

Case Report

Successful Treatment of Cardiotoxicity of Aluminium Phosphide Poisoning with Extracorporeal Membrane Oxygenation (ECMO): A Case report

Munish Chauhan^{1*}, Sandeep Dewan¹, Sandeep Attawar², Sahish Kamat¹, Vishal Kumar¹, Vitul Manhas¹, Nitin Jain¹, Milind V. Talegaonkar¹, Pooja Wadwa¹

¹Department of Critical Care Medicine, Fortis Memorial Research Institute, India

²Dept. of Cardiothoracic and Vascular Surgery, Fortis Memorial Research Institute, India

***Corresponding author**

Munish Chauhan, Department of Critical Care Medicine, Fortis Memorial Research Institute, Sector 44, Gurgaon, Haryana, India 122002. Tel +91-9650773633; E-mail: drchauhanmunish@gmail.com

Submitted: 30 April 2015

Accepted: 10 August 2015

Published: 12 August 2015

ISSN: 2333-7079

Copyright

© 2015 Chauhan et al.

OPEN ACCESS**Keywords**

- Extracorporeal Membrane Oxygenation (ECMO)
- Poisoning
- Toxicology
- Cardiovascular
- Aluminium phosphide

Abstract

Introduction: Aluminium phosphide poisoning is one the commonest pesticide used in India and also the most lethal with mortality approaching almost 100%; majority in the first 24 hours. Its lethality is accentuated by its rapid toxicity, non-availability of an antidote and debilitating cardiac dysfunction.

Objective: We discuss here a case of aluminium phosphide induced severe cardiac dysfunction and shock managed aggressively and successfully with early initiation of VA-ECMO propelled by the belief, though scant literature, that the cardiac injury induced by this poison is reversible.

Case study: This report pertains to a young man, admitted with reported oral ingestion of a lethal dose of aluminum phosphide with suicidal intent. He presented in a critical state of cardiovascular collapse requiring prompt management with a modality used rarely for this kind of intoxication: ECMO

Conclusion: With this report, we would like to support the belief that cardio toxicity due to aluminium phosphide poisoning is reversible. With V-A ECMO emerging as an upcoming modality with increasing availability and acceptable risk-benefit ratio, we suggest that it should be further studied as a promising treatment option to tide over the acute phase and act as a "bridge" to recovery of the cardiac function before the onset of multi organ failure (MOF) in a specific subset of patients.

ABBREVIATIONS

V-A ECMO: Veno-Arterial Extra Corporeal Membrane Oxygenation, LV: Left Ventricle, ECG: Electrocardiography, RVSP: Right Ventricular Systolic Pressure, TR: Tricuspid Regurgitation, MR: Mitral Regurgitation, EF: Ejection Fraction, ARDSnet: Acute Respiratory Distress Syndrome Network, ScvO₂: Central Venous Oxygen Saturation, APACHE: Acute Physiology and Chronic Health Evaluation, ATN: Acute Tubular Necrosis. IABP: Intra Aortic Balloon Pump

INTRODUCTION

Aluminium Phosphide is the most common farm pesticide in India, with humans commonly exposed to it accidentally or with suicidal tendencies. It causes cellular level damage and end organ damage; cardiac toxicity being the major trauma inflicted. There are only supportive therapies postulated but no specific antidote. We present a case of severe Aluminium Phosphide poisoning in a young male managed with aggressive hemodynamic support and a belief supported by scarce literature that the cardiac toxicity caused by the poison is reversible over a 10-14 day period

