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Aluminum Phosphate as a Killer Pesticide in Human Body

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ABSTRACT

Aluminium Phosphate (AlP) is a commonly used pesticide. It is a cheap and solid fumigant that showsa high level of toxicity and is one of the most common reasons for poisoning by agricultural pesticides. It is also known as rice pills or wheat pills. The composition of AlP includes 56% Aluminium Phosphide and 44% inert ingredients which prevent the tablet from decomposition. The toxicity aroused due to AlP gained popularity in the last four decades due to the increasing use of pesticides in agricultural and non-agricultural activities. The pesticide has easy availability in markets due to which it is being diagnosed in many suicidal cases. The mortality rate of AlP is more than 50% in intoxication. When AlP comes in contact with the moisture present in the environment or with HCl present in the stomach, it liberates phosphine gas which is the active component. The liberation of gas leads to cell hypoxia, inhibiting the utilization of cellular oxygen and thus inducing lipid peroxidation. The particular targets of AlP toxicity are the vascular and cardiac system thus causing congestive heart failure, refractory hypotension and other electrocardiographic abnormalities. The clinical diagnosis of AlP is dependent on the history or clinical suspicion, and can be confirmed by performing Silver Nitrate test of gastric content or breathe. Till date there is no specific antidote available for treatment of AlP toxicity. The only treatment method includes the supportive care. This review article explains the effect of Aluminium Phosphate inside the human body.

Keywords: Aluminum Phosphate, pesticide, phosphine gas, poisoning, supportive care

INTRODUCTION

Aluminium Phosphide (AlP) is a solid, fumigant pesticide which is extensively as an indoor and outdoor pesticide for protection, storage and transportation of crops since 1940's (Akkaoui *et al*., 2007). It is readily traded in India under different names like Synfume, Celphos, Phosfume or Quickphos. In Iran, AlP can be purchased from local shops under the name of rice tablet. AlP is considered as near to ideal grain fumigant due to its properties like toxicity to all stages of

free of toxic residues. According to latest figures, AlP is found to be one among the most common reason for deaths due to poisoning in India, Iran, Morocco, Oman and Sri Lanka (Anand *et al*., 2011). Due to its easy availability and absence of an effective antidote, the pesticide is emerging as a common suicidal poisoning agent throughout world (Anger *et al*., 2000) . The estimated mortality rate of AlP poisoning ranges from 37-100%. For recent scenario, due to immediate release of lethal gas, AlP is suspected as a threat in chemical terrorism (Arora *et al*., 1995).

CHEMISTRY OF alp

Aluminium phosphate is prepared by exposing soluble aluminium salts to alkaline conditions contains hydrated aluminium orthophosphate with the formula $AlPO_4$. The highly viscous aluminium phosphate solutions tend to form polymeric aggregates, and equilibria is reached at a slow rate [AT, Proudfoot 2009]. It reacts slowly with gastric acid to form soluble aluminium salts and phosphoric acid. AlP is available in the markets in form of tablets as 3g Bhostoxin/Phostoxin/Quickphos Phosphume Phostek which releases 1g PH_3 or in the form of pellets of 0.6g Alphos/ Cellphos/Quickphos. The tablets contain 56% AlP and 44% $Al_2(CO_3)$ and are available in brown, gray or green colors.

Aluminium phosphate reacts with hydrochloric acid forming phosphoric acid and aluminium trichloride [Bogle R *et al*. 2006].

$$AlPO_4 + 3HCl \rightarrow AlCl_3 + H_3PO_4$$

The active ingredient in the mixture is AlP, which releases highly poisonous phosphine gas when it comes into contact with atmospheric moisture or hydrochloric acid in the stomach (Chopra *et al.,* 1986). As a result, when tablets or pellets are exposed to the air, they release phosphine gas and leave behind a harmless residue in the form of aluminium hydroxide.

Phosphine gas is colourless and odourless in its pure form, but it has a foul odour that resembles decomposing fish or garlic due to the presence of substituted phosphines and diphosphines. Phosphine is normally undetectable in both air and water (Davey Fumigation, 2013). It is combustible and may spontaneously ignite in air at room temperature at concentrations over the 1.9 percent (v/v) threshold limit range (Gargi *et al*. 2006). It is soluble in water and organic solvents; however, it reacts with OH radicals in the air and is eliminated through this method.

The ammonium carbamate component is included in commercially available tablets to prevent phosphine from degrading into carbon dioxide and ammonia and causing combustion (Goel and Aggarwal, 2007). Aluminum oxide and diphosphine gas are two further by-products of commercial tablets. The amount of diphosphine gas, which is spontaneously combustible in the air (Gupta and Ahlawat, 1995), is proportional to the amount of phosphorous as compared to aluminium present in the tablets.

