

## Case Report

# Acute on chronic liver failure presentation of zinc phosphide poisoning: a concept elucidating case report

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## ABSTRACT

Zinc phosphide is an inorganic compound that is used as a rodenticide. A case of a young female is described who developed acute on chronic liver failure (ACLF) precipitated by deliberate self-harm (DSH) with zinc phosphide. She had underlying cirrhosis due to surreptitious alcohol intake. She recovered propitiously following meticulous intensive care management of the acute event. This case in itself elucidates the concept of ACLF.

**Key words:** Zinc phosphide, DSH, ACLF

## INTRODUCTION

Zinc phosphide is used as a rodenticide and is available as paste, bait pellets, granules, dust, and tracking powder formulations. In Kerala state zinc phosphide has second highest incidence for intoxicant poisoning after organophosphates.<sup>1</sup> Zinc phosphide following ingestion gets decomposed by hydrochloric acid in stomach, and liberates highly toxic phosphine gas which is a respiratory chain and mitochondrial poison. We present the unusual case of a young female who attempted DSH with zinc phosphide and presented as ACLF.

## CASE REPORT

A 24 year old female was referred to our tertiary centre with jaundice, ascites and altered sensorium following alleged consumption of zinc phosphide poison. She had consumed about 4 grams of Ratol® mixed with soft drink followed by few episodes of vomiting. Following the event she was admitted in a local hospital and was recovering from initial respiratory symptoms when she developed jaundice followed by ascites and altered

sensorium over the next three weeks and was referred as liver failure. At presentation her vital signs were normal. She had pallor, icterus and pedal edema. Abdominal examination showed ascites and notably firm hepatomegaly. Bowel sounds were normal. She had West Haven criteria grade 3 hepatic encephalopathy. Investigations revealed hemoglobin 80 g/l, high total count 11550 /mm<sup>3</sup>, high ESR of 30 mm at one hour, low platelet count 1.3 Lakh/mm<sup>3</sup>, low MCV, peripheral smear showed hypochromic microcytic anemia, low blood glucose 3.33 mmol/l, blood urea nitrogen 7.1 mmol/l, creatinine 124 mmol/L, hyperbilirubinaemia (total bilirubin 340 mmol/l, direct bilirubin 187mmol/L), raised hepatic enzymes (aspartate aminotransferase 801 U/l, alanine aminotransferase 1662 U/l), ALP 128 U/L INR 2.2, normal amylase(100 U/L) and lipase (420 U/L), serum sodium 133 mmol/L, hypokalemia (3.3 mmol/l), hypoalbuminaemia (32 g/l), normal serum calcium (1.9 mmol/l), high serum ammonia 112 mcg/dL, acute hepatitis etiological evaluation including viral markers, autoimmune hepatitis and metabolic causes were negative. Blood and urine cultures were sterile, ECG, cardiac enzymes CPK and Troponin were essentially normal, ABG was normal.

Ultrasonography showed hepato splenomegaly with coarse echo texture of liver, moderate ascites, portal vein (PV) was 13.5 mm and with features of portal hypertension (PV velocity 14 cm/s, congestive index calculated was 0.1, hepatic venous wave form was biphasic). She was meticulously managed in our intensive care unit and along with other medications was also given N acetyl cysteine infusions. She showed signs of clinical improvement and recovered from hepatic encephalopathy. Later she successfully underwent upper gastrointestinal endoscopy which showed significant esophageal varices and portal hypertensive gastro pathy.

In Kerala state, women have a very low prevalence of alcohol intake or tobacco use.<sup>2</sup> To our surprise she revealed surreptitious use of cirrhotogenic dose of alcohol about 60 grams for last 12 years. A detailed evaluation of her mental state was done by psychiatrist and she was diagnosed to have adjustment disorder with depression which had lead to deliberate self-harm (DSH). At 3 weeks her liver parameters showed total bilirubin 68 mmol/L, direct bilirubin 35.7 mmol/L, aspartate aminotransferase 132 U/L, alanine aminotransferase 77 U/L, INR 1.6, serum sodium was 138 mmol/L and serum potassium was 3.6 mmol/L. Her MELD score improved from 29 to 17. Patients with ACLF have two hepatic insults, namely, acute liver injury on top of chronic liver disease. Our patient is a classic case yet rare clinical presentation of ACLF. She is under regular follow up and surveillance for cirrhosis liver and under treatment from psychiatrist for adjustment disorder and depression.

