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Multidisciplinary Approach to the Management of Aluminium Phosphide Poisoning – Experience from a Tertiary Care Hospital

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Abstract

A usual ingredient of rodenticide, aluminium phosphide is known for its poisoning which happens to be one of the common causes of suicides in India. Signs and symptoms of toxicity with aluminium phosphide are well-known. Circulatory failure plays an important role in mortality with aluminium phosphide poisoning. Aluminium phosphide poisoning is associated with high mortality as there is no specific antidote available yet. There is a need for correct treatment approach to manage this fatal poisoning. In this retrospective analysis we present a data of forty cases registered at a tertiary care hospital in Mumbai. We developed a multidisciplinary treatment approach to aluminium phosphide poisoning which may help in better patient outcomes. Correct treatment protocol with supportive therapy resulted in better survival in these patients. Hence we propose this aggressive, appropriate management with continuous haemodynamic monitoring and multidisciplinary treatment approach to reduce the mortality in aluminium phosphide poisoning.

Keywords: Aluminium Phosphide Toxicity, Multidisciplinary Treatment, Rodenticide Poisoning

1. Introduction

Aluminium phosphide is commonly used as a rodenticide and pesticide in grain storage facilities. Aluminium phosphide poisoning occurs as a result of excessive exposure to aluminium phosphide, which is readily available as a fumigant for stored cereal grains or as a rodenticide and sold under various brand names such as QuickPhos, RatKil, Salphos and Celphos. It is highly toxic, especially when consumed from a freshly opened container[1,2]. After ingestion; toxic features usually develop within a few minutes. It has a fatal dose between 0.15 and 0.5 grams[3].The mortality rates from aluminium phosphide poisoning vary from 35 to 85% in various studies[1].The major lethal consequence of aluminium phosphide ingestion is profound circulatory collapse and is due to the liberation of phosphine gas, a cytotoxic compound that causes free radical mediated injury, it inhibits vital cellular enzymes and is directly corrosive to tissues, which leads to direct effects on cardiomyocytes, fluid loss and adrenal gland damage[4,5]. It produces phosphine gas which is a mitochondrial poison. It has a very destructive effect on myocardial cells and leads to myocarditis. The degree of myocarditis can vary from mild to severe and it can cause heart failure, various cardiac arrhythmias like atrial

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fibrillation, ventricular tachycardia and bradyarrhythmias. It can also cause ventricular fibrillation and sudden death.

The signs and symptoms of aluminium phosphide poisoning are nonspecific, dose dependent and evolve with time. Severe poisoning also has the potential to induce multiorgan failure. The dominant clinical feature is severe hypotension refractory to dopamine therapy and metabolic acidosis[6]. Other features may include dizziness, fatigue and tightness in the chest, headache, nausea, vomiting, diarrhoea, ataxia, numbness, paraesthesia, tremor, muscle weakness, diplopia and jaundice[7–10]. In severe cases, the patient may develop Acute Respiratory Distress Syndrome (ARDS), heart failure, arrhythmias, convulsions and coma and death. Late manifestations include liver and kidney toxicities[7–10]. Death can result from profound shock, myocarditis and multi-organ failure[11], Several ECG changes ranging from ST segment elevation/depression, PR and QRS interval prolongation, complete heart block to ectopic and fibrillation have been observed. Reversible myocardial injury has also been reported[4,7,8]. The breath of patients who have ingested aluminium phosphide has a characteristic garlic-like odour. Confirmation of diagnosis is based on the patient's history.

Previously, the laws and legislations for the sale of such chemicals were not that strict and it was easily available over the counter. In the last few years, stricter norms have reduced its easy availability. However, it's not enough to reduce the suicidal rate due to its consumption, which traumatizes many families. Since 1992, when aluminium phosphide became freely available in the market, it had reportedly overtaken all other forms of deliberate poisoning, such as organophosphorus and barbiturate poisoning particularly in North India[12]. In a 25-year-long study on 5933 unnatural deaths in northwest India, aluminium phosphide poisoning was found to be the major cause of death among all cases of poisonings[13]. It has been reported to be the most common method of suicidal death in North India[14].