CASE PRESENTATION

A 17 year old boy, with no known comorbidities, presented to our hospital, a tertiary care multispecialty referral center, with vomiting and breathlessness after alleged history of consumption of 3gm Aluminium Phosphide tablet 4 hours prior to the symptoms. He was given gastric lavage at a local private hospital with potassium permanganate almost 2 hours after the consumption of the poison and then referred to our institute. On first examination, the patient was conscious, oriented, irritable, severely dyspnoeic, heart rate 126/m, blood pressure 90/50mmHg on high vasopressor support (norepinephrine at 0.8 mcg/kg/min and adrenaline 0.2mcg/kg/min) with signs of poor perfusion and high lactates (9mmol/lit going upto 15mmol/lit). Severe metabolic acidosis in the first arterial blood gases was there {with a pH of 7.27/PCO₂ 29.6 torr (3.9kPa) / PO₂ 264.8 torr (35.3kPa) / Base deficit 11.4mmol/L/HCO₃ 15.5 mmol/L/anion gap 21.5}; pH in the subsequent hour worsened to 7.1. Electrocardiography (ECG) showed QRS widening and generalized ST segment depression pointing to severe myocardial depression (Figure 1). Transthoracic 2D Echocardiography was showing severe global Left ventricular (LV) dilatation and hypokinesia with Ejection Fraction (EF) of 15-20% and Right Ventricular Systolic Pressure (RVSP) of 30mmHg. Mild Tricuspid Regurgitation (TR), Mitral Regurgitation (MR) and diastolic dysfunction was found. Initial laboratory parameters were showing leukocytosis with mildly deranged liver functions, normal renal functions and normal coagulation profile.

The patient was endotracheally incubated, mechanically ventilated as per ARDSnet (Acute Respiratory Distress Syndrome Network) protocol and all invasive lines established. Central Venous Oxygen Saturation (ScvO₂) was measured to be 65%. After adequate fluid resuscitation as guided by the advanced hemodynamic parameters, epinephrine was added to support the blood pressure. Electrolyte correction was given for magnesium and calcium. Supportive care was continued and ICU protocols/bundles followed.

In view of worsening hemodynamics, lactic acidosis (16mmol/lit), cardiac dysfunction, vasopressor refractory shock,

decision for Venous-Arterial (V-A) Extracorporeal Membrane Oxygenation (ECMO) was taken. ECMO initiation was done within 5 hours after admission to ICU. Femoral cannulation was done and V-A ECMO initiated as per the institutional ECMO protocol using cannula size 18F for arterial and 20F for venous access (Edward Life sciences, Irvine, CA, USA). Initial ECMO pump flows were set to 3.6-3.8L/min (using Medos Inc, Stolberg, Germany) aiming to attain 60-70 % of the estimated cardiac output of the patient. Within 6 hours of initiation of ECMO vasopressors were tapered to minimum doses of nor epinephrine (0.01mcg/kg/min), epinephrine was stopped. During initial 4 hours, lactate went out of range but became measurable again at 19.8mmol/l after 7 hours of ECMO and then went down continually to reach normal range on 34 hours of ECMO

Daily lab parameters were monitored and APTT maintained 2 -3 times above normal upper limit with i.v heparin infusion. Surveillance cultures as per protocol were taken daily. Daily Trans-thoracic echocardiography was done to assess the left ventricular function. First LV assessment post ECMO had an EF of 10-15% and presence of Spontaneous echo contrast (SEC) (Figure 2). By day 3, EF had improved marginally to 15-20% but LA was dilated with high pressures. Things started turning around by day 5 of ECMO with an improving EF of 25-30% and fall in RVSP with improving RV function. It was closely mirrored by the ECG with near normalization of the nonspecific ST-T changes

There was appearance of ATN (Acute Tubular Necrosis) with polyuria reaching up to 34L a day in the first two days requiring close but aggressive fluid replacement. The cause was inexplicable and was attributed either to direct cellular damage by the poison and/or SIRS due to ECMO leading to nephrogenic diabetes insipidus.

