CASE REPORT

Aluminium phosphide poisoning with severe cardiac dysfunction and the role of digoxin

Khalid Hamid Chungal,¹ Muzamil Latief,² Manzoor Parry,² Farhat Abbas³¹Department of Internal Medicine, Mercy St. Vincent's Medical Center, Toledo, Ohio, USA²Department of Internal Medicine, Maharishi Markandeshwar University, Mullana, India³Department of Internal Medicine, Government Medical College Srinagar, Srinagar, India**Correspondence to**

Dr Khalid Hamid Chungal, khalidchungal@gmail.com

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SUMMARY

Aluminium phosphide (ALP) is a common cause of suicidal poisoning in India where it is easily available and commonly known as 'rice tablet'. In rural areas of India, it is still used to protect rice and stored grains from rodents and pests.¹ There is no specific antidote for phosphide poisoning and treatment involves meticulous supportive care. Ingestion can lead to severe cardiac suppression and cardiogenic shock. For patients poisoned with ALP who continue to have refractory shock with persistent myocardial suppression despite the use of adrenergic inotropic agents, the addition of digoxin may be beneficial. We present a case where digoxin was utilised with beneficial patient outcomes.

CASE PRESENTATION

A 20-year-old man was presented 3–4 hours after accidental consumption of 4–8 g of celphos (aluminium phosphide (ALP)). On hospital presentation, he was noted to have altered sensorium. His vital signs were pulse of 133/min and a blood pressure of 70/50. He was tachypneic and pale. Arterial blood gas showed lactic acidosis (6 mmol/L). His blood counts, renal function tests and cardiac enzymes were normal. ECG revealed non-specific ST/T changes (figure 1). His medical history was significant for a seizure disorder managed with phenytoin.

The patient was managed with gastric lavage with activated charcoal and potassium permanganate. A diagnosis of ALP poisoning was confirmed by silver nitrate testing performed on the gastric aspirate. Further management included intravenous fluids, magnesium sulfate 1 g every 6 hours and vasopressors. The patient did not respond to dopamine infusion and subsequently dobutamine and norepinephrine were added. Echocardiography demonstrated severe left ventricular (LV) systolic dysfunction with an ejection fraction (EF) of 20% and severe LV hypokinesia (figure 2).

Over the next 36 hours his clinical status worsened. His mentation deteriorated, urine output decreased and his lactic acid level increased from 6 mmol/L to 9 mmol/L. The decision was made to add digoxin to increase inotropy. Rapid intravenous digitalisation was performed with digoxin 0.5 mg every 6 hours for 48 hours followed by 0.25 mg daily. Within 24 hours of the introduction of digoxin, all clinical parameters improved including haemodynamics, mental status and urine output. Weaning of vasopressors commenced at

24 hours and after 36 hours all vasopressors were stopped. ECG changes normalised (figure 3) and the acidosis resolved over a period of days. By hospital day 7, echocardiogram revealed marked improvement with the EF increasing to 45%. Oral digoxin was continued for two more weeks. At the patient's 2-week follow-up, a repeat echocardiogram demonstrated further improvement with resolution of ventricular hypokinesia. The addition of digoxin was temporally correlated with clinical improvement, supporting our clinical decision to use digoxin as an intervention.

GLOBAL HEALTH PROBLEM LIST

- ▶ Aluminium phosphide poisoning.
- ▶ Use of digoxin in aluminium phosphide poisoning.

GLOBAL HEALTH PROBLEM ANALYSIS

Every year, approximately 800 000 people commit suicide and 135 000 (17%) are in India.² Poisoning (33%), hanging (38%) and self-immolation (9%) are the most common methods used to commit suicide.³ The incidence of ALP poisoning has been increasing steadily and is now the most common method of suicide in the Northern India agricultural community.^{4 5} Economic and social factors such as unemployment in the poor, breakdown of traditional community and family relationships, urban migration and the social stigma and cultural beliefs associated with diseases like schizophrenia and AIDS likely contribute to increasing rates of suicide.⁶ The Indian health system has received criticism because of its lack of emphasis on mental healthcare. While it cannot address many of these predisposing factors, they have not been effective in increasing the limited number of mental health facilities or the number of professionals providing mental healthcare.^{6 7}

ALP is a cheap, solid fumigant and a highly toxic pesticide which is commonly used to protect grain stores from pests. ALP can be manufactured with a high degree of purity resulting in a phosphide content of 90%–98% by heating aluminium and phosphorus.⁸ It can also be produced from red phosphorus and aluminium powder and from aluminium and zinc phosphide.⁹ It is formulated in the form of tablets, pellets, granules or as dust and can be mixed with carbamate insecticides.¹⁰ ALP has significant morbidity and mortality. One study attributed 68% of suicides to ALP exposure making it the most common suicide modality, with a 60% mortality rate.¹¹

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Figure 1 ECG at the time of admission shows non-specific T wave inversion in all leads.

When ALP comes into contact with water, phosphine gas is released. It is the phosphine gas that is responsible for ALP's toxicity. Phosphine inhibits cellular respiration by inhibition of cytochrome C, preventing cellular respiration, leading to the creation of reactive oxygen species and severe organ dysfunction.¹² Phosphine also creates hydroxyl radicals that cause further oxidative stress.^{13 14} Phosphine gas is rapidly absorbed through the lungs and gut and enters the central circulation where it affects many organ systems through a variety of mechanisms. Toxic features usually develop rapidly within minutes of ingestion.

