with normalization of SGOT and SGPT. Clinical improvement followed with successful extubation and eventual discharge.

**Conclusion**: This case series highlights the potential role of therapeutic plasma exchange as an adjunctive treatment in severe paracetamol toxicity when patients deteriorate despite NAC therapy and are not candidates for liver transplantation.

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## INTRODUCTION

Acute liver failure (ALF) is a rare but life-threatening clinical syndrome characterized by the rapid deterioration of liver function, resulting in coagulopathy and hepatic encephalopathy in individuals without pre-existing liver disease. Among the various etiologies, acetaminophen (paracetamol) toxicity remains the most common cause of ALF in many parts of the world, particularly in developed and developing countries alike (1). The widespread availability and perceived safety of acetaminophen contribute to its frequent misuse, leading to both intentional and unintentional overdoses (2).

The pathophysiology of acetaminophen-induced liver injury involves the accumulation of a toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI), which is normally detoxified by glutathione. In overdose situations, glutathione stores become depleted, allowing NAPQI to bind to hepatocellular proteins, leading to oxidative stress, mitochondrial dysfunction, and ultimately hepatocyte necrosis (3). Clinically, patients may initially present with nonspecific symptoms such as nausea, vomiting, and malaise, which can rapidly progress to jaundice, coagulopathy, encephalopathy, and multi-organ failure (4). Early administration of N-acetylcysteine (NAC) is the cornerstone of treatment and has been shown to significantly reduce morbidity and mortality when given promptly (5). However, in cases of delayed presentation or massive overdose, NAC therapy may be insufficient to prevent progression to fulminant hepatic failure. Liver transplantation remains the definitive treatment for patients who fail medical therapy, but its application is limited by donor organ availability, high cost, and strict selection criteria (6). Therefore, there is a critical need for alternative or bridging therapies that can support patients during the acute phase of liver failure.

Therapeutic plasma exchange (TPE), also known as plasmapheresis, has emerged as a potential rescue therapy in patients with ALF. TPE involves the removal of a patient's plasma and replacement with donor plasma or albumin, thereby eliminating circulating toxins, inflammatory mediators, and harmful metabolites (7). In

the context of acetaminophen toxicity, TPE may aid in reducing circulating levels of toxic substances and modulating the systemic inflammatory response associated with liver injury (8). Recent studies have suggested that high-volume plasma exchange can improve transplant-free survival in patients with ALF by stabilizing hemodynamic, improving coagulation parameters, and reducing the severity of encephalopathy (9). Additionally, TPE may serve as a bridge to liver transplantation or, in some cases, allow for spontaneous hepatic recovery, thereby avoiding the need for transplantation altogether (10). Despite these promising findings, the use of TPE in acetaminophen-induced ALF is still not universally standardized, and further evidence is required to establish clear clinical guidelines.

This case report aims to highlight the role of plasma exchange as a rescue therapy in a patient with acute liver failure secondary to acetaminophen toxicity. It underscores the potential benefits of early intervention with TPE in critically ill patients who do not respond adequately to conventional medical management, thereby contributing to the growing body of evidence supporting its use in this setting.

## CASE SERIES:

### Case 1

A 34-year-old female with no known comorbidities presented to the emergency department with a history of intentional ingestion of approximately 25 g of paracetamol tablets 10 hours prior to admission. She complained of nausea, repeated vomiting, and epigastric abdominal pain. On examination, she was conscious but lethargic, with mild dehydration and stable hemodynamic parameters. Initial laboratory investigations revealed markedly elevated liver enzymes with SGOT of 4,850 U/L and SGPT of 5,120 U/L, serum bilirubin of 2.1 mg/dL, and an INR of 2.3. Serum paracetamol level was 32 µg/mL. A diagnosis of severe paracetamol poisoning with acute hepatocellular injury was made, and intravenous N-acetylcysteine (NAC) therapy was initiated using the standard 21-hour protocol, followed by an extended 72-hour regimen along with glutathione supplementation and vitamin K.

Despite appropriate treatment, the patient's condition deteriorated with further elevation of liver enzymes and development of metabolic acidosis (arterial pH 7.18, lactate 6.2 mmol/L). She became progressively drowsy and required endotracheal intubation and mechanical ventilation. Although she had significant hepatic injury, she did not meet King's College criteria for liver transplantation. Therefore, therapeutic plasma exchange (TPE) was initiated using albumin, fresh frozen plasma, and normal saline as replacement fluids. After four sessions of TPE, there was a significant decline in transaminase levels and improvement in metabolic parameters. The patient was successfully extubated and discharged with near-normal liver function tests.