Encouraged by the constant improvement of LV function ECMO was discontinued after 129 hours and 14 minutes successfully. His course subsequently was riddled with hospital associated infections and requirement of renal replacement therapy for persistent metabolic acidosis; but he improved continually. He was weaned off the ventilator 5 days later (day 12). His LVEF on day 14 of admission was 40% with a RVSP of

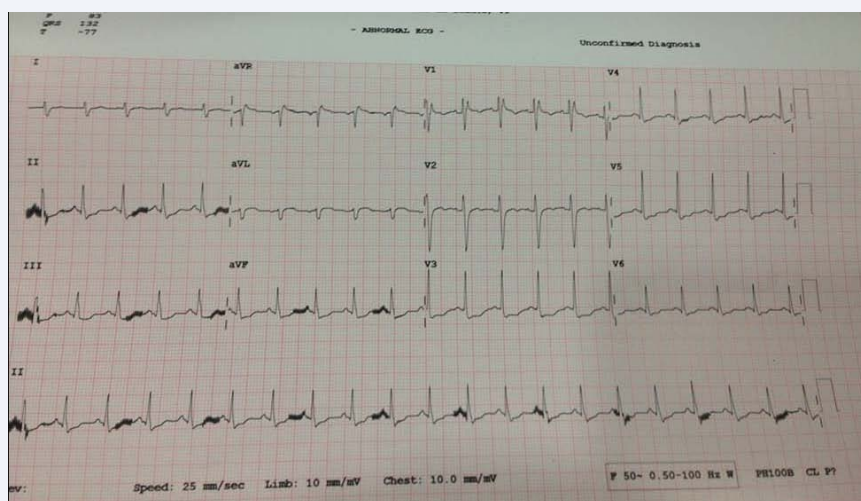


Figure 1 ECG at the time of admission exhibiting non specific ST-T wave changes.

21mmHg (Figure 3). His APACHE (Acute Physiology and Chronic Health Evaluation) II score had worked out to 15, and SAPS (Simplified Acute Physiology Score) II to 34. He was shifted out after 16 days in the ICU. His cardiac function was normal on follow up at 1 month admission. Table 1 highlights the important parameters pre, during and post ECMO.

DISCUSSION

Aluminium phosphide is an extremely lethal poison used as rodenticide and pesticide in grain storage facilities. Like all other agricultural poisons, ingestion is usually suicidal in nature and less commonly accidental [1]. The lethal dose (LD50) is 10mg/kg of body weight. The fatal dose is 0.15-0.5gm; well below the amount ingested by our patient [2,3].

The high mortality (upwards of 70%, even upto 100% in some studies) [4,5] related to Aluminium phosphide ingestion

is due lack of specific antidote and the mechanism of action of phosphine gas, that is, acting at the mitochondrial level; causing cellular hypoxia [6]; heart being the prime target. The average time interval between ingestion and death is reported to be 3 hours (range 1-48hrs); with 95% mortalities occurring within 24 hours: cause cardiac dysrhythmias [6]. Focal myocardial necrosis and membrane action potential changes occur due to altered permeability to sodium, calcium and magnesium leading to various ECG changes and arrhythmias [2].

No different from our case, acute onset cardiovascular collapse has been reported as the commonest clinical presentation [7]. It has been confirmed on autopsy findings also in the form of myocardial congestion and necrosis, vacuolar changes in myocytes and cellular infiltration by neutrophils and eosinophils [8,9]. As mentioned earlier our patient also had non-specific ST-T changes in multiple leads which were reversed as cardiac function