The management of aluminium phosphide poisoning remains purely supportive, because there is no specific antidote or cure for aluminium phosphide poisoning5. Treatment consists of gastric lavage with potassium permanganate solution, oral administration of charcoal and sorbitol suspension, intravenous administration of fluids, inotropes, sodium bicarbonate, magnesium sulphate, calcium gluconate, corticosteroids and other supportive care. Correction of metabolic acidosis is a cornerstone of treatment[15]. We undertook a retrospective analysis of cases of aluminium phosphide poisoning at the Intensive Care Unit (ICU) of our institute. We adopted a multidisciplinary approach taking the help of a physician, intensivists, cardiologists, nephrologists, neurologists, psychiatrist and clinical pharmacologist as well as a toxicologist for the treatment of aluminium phosphide poisoning. Hence, this analysis was aimed at observing the clinical profile and outcome of aluminium phosphide poisoning with a multidisciplinary approach in our institute.

2. Materials and Methods

The data was curated for the period of three years from January 2011 to December 2014, for all the patients with an alleged history of aluminium phosphide poisoning. Only registered cases with the tertiary care municipal corporation hospital from Mumbai were selected. The archived case files were opened to study the patient profiles along with the treatment protocols used. The data was further compiled in excel sheets and the retrospective analysis was planned to understand the multidisciplinary treatment approach used to assess the outcome. As a routine practice patient's consent was taken on admission regarding possible use of the data for publication. Statistical analysis was carried out and data was presented as absolute numbers and percentage.

3. Results

Data of total 40 patients admitted with aluminium phosphide poisoning was found in the case record files. This data is only for the patients admitted at this institute during January 2011 to December 2014. There were no reported cases of death on arrival at emergency department due to aluminium phosphide poisoning during the given period.

The age of the patients ranged from 14 to 80 years with a mean age of 37.8 years. The majority of patients were young with 50% of patients in the 20 to 40 years age group. Out of 40 patients, 26 were male and 14 female. Demographic details of the patients are summarized in Table 1. According to the educational level, 4 patients were illiterate, 16 were studied up to secondary school, 14 patients were graduates and 6 patients were postgraduate, indicating aluminium phosphide was seen less likely in educated than illiterate people. According to professional status, six people were not working or unemployed, 12 were employed and 22 were self-employed.

Most of the patients had features of hypotension, cardiogenic shock and arrhythmias, while few got admitted with respiratory distress and the rest of them had a multitude of symptoms related to different organ systems. On admission, sinus tachycardia was present in 20 patients. Wide Complex Tachycardia was present in 6 patients;

sinus bradycardia was seen in 2 patients. Complete heart block was seen in 1 patient and junctional rhythm was seen in 1 patient, both of which required a temporary pacemaker, and patients later resumedspontaneous sinus rhythm. On admission, Left ventricular (LV)dysfunction was present in 28 patients (mild 14, moderate 8 and severe 6). Twelve patients out of 14 (85.7%) survived with mild LV systolic dysfunction, 6 patients out of 8 (75%) survived with moderate LV systolic dysfunction and 3 patients out of 6 (50%) survived with severe LV systolic dysfunction. It indicates that Left Ventricular ejection fraction/systolic dysfunction has an important impact on the survival of patients with aluminium phosphide. The maximum number of patients was 30 (75%), presented clinically with cardiovascular system involvement, either in the form of tachycardia, hypotension or arrhythmias, or ST-T changes, which was clinically significant. Clinical presentation of these patients is summarized in Table 2.

