

Aluminum phosphide poisoning: Possible role of supportive measures in the absence of specific antidote

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Abstract

Aluminum phosphide (ALP) poisoning is one of the major causes of suicidal deaths. Toxicity by ALP is caused by the liberation of phosphine gas, which rapidly causes cell hypoxia due to inhibition of oxidative phosphorylation, leading to circulatory failure. Treatment of ALP toxicity is mainly supportive as there is no specific antidote. We recently managed 7 cases of ALP poisoning with severe hemodynamic effects. Patients were treated with supportive measures including gastric lavage with diluted potassium permanganate, coconut oil and sodium-bicarbonate first person account should be avoided in a scientific paper. Intravenous magnesium sulfate, proper hemodynamic monitoring and vasopressors. Four out of 7 survived thus suggesting a role of such supportive measures in the absence of specific antidote for ALP poisoning.

Keywords: Aluminum phosphide, coconut oil, magnesium sulfate, phosphine gas, potassium permanganate

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Introduction

Aluminum phosphide (ALP) is a major cause of suicidal poisoning in many countries.^[1,2] Toxicity by ALP is caused by the liberation of phosphine gas, which causes cell hypoxia due to inhibition of oxidative phosphorylation leading to circulatory failure.^[2] Treatment of ALP toxicity is mainly supportive as there is no specific antidote. Mortality with ALP poisoning is very high, ranging from 37% to 100%.^[3,4] We recently managed 7 cases of ALP poisoning with severe hemodynamic effects. Patients were treated with supportive treatment including gastric lavage with diluted potassium permanganate, coconut oil, sodium-bicarbonate, intravenous magnesium sulfate and vasopressors. Four out of 7 patients survived, thus suggesting a role of such supportive measures in the absence of specific antidote for ALP poisoning.

Materials and Methods

All patients were managed in medical intensive care unit (MICU). Diagnosis of ALP ingestion was confirmed by history and typical odor of ALP. Number of tablets ingested or amount of powder used, date of opening of container, nature of poisoning (suicidal or accidental), time lag to medical attention from time of ingestion were collected in baseline demographic data. Presenting complaints, clinical characteristics and laboratory data were recorded at the time of admission. Gastric lavage was performed with diluted potassium permanganate (1:10000 dilution), coconut oil, sodium-bicarbonate and activated charcoal. Airway protection was given before gastric lavage in required patients. Supportive treatment included intravenous (IV) fluids, vasopressors and inotropic drugs, sodium-bicarbonate infusion, magnesium sulfate infusion and proton pump inhibitors. Close monitoring of hemodynamic parameters, urine output, arterial blood pressure and arterial blood gas was regularly done. The primary outcome was categorized as survivor and nonsurvivor.

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Results

Totally, 7 cases of ALP poisoning were managed. Of these, 5 were males, and the mean age of patients was 36.85 years. The mean time lag to MICU transfer was 3 h 50 min. Mean dose of ingested ALP was 5.14 g. Mean systolic blood pressure on presentation was 84 mm Hg. Survivors were 4 (57.14%). We used gastric lavage with KMnO_4 and sodium-bicarbonate in all patients while coconut oil was used in 4 (57.14%). Incidentally all patients with coconut oil use survived. 6 patients were intubated and mechanically ventilated. Two-dimensional echo revealed low left ventricular ejection fraction (LVEF) (mean LVEF of 27.85%) in all patients. Magnesium sulfate was used in all subjects. All survivors had initial electrocardiogram (ECG) of normal sinus rhythm or sinus tachycardia. All nonsurvivors had cardiac arrhythmias on presentation including ventricular Fibrillation in 2 cases and Atrial Fibrillation in one case. Average Intensive Care Unit stay of survivors was 5 days and in nonsurvivors was 1.33 days.

Discussion

Aluminum phosphide poisoning is known worldwide, especially in developing countries like India and Iran.^[1,2] Lethal dose of ALP is 1–1.5 g. Deaths are reported even with a dose of 150–500 mg.^[5] ALP, when ingested, liberates a lot of phosphine gas. Phosphine leads to noncompetitive inhibition of the cytochrome oxidase of mitochondria, blocking the electron transfer chain and oxidative phosphorylation, producing an energy crisis in the cells. The severe toxicity of ALP particularly affects the cardiac and vascular tissues, which manifests as profound and refractory hypotension, congestive heart failure, ECG abnormalities, myocarditis, pericarditis and subendocardial infarction. The frequency of hypotension varied from 76% to 100%, which is a cardinal feature in ALP toxicity.^[6] Cardiac arrhythmias were noted in all 3 patients with mortality in our cases. Cardiac arrhythmias,^[7] respiratory failure and requirement of mechanical ventilation^[7,8] are poor prognostic markers with ALP poisoning. Metabolic acidosis is again common probably due to the accumulation of lactic acid caused by blockage of oxidative phosphorylation and poor tissue perfusion. Severity of metabolic acidosis is also a prognostic indicator in ALP toxicity.^[9] We also noted severe metabolic acidosis in all 3 patients with mortality in our cases.

