

## Liver transplantation for fulminant hepatic failure in yellow phosphorus poisoning

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### ABSTRACT

Yellow phosphorus (YP) containing rodenticides is a readily available poison that may be accidentally or deliberately ingested, leading to symptoms ranging from simple gastrointestinal symptoms to fulminant hepatic failure, depending on the amount ingested. As there is no specific antidote, the treatment requires early gastric lavage and institution of supportive measures such as acetyl cysteine infusion and Vitamin K. Progression to fulminant hepatic failure is characterized by rapid deterioration of liver function tests, worsening coagulopathy, and sensorium. The only definitive treatment at this stage is a liver transplant and therapeutic plasma exchange (TPE) can serve as a bridge therapy until a compatible liver donor is found. We present a case of YP-containing rodenticide poisoning, in which the patient progressed to fulminant hepatic failure despite aggressive supportive therapy and was successfully managed with TPE until liver transplantation.

**Key words:** Acute liver failure, Plasmapheresis, Rodenticide poisoning, Yellow phosphorus

Rodenticides are readily available household poison commonly involved in accidental or deliberate poisoning [1]. They contain either yellow phosphorus (YP) (2–5%) or metallic phosphides such as aluminium phosphide and zinc phosphides [2]. YP is a toxic chemical that is rapidly absorbed and metabolized in the liver [3]. The only definitive treatment is liver transplant, but a few people have even survived without it.

We present a case of phosphorus-containing rodenticide ingestion with acute liver failure (ALF) who underwent a successful liver transplant.

### CASE REPORT

A 39-year-old female with no comorbidities presented with a history of recurrent vomiting, abdominal cramps, and giddiness following usage of YP-containing rodenticide for home pest control without any protection 4 days ago. She had been treated at a local hospital and referred here in view of worsening coagulopathy.

She was conscious and oriented on arrival, with a heart rate of 92 beats/min, respiratory rate of 18 cycles/min, blood pressure of 112/72 mm Hg, and temperature of 98°F.

Initial laboratory investigations including liver function and hepatitis work-up were normal, except for the deranged


international normalized ratio (INR) (2.4) (Table 1). She was initiated on acetyl cysteine infusion of 150 mg/kg over 1 h, then 50 mg/kg over 4 h and 100 mg/kg over 16 h, in 5% dextrose and Vitamin K 10 mg once daily and admitted to the intensive care unit (ICU) for monitoring. On day 2 of admission, she developed fever, and serum bilirubin (4.47 mg/dL) and INR (3.8) worsened, following which the liver transplantation team was alerted, and fresh frozen plasma (FFPs) were transfused.

She continued to deteriorate, with Grade 2 encephalopathy along with worsening serum ammonia (145 µmol/L) (normal range 15–45 µmol/L) levels, for which sustained low-efficiency dialysis (SLED) was initiated. She also underwent two sessions of therapeutic plasma exchange (TPE) over the next 2 days, using 8 units of FFPs with 5 units of albumin, with a total of 3l plasma volumes replaced each session. As her MELD (Model for End-stage Liver Disease) score further rose to 36, she underwent a live-donor liver transplant (LDLT) on day 8 of ICU admission, with her sister being the donor.

Post-transplant, there was a steady improvement in bilirubin and other liver parameters. She was started on tacrolimus and prednisone and discharged by day 18.

### DISCUSSION

YP is a toxic substance widely used in rodenticide products [1] in a concentration of 2%–5%. Accidental poisoning of the substance

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Table 1: Daily levels of total bilirubin, serum lactate, INR and encephalopathy grade before and after transplantation

Day in ICU	Total bilirubin (mg/dL)	Serum lactate (mmol/L)	INR	Encephalopathy grade (West Haven)
After admission				
Day 1	1	1.8	2.4	0
Day 2	4.47	2.6	3.8	0
Day 3	4.81	4.1	3.9	0
Day 4	6.04	6	4	0
Day 5	7.14	8.4	3.7	1
Day 6	11.11	9	2.7	1
Day 7	17.4	10	2.4	2
After transplantation				
Day 1	8.4	5.8	3.1	2
Day 2	5.72	2	2.5	1
Day 3	2.74	0.9	2.1	0
Day 4	2.44	1.1	1.5	0
Day 5	3.14	0.8	1.7	0
Day 6	2.57	1.7	1.7	0
Day 7	2.63	0.8	1.5	0

INR: International normalized ratio

is common in developing countries although suicidal ingestion is not rare. ALF, acute tubular necrosis, cardiac arrhythmias, convulsions, coma, and circulatory collapse are the possible consequences of intoxication which may be fatal [3,4].