### Case 2

A 41-year-old male presented with altered sensorium and severe abdominal pain following ingestion of approximately 30 g of paracetamol tablets 14 hours prior to admission. On examination, he was confused, tachycardia, and dehydrated. Laboratory investigations showed severe hepatocellular injury with SGOT of 6,420 U/L and SGPT of 6,980 U/L, serum bilirubin of 3.4 mg/dL, and an INR of 3.1. Serum paracetamol level was 38 µg/mL. A diagnosis of massive paracetamol overdose with progressive hepatic dysfunction was made, and intravenous NAC therapy was initiated and continued beyond the standard duration due to worsening liver injury. Supportive treatment included glutathione infusion and vitamin K.

Despite aggressive management, the patient developed worsening metabolic acidosis (pH 7.12, lactate 7.4 mmol/L) and required mechanical ventilation. Imaging revealed hepatomegaly without evidence of chronic liver disease. Although the biochemical abnormalities were severe, he did not fulfil criteria for liver transplantation. Therapeutic plasma exchange was therefore initiated using albumin and fresh frozen plasma as replacement fluids. After six sessions of TPE, there was marked improvement in liver enzyme levels, coagulation profile, and metabolic acidosis. The patient was gradually weaned off ventilatory support and discharged in stable condition with improving liver function.

### Case 3

A 29-year-old female presented with a two-day history of persistent vomiting, abdominal pain, and progressive drowsiness after ingestion of approximately 20 g of paracetamol tablets. On examination, she was drowsy but arousable and showed signs of dehydration. Laboratory investigations revealed SGOT of 3,980 U/L and SGPT of 4,210 U/L, total bilirubin of 1.8 mg/dL, and an INR of 2.0. Serum paracetamol level was 27 µg/mL. A diagnosis of delayed presentation of paracetamol toxicity with acute liver injury was made, and intravenous NAC therapy was initiated using the standard protocol followed by extended infusion due to persistent hepatotoxicity.

Despite treatment, the patient's condition worsened with development of metabolic acidosis (pH 7.21, lactate 5.8 mmol/L) and declining mental status, necessitating mechanical ventilation. As she did not meet liver transplantation criteria but continued to deteriorate, therapeutic plasma exchange was initiated. After three sessions of TPE, there was a significant reduction in liver enzyme levels and correction of metabolic acidosis. The patient showed gradual clinical improvement, was successfully extubated, and discharged with normalization of liver function tests on follow-up.

**DISCUSSION:**

Acetaminophen-induced acute liver failure (ALF) remains a major clinical challenge worldwide, representing one of the most common causes of drug-induced hepatotoxicity and ALF in both developed and developing countries (1). Despite the widespread availability of N-acetylcysteine (NAC) as an effective antidote, a subset of patients continues to progress to severe liver injury, underscoring the need for additional therapeutic strategies. The present case series highlights the potential role of therapeutic plasma exchange (TPE) as an adjunctive treatment modality in patients with severe acetaminophen toxicity who fail to respond adequately to standard medical therapy.

The pathogenesis of acetaminophen toxicity is well established and involves the accumulation of the toxic metabolite N-acetyl-p-benzoquinone imine (NAPQI), which overwhelms hepatic glutathione stores and leads to hepatocellular necrosis (3). While early administration of NAC replenishes glutathione and neutralizes NAPQI, delayed presentation or massive ingestion can render NAC insufficient, allowing the progression of oxidative stress, mitochondrial dysfunction, and systemic inflammatory response (4, 5). In the cases described, all patients received timely and extended NAC therapy, yet they exhibited worsening biochemical and clinical parameters, emphasizing the limitations of NAC in advanced stages of toxicity.

Therapeutic plasma exchange offers a mechanistically distinct approach by directly removing circulating toxins, inflammatory cytokines, and harmful metabolites from the bloodstream (7). In acetaminophen-induced ALF, TPE may contribute to improved outcomes through several mechanisms. First, it facilitates the clearance of residual acetaminophen and its toxic metabolites, thereby reducing ongoing hepatocellular injury. Second, it modulates the systemic inflammatory response, which plays a crucial role in the progression of ALF and multi-organ dysfunction (8). Third, TPE provides coagulation factors and albumin, which can improve coagulopathy and hemodynamic stability, both of which are commonly impaired in ALF (9).