Phosphine toxicity can cause severe cardiac damage and lead to altered haemodynamics, shock, ECG changes, dysrhythmias and cardiac necrosis. The mechanism of refractory shock is multifactorial and includes myocardial damage, peripheral vasodilatation, fluid loss, cellular energy failure or cytokine-mediated

dysfunction.¹⁵ Autopsy results on hearts of poisoned patients show congestion of cardiac muscles, separation and fragmentation of myocardial fibres, vacuolation of myocytes, focal necrosis and neutrophilic and eosinophilic infiltration. The myocardial necrosis and changes in membrane action potentials result in non-specific ST/T wave changes in the ECG.¹⁶ Cardiac arrhythmias are common and are a major contributor to mortality. In a study done by Siwach *et al*,¹⁷ it was noted that ventricular tachycardia occurred in 40% of patients poisoned with ALP cases, ventricular fibrillation in 23.3%, supraventricular tachycardia in 46.7% and atrial flutter/fibrillation in 20%.

Other clinical features include inflammation of airways, dyspnoea, lightheadedness, malaise, chest tightness, headache, nausea/vomiting, diarrhoea, unsteady gait, paresthesias, tremors, muscular weakness, double vision, jaundice, acute respiratory distress syndrome, seizures and coma.^{10 11} Diagnostic tests for

Figure 2 Echo at admission shows dilated left ventricle.

Figure 3 ECG on fifth day of admission shows reversal of T wave inversion to normal in most leads.

ALP exposure includes silver nitrate testing performed on gastric aspirates and gas chromatography with a nitrogen–phosphorous detector.^{18 19}

On exposure to phosphine, the affected person should be moved to clean air. Due to the possibility of phosphine being absorbed through the skin, it is important that rapid and thorough decontamination of skin and eyes be done with clean water.¹⁰ Early gut decontamination with potassium permanganate and activated charcoal may be effective if used within 1–2 hours of exposure. As the metabolic components of ALP are excreted via the urine, it is important that adequate renal perfusion and diuresis be maintained to remove the toxins from the body.²⁰

There is no effective antidote to ALP and therapy is only supportive until the effects of the phosphine subside. Early arrival to the healthcare facility, appropriate resuscitation, prompt diagnosis, intensive monitoring and supportive therapy may improve the survival of patients.²⁰ Many therapeutic agents have been tried in experimental animal studies. These include N-acetylcysteine and glutathione,^{21 22} hydroxyethyl starch,²³ hyperbaric oxygen²⁴ and trimetazidine,²⁵ but the evidence is not very convincing as they have not shown definitive improvement. The role of steroids is not well studied in ALP toxicity.²⁶ The treatment challenge for ALP poisoning is to effectively manage the resistant hypotension and shock due to decreased cardiac contractility. Management of cardiovascular failure is of the highest priority. While vasopressors can support haemodynamics, they are not without harm. For patients poisoned with ALP who continue to have refractory shock despite the use of usual vasopressor and inotropic agents with persistent myocardial suppression, the addition of digoxin may be beneficial.

Digoxin is a sodium–potassium ATPase inhibitor that increases myocardial contractility and inotropy without appreciable effect on the peripheral vasculature. Digoxin's positive inotropic effects are due to the reversible inhibition of the cellular membrane sodium–potassium pump. There is an increase in intracellular sodium concentration, a reduction in cytoplasmic potassium and ultimately an increase in cytoplasmic calcium that promotes myocardial contractility.²⁷ In a poorly contracting heart where this decreased inotropy is contributing to the shock state, digoxin may be a consideration. In 2011, Mehrpour *et al* reported

successful treatment of an ALP phosphide poisoning with rapid digitalisation along with other supportive treatment.²⁸ We did a similar rapid digitalisation that lead to an earlier withdrawal of other vasopressors. In our patient, ALP toxicity caused severe myocardial depression and digoxin produced a rapid reversal of myocardial depression and did not cause any arrhythmias. While it is possible that digoxin improved the haemodynamic parameters, it is also possible that the patient was beginning to recover or the therapies previously employed were sufficiently effective to support his recovery. Regardless, the addition of digoxin did not appear to cause harm (eg, bradycardia, hyperkalemia, etc) and was well tolerated.

Only prospective randomised controlled studies will be able to demonstrate the clinical benefit of digoxin in this setting. It is possible that the few reported cases of the beneficial effects of digoxin represent a publication bias as any reports where digoxin was harmful have never been published. Based on our experience in this single case report as well as previously documented other cases, we believe it is a reasonable consideration until further evidence emerges.

Contributors KHC was involved in the planning, conduct, reporting, conception and design, acquisition of data or analysis and interpretation of data and writing the manuscript. ML, MP and FA were responsible for the acquisition, analysis and interpretation of the data and editing the manuscript.

Competing interests None declared.

Patient consent Obtained.

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Learning points

- Aluminium phosphide (ALP) poisoning is common in India and treatment is mainly supportive.
- Rapid digitalisation may be helpful in ALP-induced myocardial suppression.

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