Rodenticide (Yellow Phosphorus) Induced Acute Hepatitis
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ABSTRACT
Rodenticides for many years have been an important cause of significant morbidity and mortality in patients who present to a medical emergency with deliberate self-harm. Yellow phosphorous component present in rodenticide, if ingested leads to severe liver consequences. The present manuscript describes a patient with rodenticide poisoning who had severe hepatic dysfunction which was successfully managed with early N-Acetyl cysteine therapy.

Key-words: Yellow phosphide, Fulminant hepatitis, N-Acetyl cysteine

Introduction:
Rodenticides are commonly used suicidal poison in India. An annual incidence of 500,000 cases has been reported¹. The varieties of rodenticides used over the years all over the world are heavy metals (arsenic, thallium), red squill, alpha naphthylthiourea, strychnine, cholecalciferol containing rodenticides, warfarin-type anticoagulants, phosphorous. According to national poison data centre in India, zinc phosphate, barium carbonate, aluminium phosphide remain the most common cause of household and agricultural rodenticide poisoning, and deaths frequently occur. Elemental phosphorus exists in two forms red and yellow. Phosphides used as rodenticides include: aluminium phosphide, calcium phosphide, magnesium phosphide, zinc phosphide. The acid in the digestive system of the rodent reacts with the phosphide to generate the toxic phosphine gas. Red phosphorus is non-volatile, water insoluble, and unabsorbable, and therefore nontoxic when ingested. Yellow phosphorus (also referred to as white phosphorus), on the other hand, is a severe local and systemic toxin causing damage to gastrointestinal, hepatic, cardiovascular, and renal systems. White phosphorus is used as rodenticides and in fireworks. In India, suicidal or accidental poisoning with rodenticides containing metal yellow phosphorous (Ratol) which has Zinc Phosphide containing 3% yellow phosphorous is a more frequent cause of drug-induced acute liver failure.

Here we describes a patient with rodenticide poisoning who had severe hepatic dysfunction which was successively managed.

Case Report:
A 22 year old housewife presented to the emergency medical ward with alleged history of consumption of one packet of ratol; a rodenticide containing 3% of yellow phosphorus equivalent to a total cumulative dose of 3 g of yellow phosphorus. Patient presented nearly four hours after ingestion with complaints of 2 episodes of vomiting on admission. There was no history of breathlessness, hematemesis and hemoptyis. On examination; pulse 80 / min, respiratory rate - 18 / min, blood pressure - 126/78 mmHg, no pallor, no icterus and systemic examination was within normal limits. She was treated with stomach wash (gastric lavage) and intravenous saline, proton pump inhibitor and antiemetic. The Blood investigations on admission revealed hemoglobin 9.5 gm%, TLC 5300/mm³, blood sugar 90 mg/dl. Liver functions were: total bilirubin 0.5 mg/dl, AST 24 U/L, ALT 59 U/L, Alkaline phosphatase 153 U/L, total protein 7.1 mg/dl, albumin - 3.6 mg/dl, globulin 3.5 mg/dl, Prothrombin time was 14 seconds and INR was 1. Blood urea Nitrogen, serum creatinine and serum electrolytes were within normal range. USG abdomen and chest radiograph

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Blood investigations were repeated daily which showed improvement gradually, liver functions improved and on 13th day AST/ALT were 41/46 IU, total bilirubin 0.5 and INR was 1. With all parameters being normal, she was discharged on 23rd day.

Discussion:

Yellow Phosphorus is one of the common mode of suicidal poisoning in developing countries which is readily available as rodenticides, military ammunition, fire crackers, and fertilizers. A recent study conducted in South India showed that yellow phosphorus was the most common rodenticide used in suicide attempts in the region and carried a 30% mortality despite maximal supportive therapy. The LD50 dose in yellow phosphorus poisoning is 10 mg/kg body weight; however, ingestion of a dose as low as 100 mg has been seen to result in death. Inorganic phosphorus is a potent hepatotoxic agent that is still widely available in our country as a household rodenticide. The mechanism of toxicity of yellow phosphorus is by means of an exothermic reaction producing phosphoric acid that causes direct tissue damage due to the production of free radicals against organic molecules. This, in turn, will bring about changes in ribosomal function and protein synthesis, failure of regulation of blood glucose, and fatty degeneration of multiple organs. The reason for an increased predilection to cause liver toxicity is, however, not fully understood. The acid in the digestive system of the rodent reacts with the phosphide to generate the toxic phosphine gas. It is a protoplastic poison which inhibits various enzymes and protein synthesis leading to multi organ failure. It usually goes into three phases. First phase within 24 hours which is asymptomatic period and the patient may be discharged prematurely. Second phase is asymptomatic elevation of liver enzymes. Third phase of advanced liver disease and resolution after few days of poisoning. Rodenticide poisoning usually presents with gastrointestinal effects which may proceed to cause acute hepatic failure, coagulopathy, and deranged liver function as was observed in our patient. Features of hepatotoxicity with inorganic phosphorus often
develop 72 hours after ingestion of the poison. During this time, the patient has only minor gastrointestinal symptoms or no symptoms at all.\textsuperscript{10} Early elevations in transaminase, alkaline phosphatase, derangement in prothrombin time, metabolic acidosis associated were significantly associated with mortality.\textsuperscript{11}

Management of this condition is purely supportive as there is no specific antidote available to date. NAC, a glutathione precursor, has been shown to neutralize the active metabolite of acetaminophen by replenishing the glutathione stores in the liver, resulting in improved prognosis in acetaminophen overdose. The possibility of similar effects of NAC in yellow phosphorus has been evaluated in recent studies with limited success. A meta-analysis involving 616 patients, conducted to assess the role of NAC in non-acetaminophen-related acute liver failure, showed no significant difference in overall survival of the patients.\textsuperscript{12,13} Other studies that specifically looked at the role of NAC in the treatment of liver injury in yellow phosphorus overdose have yielded mixed results.\textsuperscript{14} However, it was noted that survival was greater among patients who received NAC early, compared to those who received it later during the course of illness.

The individual in this report had consumed a large dose of yellow phosphorus (3 g) and had elevation of liver enzymes, both of which were indicators of a poor prognosis. She was initiated on NAC at an appropriate dose with which she showed a complete resolution of liver injury. She developed no side effects or complications.

Poor prognostic factors are shock, altered mental status, high SOFA score, acute kidney injury, low prothrombin rate, leucocytosis, requirement of mechanical ventilation, lack of vomiting after ingestion, hyperglycaemia and time lapsed after exposure.\textsuperscript{14} Unless looked for specifically clinical evidence of icterus or an abnormality in liver function tests, it can be missed and elevation of prothrombin time can be wrongly attributed to a warfarin containing rodenticide.

**Conclusion:**

When high mortality results from the lack of a specific antidote, our patient emphasizes the possible survival benefit of early intravenous NAC in yellow phosphorus poisoning. More research is required to determine the efficacy, dosage, and side effects of the same.

**References:**