Table 1. Demographic profile and patient characteristics

Gender	Male	26 (65%)
	Female	14 (35%)
Age	Below 20 years	9 (22.5%)
	20 to 40 years	20 (50%)
	40 to 60 years	10 (25%)
	Above 60 years	1 (2.5%)
Educational status	Illiterate	4 (10%)
	Up to Secondary school	16 (40%)
	Graduate	14 (35%)
	Postgraduate	6 (15%)
Professional status	Unemployed	6 (15%)
	Employed	12 (30%)
	Self-employed	22 (55%)

Table 2. Clinical presentation* of patients in ICU

Clinical presentation	Number of patients (%)
Cardiovascular complications / Arrhythmia	30 (75%)
Respiratory distress / failure	10 (25%)
Acidosis	24 (60%)
Gastrointestinal bleed	2 (5%)
Altered sensorium	2 (5%)
Combined respiratory / Cardiovascular /CNS involvement	6 (15%)

*Clinical presentation was overlapping.

Out of the 40 patients, 12 patients (30%) required mechanical ventilation and 28 patients (70%) needed inotropic support for maintaining stable hemodynamic parameters. Seven patients (17.5%) needed defibrillation or other antiarrhythmic treatment, 2 patients (5%) required temporary pacemaker insertion and both patients later regained spontaneous sinus rhythm. Only 2 patients (5%) required haemodialysis for renal impairment. The stay in ICU varied from 3 to 14 days, with a mean stay of 6 days. We were able to save 26 patients (65%) without any end organ damage, which is quite significant, but the rest 14 (35%) succumbed to poisoning.

Table 3. Systemic involvement and related mortality

Number of organs involved	Number of patients	Number of deaths (% mortality)
1	5	01 (20%)
2	12	03 (25%)
3	17	06 (44%)
4	4	04 (100%)

In our study, 14 patients died due to aluminium phosphide and the mortality increased with progressive involvement of the number of organ systems. Organ system involvement and mortality is summarized in Table 3, where it indicates that the mortality reached 100% if four or more organs are involved.

Three of our patients consumed three or more than three tablets of the aluminium phosphide containing poison, while four of the patients were brought to the hospital almost more than four hours of ingestion of these pellets which we believe led to the increase of mortality rate among our patients.

Treatment protocol used was as follows, extensive gastric lavage was done with potassium permanganate and charcoal on admission to casualty. Initial 30 ml lavage was sent to the forensic laboratory for toxicological analysis. On admission to ICU, the patients were made comfortable on the bed, monitoring gadgets were attached for Heart Rate (HR) and rhythm, Non-Invasive (NIBP) or invasive blood pressure monitoring, ECG, Pulse Oximetry (SpO_2). Endotracheal intubation for the indicated patients was done with an appropriate size cuffed endotracheal tube and patients were put on mechanical ventilation. Symptomatic treatment was initiated on a patient to patient basis. Intravenous normal saline, magnesium sulphate, dopamine, dobutamine, amiodarone infusion, antibiotics and other appropriate Intravenous (IV) drugs were given depending on the patient's clinical presentation and symptomatology, as well as arrhythmias and blood pressure variations. Urine output was monitored through Foley's catheter attached to a urobag with a uroflow-meter. Patients who required mechanical ventilation were kept sedated with injection midazolam and paralyzed with injection vecuronium. During this period, strict and vigil monitoring of all vital parameters was done and treatment regimens were titrated according to the clinical condition of the patients.

All patients were managed in ICU with the objective to provide symptomatic and supportive aid. Central venous line was used for CVP monitoring, IV fluids and inotropic support. Arterial line was used for invasive BP monitoring in all the patients. Intravenous sodium bicarbonate was administered for metabolic acidosis. Patients who required mechanical ventilation were kept sedated with injection midazolam and paralyzed with injection vecuronium. Magnesium sulphate two grams in dextrose was given as intravenous infusion every six hourly. Continuous cardiac monitoring and injection amiodarone, defibrillation or temporary pacemaker insertion was used whenever required. Prophylactic antibiotics were given. Bedside 2D echo was done for all the patients

