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Recent Advances in Management of Aluminium Phosphide Poisoning

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Abstract

Aluminium phosphide (AIP), commonly known as celphos is a household name in villages of Punjab. This cheap solid fumigant and a highly toxic pesticide is commonly used for grain preservation. The post “green revolution” era saw alarmingly increased mortality by consumption of celphos for suicidal intent. Till date, there is no specific antidote for its intoxication and the poisoning carries extremely high mortality. The article will throw some light upon the recent advances that have been made regarding the management of acute aluminium sulphide poisoning (AAIPP).

Keywords: Aluminium phosphide poisoning; Celphos poisoning; AAIPP; ECMO; boric acid as an antidote to AAIPP

Introduction

AIP, a mitochondrial poison, exerts its toxicity due to deadly phosphine gas that is liberated when it reacts with water or hydrochloric acid in the stomach. Phosphine gas (PH₃), the active pesticide component of AIP, is rapidly absorbed by inhalation, ingestion, and skin or mucosal contacts. The mechanism of toxicity includes cellular hypoxia due to the effect on mitochondria, inhibition of cytochrome C oxidase and formation of highly reactive hydroxyl radicals. The signs and symptoms are nonspecific

and instantaneous. The mortality ranges from 45% to 100%.

Discussion

In Northern India, when it comes to choosing a poison for suicidal intent, celphos is perhaps the favourite choice of victims- way ahead of barbiturates, organophosphorus or copper sulphate¹. Upon contact with moisture in the environment, AIP undergoes a chemical reaction

yielding phosphine gas. Phosphine inhibits cellular oxygen utilization and can induce lipid peroxidation. In the case of oral intake, the phosphine gas released is absorbed by the gastrointestinal tract with simple diffusion and is mainly excreted by the kidneys and lungs. Phosphine, like cyanide, inhibits mitochondrial cytochrome oxidase and cellular oxygen utilization^{2,3,4}. It can rapidly perturb mitochondrial conformation and inhibit oxidative respiration by 70%. This situation results a severe decrease in mitochondrial membrane potential³. AIP generates cellular superoxide and peroxide radicals, which trigger cellular damage by lipid peroxidation. The direct toxic effects of phosphine⁵ and phosphides⁶ on cardiac myocytes, fluid loss and adrenal gland can induce profound circulatory collapse. Death is usually a resultant of refractory myocardial depression, resistant hypotension, severe metabolic acidosis and acute respiratory distress syndrome.

Traditionally, the management of AAIPP is largely symptomatic as there is no specific antidote available. Gastric lavage with potassium permanganate (1:10,000) is done as it oxidizes PH₃ to form non-toxic phosphate⁷. Activated charcoal (approximately 100 g) given through a nasogastric tube to delay the absorption. Liquid paraffin, that accelerate the excretion of AIP and phosphine is often used⁸. For symptomatic relief from severe gastritis, antacids and proton pump blockers are employed. As AIPP is often associated with hypoglycaemia, correction of plasma glucose level with glucose containing fluids is done. Circulatory shock is dealt with 24 hr low dose dopamine (4–6 µg/kg/min) and intravenous fluids⁹. Hydrocortisone 200–400 mg every 4–6 hr has been reported to be used with good results¹⁰. Patients who land up in ARDS require intensive care monitoring and mechanical ventilation. If systolic blood pressure is >90 mm Hg, Diuretics may be used to enhance excretion as the main route of elimination of phosphine is renal¹¹. Arrhythmias are common and they are managed just as any other situation. Metabolic acidosis requires administration of intravenous sodium bicarbonate. Dialysis may be required for severe acidosis and acute renal failure.

Specific therapy and recent advances:

The clinical management of intoxication from AIP is mainly supportive. In one study, intravenous magnesium has shown significant improvement in indicators of oxidative stress and a lower incidence of mortality (20%) in comparison to control subjects (44% mortality)¹⁷. Oral administration of the anti-ischemic drug trimetazidine, which works through a metabolic mechanism of decreasing the production of oxygen-derived free radicals and stimulating the oxidative metabolism of glucose has been suggested to decrease mortality^{14,15}. Administration of sorbitol solution (at a dose of 1-2 ml/kg) as a cathartic and vegetable oils and liquid paraffin as inhibitor of phosphine release from the overdosed AIP has been suggested¹⁷. coconut oil has been shown to have a role in managing acute AIP poisoning even 6 h post ingestion¹⁸. Digoxin has been suggested for treatment of cardiogenic shock induced by acute AIP intoxication¹⁹.

Case reports and studies are available which suggest the treatment with various agents by various regimens with varying results. N-omega-nitro-L-arginine methyl ester (L-NAME)²⁰, N-acetylcysteine²⁰, hyperbaric oxygen²¹, 25Mg²⁺-carrying nanoparticles²², intragastric irrigation with sweet almond oil²², combination of vitamin C and methylene blue²³, extensive gastric lavage with coconut oil and sodium bicarbonate solution with simultaneous aspiration²⁴, intra-aortic balloon pump²⁵, have all been used in isolation or in conjunction with one another.

However, above all of them, Extracorporeal membrane oxygenation (ECMO) seems to hold the maximum promise regarding success management of this lethal poisoning. ECMO is a modified "heart-lung" machine to provide temporary cardiorespiratory support. Timely intervention with ECMO in patients with AIP poisoning-induced severe metabolic acidosis and refractory cardiogenic shock has shown significant improvement in overall survival in several trials and studies. Although EMCO is associated with significant complication rates of its own, it might come up as a promising

“bridge therapy” in cases with intractable cardiorespiratory failure caused by AIP poisoning who are not responding to conventional treatment.^{26,28,29}

Soltani et al have proposed a very interesting hypothesis stating Boric acid as a “trapping agent” for deadly phosphine gas and hence, purposes it be a specific antidote. Boric acid is a non-toxic Lewis acid which efficiently traps PH₃ gas. In this reaction, boric acid acts as a Lewis acid and phosphine acts as a Lewis base. The resulted polar reaction product which has H and OH groups can form hydrogen bonds with water molecules and hence can be excreted in urine by the body³⁰. Though the idea appears very practical in theory, the hypothesis is yet to be tested for In vitro and in vivo studies.

Conclusion

Although there is no specific treatment for AAIPP as yet, various agents have been used with reasonable success. EMCO has proved to be a game changer. Boric acid could be the answer for the future.

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