In this case series, all three patients demonstrated significant clinical and biochemical improvement following multiple sessions of TPE. Notably, there was a marked reduction in transaminase levels (SGOT and SGPT), correction of metabolic acidosis, and eventual recovery of hepatic function. These findings are consistent with previous studies that have reported improved transplant-free survival and clinical stabilization in patients with ALF undergoing high-volume plasma exchange (9). The observed improvement in metabolic acidosis and encephalopathy further supports the role of TPE in mitigating systemic toxicity and improving organ function.

An important consideration in the management of ALF is the identification of patients who may benefit from liver transplantation. The King's College criteria are widely used to assess prognosis and determine the need for transplantation (6). However, not all patients who deteriorate meet these criteria, as demonstrated in this case series. In such scenarios, TPE may serve as a valuable bridge therapy, either allowing time for spontaneous hepatic regeneration or stabilizing patients until transplantation becomes feasible (10). The successful recovery of all three patients without the need for transplantation highlights the potential of TPE to alter the clinical course in selected patients.

The timing of initiation of TPE appears to be a critical factor influencing outcomes. Early intervention, before the onset of irreversible multi-organ failure, may enhance the efficacy of TPE by limiting the extent of hepatocellular damage and systemic inflammation. In the present cases, TPE was initiated following evidence of clinical deterioration despite optimal medical therapy, including worsening transaminases, metabolic acidosis, and encephalopathy. The favourable outcomes observed suggest that timely initiation of TPE in such patients may improve prognosis.

Another notable aspect is the use of replacement fluids during TPE. The combination of albumin, fresh frozen plasma (FFP), and normal saline used in these cases not only facilitates toxin removal but also replenishes essential proteins and coagulation factors. This is particularly important in ALF, where coagulopathy and hypoalbuminemia contribute to disease severity. Previous studies have similarly emphasized the benefits of plasma-based replacement in improving coagulation parameters and overall clinical status (9).

Despite the promising results, the use of TPE in acetaminophen-induced ALF is not without limitations. The procedure is resource-intensive, requires specialized equipment and trained personnel, and may not be readily available in all healthcare settings. Additionally, potential complications such as hypotension, allergic reactions, and electrolyte imbalances must be considered. However, in critically ill patients with limited therapeutic options, the potential benefits of TPE may outweigh these risks.

The current evidence supporting TPE in ALF is growing but remains limited, particularly in the context of acetaminophen toxicity. Most available data are derived from case reports, small case series, and a limited number of clinical trials. Therefore, larger randomized controlled studies are needed to establish standardized protocols, including optimal timing, frequency, and volume of plasma exchange. Furthermore, identifying specific patient populations that are most likely to benefit from TPE will be essential in guiding clinical decision-making.

This case series contributes to the existing literature by

demonstrating consistent clinical improvement across multiple patients with severe acetaminophen toxicity who did not respond to conventional therapy. The reproducibility of outcomes across different cases strengthens the argument for considering TPE as an adjunctive therapy in similar clinical scenarios. It also underscores the importance of a multidisciplinary approach in the management of ALF, involving intensivists, hepatologists, and transfusion medicine specialists.

In conclusion, therapeutic plasma exchange represents a promising adjunctive treatment for acetaminophen-induced acute liver failure, particularly in patients who deteriorate despite standard NAC therapy and do not meet criteria for liver transplantation. By facilitating toxin removal, modulating inflammation, and improving coagulation and metabolic parameters, TPE may enhance the likelihood of hepatic recovery and reduce the need for transplantation. While further research is needed to establish definitive guidelines, the findings from this case series support the early consideration of TPE in the management of severe acetaminophen toxicity.

**CONCLUSION:**

Therapeutic plasma exchange (TPE) appears to be a valuable adjunct in the management of severe acetaminophen-induced acute liver failure, particularly in patients who do not respond adequately to N-acetylcysteine therapy and are not candidates for liver transplantation. In this case series, TPE was associated with significant clinical and biochemical improvement, leading to recovery without transplantation. By facilitating toxin removal, correcting coagulopathy, and modulating systemic inflammation, TPE may enhance hepatic recovery. Early initiation in deteriorating patients could improve outcomes, although further large-scale studies are needed to establish standardized treatment protocols and confirm its efficacy.

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