In management, the main objective is to provide effective oxygenation, ventilation and circulation till phosphine is excreted. All patients of severe ALP poisoning require continuous invasive hemodynamic

monitoring and early resuscitation with fluid and vasoactive agents. Specific management toward ALP toxicity includes reducing absorption of phosphine, reducing cellular toxicity and increasing excretion through kidney and lungs.

After ingestion, effectiveness of gut decontamination primarily depends on the duration of exposure of poison and should be done as early as possible. Potassium permanganate (1:10000) is used for gastric lavage as it oxidizes phosphine to nontoxic phosphate. Although some of the recently published articles support the use of KMnO_4 in ALP,^[10,11] Nasri Nasrabadi and Marashi published their finding that phosphine is a hard nucleophile and the free oxygen radicals from the resolution of KMnO_4 do not interact with each other.^[12] Therefore, there is no well proven basis to conclude that KMnO_4 is efficient against ALP poisoning. Slurry of activated charcoal also helps to adsorb phosphine from the gastrointestinal (GI) tract in most of the literature. Marashi *et al.* concluded that activated charcoal has a wide internal surface area consisting of pores (10 Å to 20 Å). It efficiently adsorbs toxins of moderate molecular weight (100 Da to 800 Da). The molecular weight of ALP is about 58 Da, therefore, role of activated charcoal in ALP poisoning is again doubtful.^[13]

Medicated liquid paraffin has been used to accelerate the excretion of ALP and phosphine from the GI tract. *In vitro* experimental findings suggest that vegetable oils and liquid paraffin, inhibit phosphine release from the ingested ALP due to physiochemical properties of ALP and nonmiscibility with fat.^[14] Singh Bajwa *et al.* used a regimen including coconut oil with sodium-bicarbonate for gastric lavage.^[15] In another paper, the mechanism by which coconut oil reduces the toxicity of phosphides was proposed that it forms a protective layer around the gastric mucosa, thereby preventing the absorption of phosphine gas. Secondly, it helps in diluting the HCl and again inhibiting the breakdown of phosphide from the pellet. Sodium-bicarbonate mainly neutralizes the HCl and thus diminishing the catalytic reaction of phosphide with HCl, thereby inhibiting the release of phosphine.^[16] Medicated liquid paraffin or coconut oil should be given immediately after ALP ingestion.

Liberated phosphine cannot be detoxified. Another possible help in acute ALP toxicity can be by reducing cellular toxicity of phosphine gas. Magnesium sulfate helps in scavenging free radicals through glutathione (GSH) recovery hence is effective as parenteral antioxidant in this poisoning as well as has been tried for its general membrane stabilizing effect in cardiac

cells. The dosages for magnesium sulfate were different in different studies. Chugh *et al.* studied the efficacy of magnesium sulfate in relation to dose of ALP ingested and concluded that hypo-magnesemia was more common with mortality and higher magnesium level after supplementation reduces significant mortality, irrespective of the dose of pesticide consumed.^[17,18] Singh, also reported better outcome in patients who presented within 4 h and IV MgSO₄ was started.^[19] Some workers had found no significant difference in dose-related mortality rates in patients treated with and without MgSO₄. Siwach *et al.* have observed that dose-related mortality rates in patients treated with and without MgSO₄ are not significantly different. The authors also state that magnesium is weak antiarrhythmic agent and may be useful in controlling few supraventricular arrhythmia and recommend the use of more potent antiarrhythmic agent.^[20]

Adequate hydration and renal perfusion with IV fluid enhance the excretion through urine. The role of advanced measures like use of intra-aortic balloon pump to mechanically support the heart has not been supported by a well-designed randomized though isolated successful cases have been reported.^[21,22]

Methemoglobinemia should be suspected with refractory hypoxia and treated with methylene blue (1%).^[23] Steroids have been used to combat shock, reduce the dose of dopamine, and to potentiate the responsiveness of the body to endogenous and exogenous catecholamines. Role of steroids is not well studied in ALP toxicity.^[24] Many therapeutic agents have been tried in experimental animal studies, like N-acetylcysteine and GSH,^[25,26] hydroxyethyl starch,^[27] digoxin,^[28] hyperbaric oxygen^[29] and trimetazidine,^[30] but there is a need for good human trials.

Conclusion

Aluminum phosphide poisoning has high mortality rate due to nonavailability of specific antidote. Only possible measures to save the life in poisoning with unexposed form of ALP are supportive. We have reported a case series of aluminium phosphide poisoning with a relatively high survival rate despite severe hemodynamic effects at presentation. This was achieved by optimizing supportive care.

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