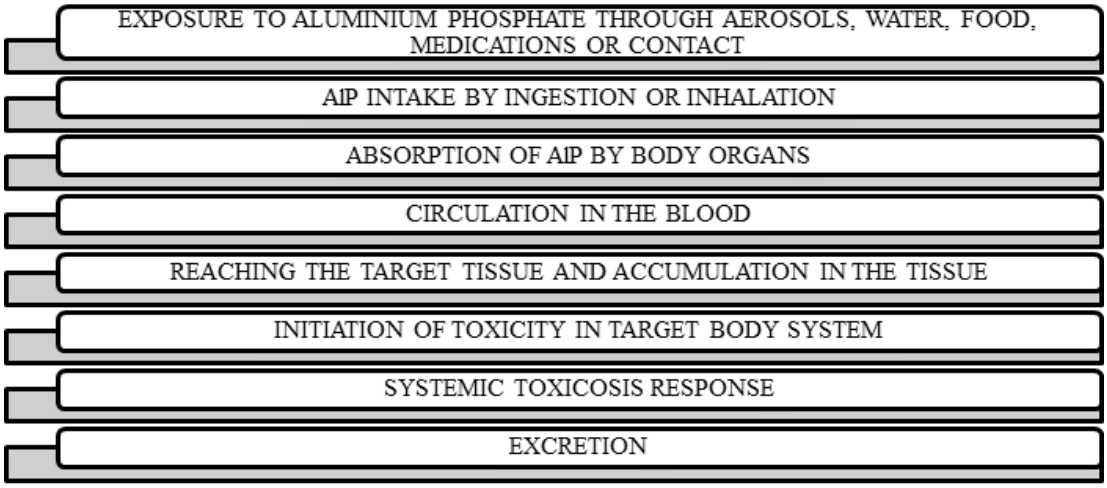

Figure 1. Development of AlK Toxicosis

Toxicokinetics

Ingestion- Phosphine is released after consumption (Gurjar *et al.* 2011) when AlP comes into touch with water or acid in the gastrointestinal (GI) tract. Some phosphide may be ingested and converted to phosphine without being hydrolyzed by the GI tract. Phosphine gas is quickly absorbed by the lungs and gastrointestinal tract. Absorption through the skin and eyes is uncommon, although it does occur. Distribution- The concentration of phosphine (Kondo et al., 1995) in the blood and liver increases after consumption. This tiny molecule is easily dispersed throughout the body.

Metabolism and Excretion- Hydrolysis converts metal phosphides to phosphine, which is then excreted. Hypophosphite is the most important phosphine urine metabolite, but phosphate and phosphite can also be found in urine. Exhalation is the only way to get rid of phosphophine. Aluminium phosphide can be excreted unaltered in the urine (LJ and Willers-Russo 1999).

Toxicodynamics

Aluminium Phosphate toxicity (Mashayekhian *et al*. 2016) in humans is caused either by ingestion or inhalation of AlP or absorption via skin. On contact with the acid present in the stomach, AlP realeases phosphine gas. The gas gets absorbed b the lining of gastrointestinal tract and leads to systematic toxicosis (Mehrpour *et al*., 2012).

Phosphine has been demonstrated to impair cellular respiration in studies. It prevents amino acids from entering the cycle of myocardial protein synthesis, as well as inhibiting cytochrome C oxidase in heart cells. These alterations in mitochondrial and myocardial proteins reduce cellular permeability to sodium, potassium, magnesium, calcium, and other ions, as well as alter the potential of cardiac cell walls. The heart, pulmonary cells, and small peripheral arteries are particularly susceptible to phosphine-induced pathophysiological alterations.

Cholinesterase is inhibited by both AlP and phosphine, however this suppression is unlikely to be clinically meaningful . Another harmful effect of phosphine is that it alters haeme capacity (Misra *et al*. 1988). Humans and rats can absorb unhydrolyzed aluminium phosphide salt, which continues to react with free haemoglobin and haemoglobin in normal red blood cells (RBCs) to create haemichrome, a derivative of methaemoglobin, in vitro investigations demonstrate.

Carbon monoxide levels, which may be measured by CO-oximetry, can aid in the diagnosis and prognosis of AlP poisoning. Specifically, phosphine may disrupt oxyhaemoglobin, which interacts with CO, resulting in dyshaemoglobinemia, which can result in elevated CO levels.

Given that phosphine produces free oxygen radicals in body tissues, organs with a higher need for oxygen (heart, lung, kidney, and liver) have been found to be more susceptible to phosphine gas damage, which is consistent with post-mortem histological alterations in these organs (Mittra *et al*. 2001). Furthermore, in poisoned patients, Heinz bodies, which indicate haemoglobin breakdown in vitro, rise to 1.25 g mL-1.

