Case Report

White Phosphorus Poisoning Successfully Managed With Oral N-Acetylcysteine: A Case Report

Mahesh M*, Mohan Goudar, Venkatesh CR, Tejaswini CJ

ABSTRACT

Poisoning by white phosphorus is being encountered more commonly due to easy availability of rodenticides containing this deadly substance. White phosphorus is highly toxic and afflicts multiple systems and is associated with a high mortality. Intravenous N-acetylcysteine is recommended by most authorities in addition to symptomatic and supportive therapy.

We report our experience of a case of white phosphorus poisoning with hepatic dysfunction managed successfully with oral N-acetylcysteine, which had to be used because of non-availability of intravenous N-acetylcysteine.

Key Words: White phosphorus; Yellow phosphorus; Rodenticide; Rat poison; Hepatotoxicity; N-acetylcysteine

Introduction

Case Report: Mr. T, a 25-year-old male was brought to the hospital emergency room with history of consumption of a tube (15 gm) of "*Ratol*" rodenticide paste (3% white phosphorus) with suicidal intent, 2 days prior to admission. He had symptoms of nausea and retrosternal burning sensation, and was passing dark coloured urine over the past 24 hours. He had no significant medical illnesses in the past. He was not an alcoholic.

On examination, the patient had a temperature of 98.6°F, pulse of 86 beats per minute, respiratory rate of 18 breaths per minute, and blood pressure of 120/70 mmHg. He had moderate icterus. Abdominal examination revealed no organomegaly. Nervous system examination revealed a conscious, oriented patient with no motor weakness and no asterixis. Bilateral plantar flexor response was present. The respiratory and cardiovascular systems were normal.

Laboratory investigations revealed the following: haemoglobin 10.6 g/dl, haematocrit 35.4 %; leukocyte count 7900 /mm^3 (72% granulocytes, 18% lymphocytes); platelet count 2.62 L/mm^3; erythrocyte sedimentation rate of 05 mm, RBS 73 mg/dL, serum electrolytes- sodium 138 mol/L, potassium 3.2 mmol/L; blood urea 20 mg/dL; creatinine, 1.1 mg/dL; total bilirubin 6.30 mg/dL with 2.56 mg/dL of direct bilirubin, total protein 7.0 gm/dL, albumin 4.5 gm/dL, A/G ratio 1.2, AST 185 IU and ALT 136 IU; serum alkaline phosphatase 177 IU, gamma glutamyl transferase 60 IU and lactate dehydrogenase of 385 U/L. HBsAg, HCV and HIV by ELISA were negative. Coagulation profile showed normal results with PT-INR 0.93, APTT INR of 0.90 and BT of 4 minutes. Electrocardiogram was essentially normal. Chest radiograph did not demonstrate any abnormality. Ultrasound of abdomen revealed mild hepatomegaly.

A diagnosis of stage III white phosphorus poisoning was made, and symptomatic and supportive treatment was started. Prophylactic vitamin K was also administered. However, the patient did not make any significant improvement clinically over the next two days. LFT parameters continued to worsen with total bilirubin 8.30 mg/dL with 5.56 mg/dL of direct bilirubin, total protein 7.1 gm/dL, albumin 4.5 gm/dL, A/G ratio 1.2, AST 298

Dept of Medicine, JSS Medical College Hospital, Ramanuja Road, Mysore, Karnataka 570004
*(*Author for correspondence*): 106 Brigade Solitaire Apartments, Alanahally Layout, Mysore, Karnataka 570028.
Email: doctmahesh@yahoo.com

IU and ALT 320 IU, and serum alkaline phosphatase 180 IU after two days. Clinically the patient showed features of hepatic encephalopathy.

He was placed on standard hepatic encephalopathy treatment regimen. He did not show any significant response. At this juncture the Chief of Poison Control Centre, Dept of Analytical Toxicology, Amrita Institute of Medical Sciences & Research, Cochin was contacted, who suggested the use of intravenous N-acetylcysteine (NAC).

In view of the non-availability of IV preparation locally, the patient was administered N-acetylcysteine as orally: 140 mg/kg loading dose, followed by 70 mg/kg/ fourth hourly over the next three days. After initiating oral N-acetylcysteine in this manner, he steadily improved both clinically and biochemically. He later made a complete recovery and was discharged in a fit condition on the fourteenth day after admission.

Discussion

White phosphorus (also called yellow phosphorus), is a constituent of many rodenticides, cockroach poison, and fireworks in India. The most common and easily available source of white phosphorus is a rodenticide, which is often available as a powder or paste containing 2 to 5% of the chemical.

White phosphorus is a powerful toxin causing damage to gastrointestinal[1], renal[2], hepatic[3-5] and cardiovascular[6] systems. The lethal dose is about 1 mg/kg or 60 mg. Overall mortality ranges from 20-50%.