## DISCUSSION

The most widely accepted definition of ALF includes evidence of coagulation abnormality, usually an INR 1.5 or more, and any degree of mental alteration (encephalopathy) in a patient without pre-existing cirrhosis and with an illness of <26 weeks duration.<sup>3</sup> In a recent multicenter prospective study of acute liver failure (ALF) due to drug-induced liver injury (DILI), 3 week transplant free survival was poor (27%) but with liver transplantation overall survival could be improved to 66%.<sup>4</sup>

ACLF definition as per APASL is acute hepatic insult manifesting as jaundice and coagulopathy, complicated within 4 weeks by ascites and/or encephalopathy in a patient with previously diagnosed or undiagnosed chronic liver disease.<sup>5</sup> ACLF patients have short term mortality of 50-90 %.<sup>6</sup> Liver transplantation remains the only curative treatment for patients with failed medical treatment for ACLF. However, a universally accepted selection criteria for ACLF is yet to be defined. A recent study has shown excellent survival following liver transplantation in ACLF with 1 and 5 year survival rates of 87% and 82% which were comparable to the survival rates for non-ACLF patients.<sup>7</sup>

The acute insult precipitating ACLF (Table 1) are quite distinct in different parts of the world. Infections are the predominant acute insult in East although hepato toxins (as in our case) and herbal indigenous medicines are important etiologies for liver failure in the Asian countries. Alcohol and drugs are the predominant acute insult in the West. Etiologic profile of cirrhosis in ACLF is similar to aetiology of cirrhosis in general in the respective countries. Surreptitious significant alcohol intake caused cirrhosis and DSH with zinc phosphide induced acute insult precipitated ACLF in our patient.

**Table 1: Precipitating events in ACLF.**

<b>Infectious aetiology</b>
Hepatotropic - Reactivation of hepatitis B/C, superimposed viral hepatitis like hepatitis A/E
Non hepatotropic viruses like CMV, HSV
Sepsis due to SBP, spontaneous bacterial empyema, UTI, cellulitis
<b>Non-infectious aetiology</b>
Alcohol intake within 4 weeks
Hepatotoxic drugs and toxins
Autoimmune hepatitis flare
Wilson disease
Surgery
Variceal bleed
Ischemia
Portal vein thrombosis
Indeterminate

**Table 2: Postulated mechanisms of zinc phosphide toxicity.**

<b>Phosphine blocks the enzyme cytochrome C oxidase as a result of which mitochondrial oxidative phosphorylation is inhibited.</b>
Phosphine causes extensive lipid peroxidation damage to cell membranes via the formation of highly reactive hydroxyl radicals and inhibition of catalase and peroxidase.
Phosphine is known to inhibit protein synthesis and enzymatic activity
Phosphine has anti-cholinesterase effects
Denaturation of oxy-haemoglobin molecule

Zinc phosphide poisoning occurs by way of accidental or suicidal ingestion. A single dose of zinc phosphide 5 g can cause death. Zinc phosphide is practically insoluble in water and ethanol. Early vomiting improves the prognosis. Our patient though she consumed about 4 grams with soft drink had vomiting following intake which may have lessened the magnitude of severity of her acute insult. Once ingested, zinc phosphide hydrolyses into highly toxic phosphine gas by the action of dilute hydrochloric acid content of the stomach. This phosphine gas is rapidly absorbed throughout the gastrointestinal tract, reaches the blood stream, a part of it

is carried to the liver by portal vein. The postulated mechanisms of toxicity are given in table 2.

There are very limited studies on morphological changes in liver due to phosphide injury. A study conducted in Iran on liver biopsies from 37 patients who had died from zinc phosphide intoxication found that in all cases there were liver injury features, which ranged from congestion to necrosis in the liver at different stages.<sup>8</sup> A study from turkey found that autopsy revealed congestion and several necrotic areas in liver.<sup>9</sup> There is no antidote for poisoning with metal phosphides, such as zinc phosphide. A Turkish study showed 27 % mortality and the rate of mortality was twice as high in patients with high levels of liver enzymes as compared to patients with normal liver enzyme levels.<sup>9</sup> There is scarcity of studies on selection criteria for liver transplantation in zinc phosphide poisoning. A study from Kerala found MELD score of 31 on the sixth day or the presence of encephalopathy at any time after ingestion of zinc phosphide as a strong predictor of mortality without liver transplantation.<sup>10</sup> Liver transplantation is a potential therapy for patients who do not improve with supportive measures. However, the selection criteria for liver transplantation in ACLF needs to be better defined.

## CONCLUSION

Zinc phosphide poisoning can cause ALF and rarely ACLF. We present the rare but classic case presentation of ACLF in a young female after DSH with zinc phosphide poison and propitiously recovered following meticulous intensive care management. There is need for better predictors for liver transplantation in zinc phosphide poisoning and ACLF.

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