The clinical condition evolves in three stages. The first stage involves minimal gastrointestinal disturbances such as nausea, vomiting, and cramps over the initial 24 h. The second stage is an asymptomatic phase lasting for one to 3 days. The third stage occurs after three to 4 days and involves ALF with or without hemodynamic instability. A delayed presentation at this stage may carry a high mortality. This patient had multiple episodes of nausea and abdominal cramps within 24 h of ingestion of the poison, after which she was symptom-free for 3 days, followed by a rapid progression to ALF. Therefore, patients with acute YP poisoning need to be closely monitored for at least four to 7 days for deterioration.

There is no specific antidote for YP intoxication. Early gastric lavage and supportive therapy in the form of N-acetyl cysteine (NAC) infusion are important in management [1,2,5,6]. While NAC is traditionally indicated in acetaminophen-induced liver toxicity, it is also useful in non-acetaminophen induced liver failure by replenishing glutathione stores and improving the activity of glutathione transferase. However, survival rates may depend on the timing of NAC administration, with delays leading to increased mortality [7]. Survival rate was 76% when NAC was administered on the 1<sup>st</sup> day but dropped to 23% if administered on or after the 3<sup>rd</sup> day. In the present case, although the patient was treated with NAC, the late presentation and amount of poison consumed may have led to the worsening of liver function.

The American Association for the Study of Liver Diseases (AASLD) recommends the use of subcutaneous vitamin K for patients with ALF undergoing invasive procedures, with FFPs and platelet transfusions reserved for people with active bleeding [5]. AASLD guidelines also suggest the usage of proton

pump inhibitors or H2 receptor antagonists for stress ulcer prophylaxis. Although our patient did not have any evidence of bleeding manifestations, she received FFP before the insertion of a central venous catheter.

Complications and clinical outcomes differ in various reports. In a case series, 87% had some form of liver injury and 27% progressed to fulminant hepatic failure and died<sup>7</sup> while, in another case report, the mortality was 28% [8]. The MELD score can be used as a prognostic indicator: the average MELD for those who died was 40.5, compared to 11.7 for survivors. Our patient's highest recorded MELD score was 36.

Although high-volume TPE, defined as the replacement of 8-12l of plasma with FFP, may improve transplant-free survival in ALF patients, low-volume TPE, replacing about 3l per cycle, may also be beneficial, especially when initiated early [9-12]. The indication is the presence of systemic inflammatory response syndrome symptoms, with the aim of eliminating toxic factors such as circulating damage-associated molecular patterns that cause systemic disturbances associated with ALF. While studies recommend 3-5 cycles of plasmapheresis, our patient received two cycles, following which the liver donor was available.

Acute tubular necrosis is a common complication of YP poisoning resulting from direct toxicity and occasionally, rhabdomyolysis [3,6,13]. Continuous renal replacement therapy (CRRT) can be used as bridge therapy while waiting for the liver transplant. As CRRT was unavailable, our patient was initiated on SLED based on raised serum ammonia levels, raised lactate, and signs of volume overload.

Liver transplantation is the only treatment modality in ALF unresponsive to medical management. The patients who require urgent liver transplantation are identified by the kings college criteria [12]. However, this was not used in the present case as the patient was aged 39 years and her INR values were possibly skewed by multiple FFP transfusions. The need for liver transplantation

can also be based on a MELD score of 36 or greater and also encephalopathy of grade 2 or higher, as in the present case [7,14].

Transplant outcomes in YP poisoning cases are variable and would depend on underlying comorbid conditions, non-hepatic organ dysfunction, need for organ support, time of presentation, early treatment with supportive care, quantity consumed, early TPE, and absence of cardiac toxicity [12,14]. Hence, the selection of patients for liver transplantation is of utmost importance. Our patient neither had significant comorbidities nor a need for organ support. However, the delayed presentation, along with ingestion of an unknown quantity, may have led to deterioration despite aggressive measures. The availability of a suitable donor is also a challenge, as the timing of transplantation is a key factor in determining outcomes. As the patient's sister was a compatible donor, transplantation could take place without delay and with a good outcome.

## CONCLUSION

YP poisoning requires close monitoring of the patient for at least four to 5 days for any deterioration of clinical or biochemical parameters. In case of deterioration of liver function despite adequate supportive therapy, a liver transplant is the only definitive treatment. Therapeutic plasmapheresis and RRT may serve as a bridge therapy until a compatible donor is available.

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