Plenary Lecture by APAMT Honorary Fellow

Aluminium Phosphide Poisoning

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Introduction

Pesticide poisoning is an important cause of morbidity and mortality in India. We recorded our first case of aluminium phosphide (ALP) ingestion in late 1979 and after publication of our first largest series in literature in 1985, there has been an explosion of reports from different parts of India and rest of the world especially Iran, Jordan and Morocco. Aluminium phosphide is available both as greenish grey tablets of 3 gm which contains 56% aluminium phosphide and as pellets, granules and dust. At present ALP is being marketed in India mainly as granulated powder in plastic pouches [10 gm] as Celphos [Excel industries].

Mechanism of Action

Toxicity of ALP is due to phosphine (PH3) which is released when it comes in contact with moisture or hydrochloric acid. PH3 has been reported to have the odour of decaying fish or garlic-like odour which is likely to be due to impurities like substituted phosphines, diphosphines, methane, and most importantly arsine.

Clinical Features

Immediately after ingestion, almost all patients develop nausea, vomiting, retrosternal burning, epigastric discomfort and in significant poisoning, hypotension and shock develops invariably in 30 minutes to 2 hours. Signs of sympathetic overactivity such as tachycardia and sweating are common. Several electrocardiographic abnormalities have been reported. Oliguria develops in approximately half of cases. Adult respiratory distress syndrome (ARDS) commonly develops in patients with severe hypotension. Other complications include disseminated intravascular coagulation, intravascular haemolysis, gastrointestinal bleeding, fulminant hepatic failure, congestive cardiac failure and rarely pericarditis. Patients generally remain mentally clear, though restless, until cerebral anoxia due to shock supervenes, resulting in drowsiness, delirium and coma. If the patient survives shock, acute renal failure and tender hepatomegaly may develop.

Clinical outcomes correlate best with the number of vomits post-ingestion, and severity of hypotension and acidosis. The majority of deaths occur within the first 12 to 24 hours and are usually due to refractory hypotension and arrhythmias. Deaths after 24 hours may be due to ARDS, liver failure, renal failure or other complications. Findings at necropsy are congestion of liver, spleen, kidneys, adrenals, gastrointestinal tract and brain that correlates with the severity of hypotension. Histopathology does not reveal any specific changes beyond visceral congestion and patchy necrosis of liver.

Pathophysiology

The exact mechanism by which phosphine acts is not clear. Nakakita et al found that it inhibited oxygen uptake in isolated rat liver mitochondria. Phosphine inhibited ADP uncoupler and ion stimulated respiration but the exact target site was not identified. In a later detailed study, phosphine was found to be a stronger inhibitor of mitochondrial respiration in the active state (state-3) than in the resting state (state-4) in mouse liver, housefly flight muscles, granary weevils and beef heart. This inhibition could not be reversed by uncouplers suggesting that it is due to a direct effect on electron transport which is an important electrochemical link between respiration and phosphorylation in mitochondria. The spectral and dichroisim studies revealed an interaction with heme moiety of cytochrome oxidase (cytochrome-C) but is yet to be determined whether it interacts with either cytochrome a or a3 or both. In a study involving three species of stored beetles, insect catalase and not cytochrome-c-oxidase system was found to be inhibited. In a recent experimental study where parameters of energy metabolism and oxidative stress were measured in rat brain and liver, following administration of ALP in LD50 dose i.e. 10 mg/kg body weight, it was found that cytochrome-c oxidase activity in platelets was inhibited, decreasing in a concentration dependant manner. ATP synthesis was found to be decreased, particularly in both the liver and brain. These results suggest that inhibition of cytochrome oxidase disturbs electron transport, leading to impaired energy metabolism. In a recent study, cytochrome-c-oxidase activity in platelets of 26 patients with severe ALP poisoning was inhibited more than 50% compared to healthy controls ($p < 0.001$) as well as those in shock due to other causes like sepsis, massive bleed and myocardial infarction. The exact mechanism by which phosphine acts as cellular toxin, however is still not clear and further studies are needed.

Diagnosis

The following alone or in combination would help in the diagnosis:

1. History of ingestion
2. Symptoms and signs compatible with aluminium phosphide ingestion

3. Detecting phosphine in exhaled air or in stomach aspirate using silver nitrate. The phosphine in breath can also be detected using phosphine detector tubes.

For spot sampling of phosphine in air, detector tubes and bulbs are available commercially. However, the most specific and sensitive method is gas chromatography.

Management

Early recognition and management of the poisoning is essential. Induction of emesis is contraindicated. Gastric lavage should be considered if the procedure can be performed by experienced staff within 1 hour of ingestion. However, there is no evidence that gastric lavage improves outcome. Gastric lavage is generally followed by intragastric administration of a slurry of activated charcoal, however no studies are available in the literature that show that this is beneficial.

Caution: Insertion of a nasogastric or orogastric tube to patients who have ingested aluminium phosphide may release phosphine, presenting a potential toxic hazard to staff caring for the patient as phosphine may auto-ignite. However iatrogenic poisoning has not been reported in care givers in India despite thousands of cases having been managed in hospitals with varying facilities and only a single case of autoignition has been reported.

The management is unsatisfactory as there is no specific antidote so treatment is largely supportive. Intravenous fluids should be administered as leakage of fluids from intravascular to extravascular space occurs as a result of capillary dysfunction. Magnesium sulfate is a membrane stabilizer that can reverse arrhythmias but does not improve mortality. Although corticosteroids havebeen trialled, outcomes did not improve.

Prevention

An important preventive measure lies in better regulated supply of ALP which otherwise is an excellent and safe fumigant. Legislative and administrative measures have been suggested to restrict and modify its supply in India. Unfortunately, there has been a failure in application except for the largest producer of ALP in India who has started marketing it as granulated powder in a 10 gm plastic pouch. In our retrospective analysis, we observed that although the number of ALP cases have continued to increase, a consistent decline in mortality was observed from year 2000 since the bulk of ALP available in market changed to the form of granulated powder in plastic pouch.