Three stages of white phosphorus poisoning are well recognized. The first is the gastro intestinal stage with vomiting, diarrhoea and abdominal pain. There may be a garlicky odour to the breath and vomitus. Stools may be luminescent. Fumes may emanate from the stools (smoky stool syndrome).[7] The second stage is a symptom-free period of several days, and during this stage the healthcare provider may think that the patient has recovered, and discharge him, often with disastrous consequences. The third stage is dominated by acute hepatic and renal failure. Elevation of liver enzymes and bilirubin usually occur in this stage. Cardiac toxicity (hypotension, tachycardia, arrhythmias, and cardiogenic shock) with death can occur.[7] Central nervous system effects include changes in mental status like confusion, psychosis, hallucinations, and coma. The systemic effects of phosphorus after it has been absorbed are responsible for the various features of the third stage.

Management of acute poisoning includes the use of activated charcoal, and gastric lavage with potassium permanganate (1:5000), which oxidizes phosphorus to relatively less toxic phosphoric acid and phosphates. A 0.2% solution of copper sulphate for stomach wash has also been advocated, though it is not widely recommended today. Copper sulphate converts phosphorus to non-toxic copper phosphide. Supportive measures include the management of hypotension, hypoglycaemia, seizures, coagulopathy, and arrhythmias.

A single specific antidote for white phosphorus has not yet been identified. Phosphorus-induced liver damage is mediated by free radicals. Phosphorus increases the oxygen consumption of hepatocytes, and acts by uncoupling oxidative phosphorylation with resultant decrease in intra-hepatocyte ATP levels. Antioxidants are therefore recommended in diminishing and reversing tissue injury.[8]

N-acetylcysteine (NAC) is an established cornerstone therapy for acetaminophen (paracetamol) overdose. It is also useful in fulminant hepatic failure caused by various toxic and non-toxic aetiologies. NAC acts as a precursor for the synthesis of glutathione and modulates the oxidative stress and inflammatory cascade, improving oxygen delivery and extraction in various organs. Available literature on N-acetylcysteine in phosphorus poisoning indicates its effectiveness in preventing progression of hepatic damage during stage one.

Many investigators recommend N-acetylcysteine in all cases of phosphorus poisoning.[8] The suggested dose is 150 mg/kg in 200 ml of D5W for 15 min, followed by 50 mg/kg in 50 ml of D5W for 4 hrs, and 100 mg/kg in 1000 ml D5W for 16 hours. Only the IV route has been studied in hepatic failure. However oral NAC appears to confer equal benefit as exemplified by the case being reported, though this approach has not been well studied. NAC is available as a solution for IV use, and as effervescent tablets for oral administration. The recommended dose of oral NAC is 140 mg/kg loading dose, followed by 70 mg/kg every 4 hours for 72 hours.

It is unclear whether oral or IV route results in superior drug delivery to the liver. Higher serum concentrations achieved with IV route may be useful for extra-hepatic effects, whereas oral route might produce higher intra-hepatic concentrations.[8]

Conclusion

The case being reported here indicates that oral N-acetylcysteine is useful in the treatment of phosphorus-induced hepatotoxicity, and can be used in situations where the intravenous preparation is not available.

Acknowledgement

The authors are grateful to Dr VV Pillay, Chief of Poison Control Centre, Dept of Analytical Toxicology, Amrita Institute of Medical Sciences & Research, Cochin, for his suggestions.

REFERENCES

1. Talley RC, Linhart JW, Trevino AJ. Acute elemental phosphorus poisoning in man: cardiovascular toxicity. *Am Heart J* 1972; 84:139–140.
2. Santos O, Restrepo JC, Velasquez L, Castano J, Correa G, Sepulveda E, et al. Acute liver failure due to white phosphorus ingestion. *Ann Hepatol* 2009;8:162–165.
3. Fernandez OU, Canizares LL. Acute hepatotoxicity from ingestion of yellow phosphorus-containing fireworks. *J Clin Gastroenterol* 1995;21:139–142.
4. Mauskar A, Mehta K, Nagotkar L, Shanbag P. Acute hepatic failure due to yellow phosphorus ingestion. *Indian J Pharmacol* 2011;43(3):355–358.
5. Nayyar KS. Rodenticide induced hepatotoxicity. *J Assoc Physicians India* 2003;51:816–817.
6. George P. An unusual cause of pulmonary edema and its successful management: a case of phosphorus poisoning. *J Clinical Diag Res* 2010;34:3554–3557.
7. Simon FA, Pickering LK. Acute yellow phosphorus poisoning. "Smoking stool syndrome". *JAMA* 1976;235:1343–1344.
8. Nikkanen HE, Ewald MB. Phosporus. In: Flomenbaum N, Goldfrank LR, Hoffmann S, Howland MA, Lewin NE, *et al*. (eds). Goldfrank's Toxicologic Emergencies. 2006. New York: McGraw-Hill Professional.