4. Discussion

Rodenticides and insecticides like Celphos are formulated as a greenish or grey tablet of aluminium phosphide, which releases phosphine gas in the presence of moisture or hydrogen chloride. Phosphine gas gets rapidly absorbed from the gastric mucosa and once it gains access to the bloodstream, it reaches various tissues and at the cellular level inhibits the mitochondrial respiratory chain and hence leads to cell necrosis and death. It inhibits myocardial cellular metabolism and necrosis of the cardiac tissue, resulting in the release of reactive oxygen intermediates[16]. Refractory myocardial depression from aluminium phosphide toxicity is not uncommon and carries a very high mortality[1,17,18].These cardiotoxic effects were quite marked in our patients, as 75% of the patientsneeded inotropic support. Vascular changes may lead to marked low blood pressure/hypotension that does not respond well to vasopressor agents. Cardiotoxicity or toxic chemical myocarditis is manifested as depressed left ventricular ejection fraction, ECG changes varying from ST segment elevation or depression, PR prolongation, broad QRS complexes and right or left bundle branch block, supraventricular ectopic or ventricular tachycardia, bradyarrhythmias18. Bedside 2D echo with Doppler was done in all patients with IVC measurement, which helped us in fluid and inotropic management. Only 17.5% of our patients needed defibrillation or antiarrhythmic drugs like amiodarone, metoprolol, lignocaine in addition to

magnesium sulphate. Two patients needed temporary pacemaker insertion and both patients were salvaged and later both regained spontaneous normal rhythm.

Biochemical changes include rise in Aspartate Transaminase (AST), Creatine Phosphokinase-MB (CPK-MB) and Lactate Dehydrogenase (LDH). Histopathological reports showed myocytolysis, multiple areas of necrosis and congestion[19]. Hypomagnesaemia has been known to cause arrhythmias in aluminium phosphide poisoning and magnesium supplementation has been suggested as a therapeutic option[1]. The findings of our study do correlate with all above studies, as most of our patients presented with arrhythmias of varying nature and it proved fatal in some of the patients who died in our ICU. The incidence of aluminium phosphide poisoning was seen among working and non-working population, highlighting the fact that employment stress is not the only factor but rather it is the social and family factors which drive these people to commit suicide.

Toxicity that occurs after inhalation is characterized by chest tightness, cough and shortness of breath. Severe exposure can cause accumulation of fluid in the lungs, pulmonary edema and ARDS, which may have a delayed onset of 72 hours or more after exposure. Children may be more vulnerable because of relatively increased minute ventilation per kilogram and failure to evacuate an area promptly when exposed. Phosphine gas is eliminated through the lungs; hence, due to the high concentration in the respiratory alveoli, it is responsible for direct alveolar damage[8]. Only 25% of our patients also presented with respiratory distress, either alone or in combination with other organ dysfunction. Four of our patients developed severe pulmonary edema during the initial course of the treatment and we ventilated with 100% oxygen and high PEEP as the patients developed severe hypoxemia which was evident in ABG report.

Studies in the past have shown increased levels of inflammatory markers (cytokines and interleukins) in ARDS, which increase the capillary permeability. This combined effect of an increase in capillary permeability due to global hypoxia and ARDS could be responsible for the exudative effusion seen predominantly in the pleural cavity and not in other serous cavities[20]. Gastrointestinal symptoms are usually one of the first to occur after exposure. Symptoms may include nausea, vomiting and abdominal pain, and diarrhoea, hematemesis. Death due to acute hepatocellular toxicity and fulminant hepatic failure has also been reported in acute poisoning. Blood and protein in the urine and acute kidney failure due to shock can occur. Analysis of blood gases may reveal combined respiratory and metabolic acidosis. Moreover, there have been reports of significant hypomagnesaemia and hypomagnesaemia associated with massive focal myocardial damage[20,21]. In our study, mortality increased with increasing number of organ system involvement. In patients with involvement of four or more than four organ system involvement, mortality was 100%.

Gastric lavage is important in the initial stage. The management principles aim to save lives with appropriate resuscitation and supportive measures until phosphine is excreted from the body. If phosphides have been ingested, we do not induce emesis. Gastric lavage with saline or sodium bicarbonate or potassium permanganate (1:1000) has also been recommended by earlier studies[21]. As the poison itself causes a lot of gastric mucosal damage, it exposes a lot of raw area for phosphine absorption.

