Case Report

Rodenticide (Yellow Phosphorus) Induced Acute Hepatitis

Rashmi N Nagdeve[1], Sunil Bade[2], SagarBothra[3], S Hegde[3], V R Panpaliya[3]

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 reported[1]. 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 phosphide, 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.

[1]Associate Professor, [2]Senior Resident, [3]Junior Resident, Department of Medicine, Shri Vasantrao Naik Government Medical College, Yavatmal

Address for Correspondence -
Dr. Rashmi N. Nagdeve
E-mail : rashminagdeve05@gmail.com

Received on 18th December 2018 Accepted on 24th December 2018

Case Report :

A 22year 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 hemoptysis. On examination; pulse 80 / min, respiratory rate - 18 / min, blood pressure - 126/78 mmHg, no pallor, no icterusand 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/mm^3, platelet 3.33 lakhs / mm^3, 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

done on admission were normal. Later she was shifted to ward for observation.

On the third day, she had abdominal pain and multiple episodes of vomiting and altered level of consciousness. On examination, patient was drowsy, had fever of 101.5^{0}F, pulse rate 144/min, respiratory rate of 26/min and blood pressure of 90/60 mmHg in the supine position. Abdomen examination revealed hepatomegaly (2 cm below the right costal margin, liver span of 16 cm in right mid-clavicular line).There was no ascites. She was in stupor with bilaterally non elicit able plantar reflexes, GCS - 10/15. Her blood investigations revealed haemoglobin- 9.0gm%, TLC 11400/mm^3, platelet 1.77 lakhs / mm^3, RBS 96 mg/dl. Liver functions were altered to total bilirubin 1.4 mg/dl, SGOT - 266 U/L, SGPT - 487 U/L, alkaline phosphatase 153 U/L, prothrombin time was 32 seconds and INR was 2.3. Renal functions were normal. Antigen test for malaria, viral markers for hepatitis and HIV were negative. ECG (QTc 0.41 second), ABG and chest x-ray were normal. USG abdomen revealed altered echotexture of liver and hepatomegaly.

Patient was started with fresh frozen plasma, vitamin K, L-ornithine-L-aspartate, gut antibiotics and lactulose enema along with supportive care. Her GCS further deteriorated to 8/15 and she was intubated prophylactically to secure the airway. In view of acute liver failure, patient was also initiated on intravenous N-AcetylCysteine (NAC)[2].

The dose of intravenous NAC that was administered was according to the recommended clinical practice guidelines for the treatment of acetaminophen overdose - 150 mg/kg of NAC in 200 mL of 5% dextrose over 15-60 min and then 50 mg/kg in 500 mL of 5% dextrose over 4 h followed by 100 mg/kg in 1000 mL of 5% dextrose over 16 h. A cumulative dose of 300 mg/kg of injection NAC was administered over 21 h. She was placed under continuous monitoring of vital parameters in an intensive care setting. Clinical and laboratory parameters for liver function were monitored daily. After about 4 days she showed clinical improvement, and was extubated successfully. 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.[3] 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.[4,5] 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.[4] 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 protoplasmic poison which inhibits various enzymes and protein synthesis leading to multi organ failure. It usually goes into three phases[6]. 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[7] which may proceed to cause acute hepatic failure, coagulopathy, and deranged liver function[8,9] 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.[10] Early elevations in transaminase, alkaline phosphatise, derangement in prothrombin time, metabolic acidosis associated were significantly associated with mortality[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.[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.[4] 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[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 :

1. Bhat S, Kenchetty KP. N-acetyl cysteine in the management of rodenticide consumption-life saving? J ClinDiagn Res 2015; 9: OC10-3.
2. Clinical Practice Guidelines: Paracetamol Poisoning. Available from: http://www.rch.org.au/clinicalguide/guideline_index/paracetamol_poisoning/.
3. Nalabothu M, Monigari N, Acharya R. Clinical profile and outcomes of rodenticide poisoning in tertiary care hospital. Int J Sci Res Publ 2015; 5:1-12.
4. Mishra AK, Devakiruba NS, Jasmine S, Sathyendra S, Zachariah A, Iyadurai R. Clinical spectrum of yellow phosphorous poisoning in a tertiary care centre in South India : A case series. Trop Doct 2017;47:245-249.
5. Fletcher GF, Galambos JT. Phosphorus poisoning in humans. Arch Intern Med 1963; 112:846-52.
6. Brent J, Wallace KL, Burkhart KK. Phosphorus. In : Brent J, Wallace KL, Burkhart KK, Phillips SD, Donovan JW, editors. Critical Care Toxicology Diagnosis and Management of the Critically Poisoned patient. Philadelphia, PA: Elsevier Mosby; 2005. pp. 851-61.
7. Sogut O, Baysal Z, Ozdemir B. Acute pulmonary edema and cardiac failure due to zinc phosphide ingestion. J Emerg Med. 2011; 40:e1178.
8. Mauskar A, Mehta K, Nagotkar L, Shanbag P (2011) Acute hepatic failure due to YP ingestion. Indian J Pharmacol 43; 3: 355-356.
9. Santos O, Restrepo JC, Velásquez L, Castaño J, Correa G, Sepúlveda E, Yepes N, Hoyos S, Guzmán C, Osorio G, Cárdenas A () Acute liver failure due to white phosphorus ingestion. Ann Hepatol. 2009;8:162-5.
10. Haddad and Winchester. Clinical Management of Poisoning and Drug Overdose : W. B. Saunders Company. 1990; 2: 1118-9.
11. Fernandez OU, Canizares LL. Acute hepatotoxicity from ingestion of yellow phosphorus containing fireworks. J ClinGastroenterol 1995;21:139-42.
12. Lee WM, Hynan LS, Rossaro L, Fontana RJ, Stravitz RT, Larson AM, et al. Intravenous N-acetylcysteine improves transplant-free survival in early stage non-acetaminophen acute liver failure. Gastroenterology 2009;137:856-64.e1
13. Hu J, Zhang Q, Ren X, Sun Z, Quan Q. Efficacy and safety of acetylcysteine in "non-acetaminophen" acute liver failure: A meta-analysis of prospective clinical trials. Clin Res Hepatol Gastroenterol 2015;39:594-9.
14. Mehrpour O, Alfred S, Shadnia S, Keyler DE, Soltaninejad K, Chalaki N, et al. Hyperglycemia in acute aluminum phosphide poisoning as a potential prognostic factor. Hum ExpToxicol. 2008; 27:591-5.