In the industry, the allowed exposure limit for phosphine is <0.3 parts per million (ppm), and levels higher than 50 ppm are life-threatening, while 400–600 ppm is deadly within half an hour. Individuals working in AlP or methamphetamine manufacturing facilities (phosphine is a by-product) or placing AlP tablets on grain stacks, and in the proximity of application are at risk for unintended phosphine gas exposure, with few fatalities reported.

Clinical manifestations

The signs and symptoms are generic and occur instantly (Moghadamnia, 2012), depending on the amount, route of administration, and time since toxic exposure. Patients typically experience airway irritation and shortness of breath after inhalation exposure. Dizziness, chest tightness, easy fatigability, headache, vomiting, ataxia, nausea, diarrhoea, paraesthesia, numbness, tremor, diplopia, jaundice and muscle weakness are all possible symptoms. Cardiac failure, acute respiratory distress syndrome (ARDS), convulsions, cardiac arrhythmias, and coma are all possible symptoms of severe inhalation poisoning, as well as late manifestations of nephrotoxicity and hepatotoxicity are also possible.

Toxic symptoms usually appear within minutes of consumption. Vomiting, nausea, headache, diarrhoea, tachycardia and stomach discomfort or pain (Shadnia *et al*., 2011) are all common clinical symptoms of mild

poisoning, and these individuals usually recover. In moderate to severe ingestional poisoning, however, signs and symptoms related to circulatory, gastrointestinal, nervous and pulmonary system arise first, with subsequent signs of renal and hepatic failure and disseminated intravascular coagulation.

The cardiac and vascular tissues are particularly vulnerable to AlP toxicity, which appears as congestive heart failure, subendocardial infarction, significant and refractory (Valmas and Ebert, 2006) hypotension, electrocardiographic (ECG) abnormalities, pericarditis or myocarditis. As per a study, the incidence of different arrhythmias on holter monitoring in patients with AlP poisoning was found to be 46.7% supraventricular tachycardia (Shadnia *et al*. 2011), 40% ventricular tachycardia, 20% atrial flutter/fibrillation and 23.3% ventricular fibrillation. The occurrence of hypotension can vary from 76% to 100% of people. The actual cause of refractory shock is unknown; it could be caused by a variety of reasons such as peripheral vasodilation, fluid loss or cardiac injury. Following up on heart function with echocardiography in a few cases of AlP poisoning, revealed left ventricular impairment that was reversible within a few days.

Dyspnoea, cough, pulmonary edoema, cyanosis, ARDS and respiratory failure are all respiratory symptoms. Metabolic acidosis may occur as a result of lactic acid accumulation (Wahab *et al*. 2009) caused by oxidative phosphorylation inhibition and inadequate tissue perfusion. Patients may be conscious until late in the disease, but they may experience symptoms such as dizziness, headaches, convulsions, coma and altered sensorium.

Treatment

As there is no specific antidote for AIP poisoning, the cornerstone of therapy is supportive care. Timing significantly affects the prognosis. If AIP poisoning is suspected based on the history and physical examination, treatment must not be delayed until test results are confirmed. Symptomatic patients should be monitored in the intensive care unit (ICU)for at least 72 hours. They should be receiving 100% oxygen and treated for fluid and electrolyte abnormalities. Serum calcium and magnesium and liver/kidney function tests are mandatory. The following main treatment options are:

1. GI decontamination (Gastrointestinal decontamination)
2. Cardio vascular support
3. Respiratory support

And other treatments are sodium bicarbonate is used for the treatment of acidosis. Hypoglycemia, hypokalemia and metabolic acidosis are treated as usual. Calcium gluconate (Siwach *et al*. 1998) is generally recommended to stabilise cell membranes. However, the recommend IV injection dose for routine treatment. Other treatments such as melatonin, glutathione and beta carotene have also been proposed and need further evaluation. Blood exchange is a question able treatment in AIP poisoning. Before discharge, all the survivors with swallowing difficulty must undergo a barium swallow study and upper gastrointestinal endoscopy for early detection of esophageal complications due to AIP ingestion. Survivors also need psychological counselling.

More studies are needed to prove the efficacy (Wahab *et al*. 2009) of oximes in the treatment of this poisoning. For the moment, these medications are not recommended for routine treatment. Considering all of the above, the only recommend treatment of AIP poisoning is the general supportive one.

CONCLUSION

The case fatality ratio declined in the last decade due to improved intensive care. Strict implementation of nationwide pesticide regulation, including restricting the availability of poison, being aware of its toxicity and providing improved medical management in consultation with regional or national poison control centre could further reduce the mortality due to AIP toxicity as there is no antidote available presently. Aluminum phosphate is a highly effective insecticide and rodenticide. However, it is highly toxic with high mortality rate if ingested. It produces severe metabolic acidosis and cardiogenic shock with no available antidote, so management may be the only supportive treatment. Early decontamination and intervention may be helpful. Restricted use and away programs to farmers may be beneficial in prevention of toxicity.

Conflicts of interest: The authors stated that no conflicts of interest.

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