Enhancing phosphine excretion, especially through the lungs by increasing the respiratory rate in ventilated patients, which becomes easier when the patient is paralyzed, sedated and put on mechanical ventilation. Phosphine is excreted through urine. Therefore, adequate hydration and renal perfusion by low-dose dopamine 4-6 microgram/kg/minute can be considered. Arterial line is a must for invasive BP monitoring in most of the patients. Intravenous sodium bicarbonate helps to reverse metabolic acidosis. Magnesium sulphate in Dextrose IV every six hourly helps with its antioxidant and antiarrhythmic action. Continuous cardiac monitoring is essential and if needed, injection amiodarone and defibrillation for timely control of ventricular arrhythmia and temporary pacemaker insertion for heart block is required. Prophylactic antibiotic for prevention of nosocomial infection is also essential. By keeping serum magnesium and serum potassium, sodium within normal levels and taking care of other haemodynamic parameters and metabolic acidosis, there is a significantly better survival rate of patients with aluminium phosphide poisoning. Bedside 2D echo helps in the management of intravenous fluids, diuretics, and inotropes.

Besides, considering the expertise of a physician, intensivist, cardiologist, nephrologist, neurologist and psychiatrist in treating aluminium phosphide poisoning, we also took help from a clinical pharmacologist and toxicologists. Clinical pharmacologist can be of great help in such cases with their expertise in drug actions and adverse effects[22–24].

5. Conclusion

Aluminium phosphide poisoning patients can survive without any end-organ damage if aggressive and appropriate

management with continuous haemodynamic monitoring is done along with a multidisciplinary treatment approach. The outcome correlates best with the severity of hypotension, severity of acidosis, LV dysfunction or LV ejection fraction, arrhythmias and number of organ systems involved. The management of aluminium phosphide poisoning remains purely supportive because no specific antidote exists. With the multidisciplinary treatment approach, we were able to save 65% of our patients of aluminium phosphide poisoning and we recommend the use of this approach by all intensivists and physicians. Correction of metabolic acidosis is a cornerstone of treatment. The role of magnesium sulphate defibrillation and antiarrhythmic medicine as therapy in aluminium phosphide poisoning should decrease the likelihood of a fatal outcome. This multidisciplinary treatment approach can save the lives of so many patients with this emergency.

6. Acknowledgements

None

7. Conflict of interest

None

8. References

1. Chugh SN, Dushyant Ram S, Arora B, Malhotra KC. Incidence and outcome of aluminium phosphide poisoning in a hospital study. Indian J Med Res. 1991; 94:232-5.
2. Singh S, Singh D, Wig N, Jit I, Sharma BK. Aluminum phosphide ingestion - a clinico-pathologic study. J Toxicol Clin Toxicol. 1996; 34(6):703–6.PMid:8941200. https://doi.org/10.3109/15563659609013832
3. Wahab A, Zaheer MS, Wahab S, Khan RA. Acute aluminium phosphide poisoning: An update. Hong Kong Journal of Emergency Medicine. 2008; 15(3):152–5. https://doi.org/10.1177/102490790801500306
4. Chugh SN, Pal R, Singh V, Seth S. Serial blood phosphine levels in acute aluminium phosphide poisoning. J Assoc Physicians India. 1996; 44(3):184–5.
5. Gurjar M, Baronia AK, Azim A, Sharma K. Managing aluminum phosphide poisonings. J Emerg Trauma Shock. 2011; 4(3):378–84. PMid:21887030 PMCid:PMC3162709. https://doi.org/10.4103/0974-2700.83868
6. Chugh SN, Kumar P, Aggarwal HK, Sharma A, Mahajan SK, Malhotra KC. Efficacy of magnesium sulphate in aluminium phosphide poisoning - comparison of two different dose schedules. J Assoc Physicians India. 1994; 42(5):373–5.
7. Goel A, Aggarwal P. Pesticide poisoning. Natl Med J India. 2007; 20(4):182–91.
8. Sudakin DL. Occupational exposure to aluminium phosphide and phosphine gas? A suspected case report and review of the literature. Hum Exp Toxicol. 2005; 24(1):27–33. PMid:15727053. https://doi.org/10.1191/0960327105ht496oa
9. Gupta S, Ahlawat SK. Aluminum phosphide poisoning - a review. J Toxicol Clin Toxicol. 1995; 33(1):19–24. PMid:7837309. https://doi.org/10.3109/15563659509020211
10. Agrawal VK, Bansal A, Singh RK, Kumawat BL, Mahajan P. Aluminum phosphide poisoning: Possible role of supportive measures in the absence of specific antidote. Indian J Crit Care Med. 2015; 19(2):109–12. PMid:25722553 PMCid:PMC4339895. https://doi.org/10.4103/0972-5229.151019
11. Mathai A, Bhanu MS. Acute aluminium phosphide poisoning: Can we predict mortality? Indian J Anaesth. 2010; 54(4):302–7. PMid:20882171 PMCid:PMC2943698. https://doi.org/10.4103/0019-5049.68372
12. Singh D, Jit I, Tyagi S. Changing trends in acute poisoning in Chandigarh zone: A 25-year autopsy experience from a tertiary care hospital in northern India. Am J Forensic Med Pathol. 1999; 20(2):203–10. PMid:10414665. https://doi.org/10.1097/00000433-199906000-00019
13. Singh D, Dewan I, Pandey AN, Tyagi S. Spectrum of unnatural fatalities in the Chandigarh zone of north-west India - a 25 year autopsy study from a tertiary care hospital. J Clin Forensic Med. 2003; 10(3):145–52. https://doi.org/10.1016/S1353-1131(03)00073-7
14. Siwach SB, Gupta A. The profile of acute poisonings in Harayana-Rohtak Study. J Assoc Physicians India. 1995; 43(11):756–9.
15. Wiwanitkit V. Aluminum phosphide poisoning. Indian J Crit Care Med. PMid:20040819 PMCid:PMC2823103. https://doi.org/10.4103/0972-5229.58547
16. Lall SB, Sinha K, Mitra S, Seth SD. An experimental study on cardiotoxicity of aluminium phosphide. Indian J Exp Biol. 1997; 35:1060–4.
17. Bogle RG, Theron P, Brooks P, Dargan PI, Redhead J. Aluminium phosphide poisoning. Emerg Med J. 2006; 23:e3. PMid:16373788 PMCid:PMC2564148.https://doi.org/10.1136/emj.2004.015941

18. Mathur A, Swaroop A, Aggarwal A. ECG changes in aluminium phosphide and organo phosphorus poisoning. Indian Pract. 1999; 52:249–52.
19. Karanth S, Nayyar V. Rodenticide-induced Hepatotoxicity. J Assoc Physicians India. 2005; 51:316–7.
20. Suman RL, Savani M. Pleural effusion-A rare complication of aluminium phosphide poisoning. Indian Paediatr. 1999; 36:1161–3.
21. Chugh SN. Aluminium phosphide in Lall SB, Essentials of Clinical Toxicology. New Delhi: Narosa Publishing House; 1990.
22. Malve HO. Forensic pharmacology: An important and evolving subspecialty needs recognition in India. J Pharm Bioallied Sci. 2016; 8(2):92–7. PMid:27134459 PMCid:PMC4832912. https://doi.org/10.4103/0975-7406.171698
23. Malve H. Understanding Forensic Pharmacology: What Indian physicians need to know? J Assoc Physicians India. 2017; 65(2):74–5. https://doi.org/10.22506/ti/2016/v23/i2/146707
24. Malve H. Understanding Forensic Pharmacology: What Indian pharmacologists need to know? Toxicol Int. 2016; 23(2):205–6. https://doi.org/10.22506/ti/2016/v23/i2/146707