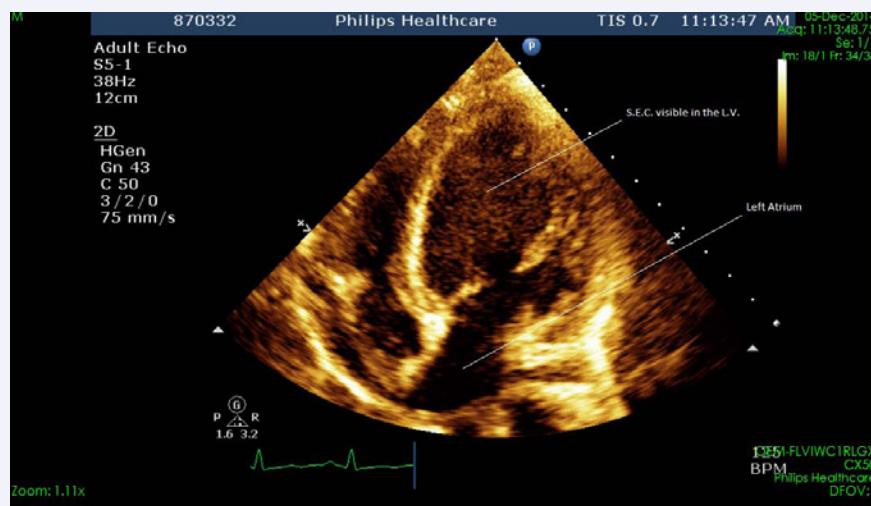


Figure 2 Transthoracic 2D Echocardiography at initiation of ECMO: apical 4- chamber view exhibiting a severely dilated left atria and left ventricle (L.V.) with Spontaneous echo contrast (SEC) in L.V. Not evident without video here is a severe L.V. dysfunction with global hypokinesia and an Ejection Fraction (E.F.) of 10-15%.

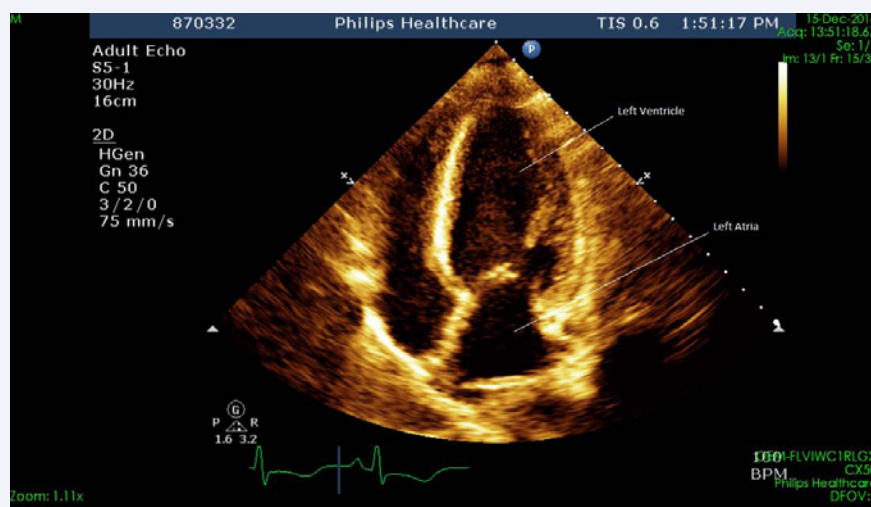


Figure 3 Transthoracic 2D Echocardiography at discharge from I.C.U: improvement in almost all parameters (vis-à-vis fig. 1) including L.V. size and function. E.F. had improved to 40% with almost complete reversal of hypokinesia.

Table 1: Important parameters during different phases of the ICU stay.

PARAMETER	PRE- ECMO	DURING ECMO	POST ECMO
White blood cell count (x 1000/ ml ³)	24.81	8.05	7.52
pH (worst)	7.16	7.30	7.45
Bicarbonate (mmol/L)	12.9	18.7	21.3
Lactate	unrecordable	Less than 2	Less than 2
S. Creatinine (mg/dl)	0.9	1.1	1.9 to 0.7 at discharge
Ejection Fraction	15-20%	10-15% to 25-30%	40%
Vasopressor support (mcg/kg/min)	Norepinephrine 0.8 Epinephrine 0.2	Norepinephrine 0.01 Epinephrine off	Norepinephrine off Epinephrine off
Sensorium	Conscious irritable	Sedated	Conscious alert oriented

improved [10]. The severity of our case was determined on the basis of several factors suggested in literature [11-13] viz. ECG changes, cardiogenic shock, metabolic acidosis with pH < 7.2 and bicarbonate levels less than 15 mmol/L [11], APACHE II and SAPS II scores, need for mechanical ventilation and hyperleucocytosis. Mathai et al [11] reported mortality rates of 73 % in cases with APACHE II scores of more than 8, and 69.2% in cases with SAPS II score in excess of 30. APACHE II score was found to be better correlated with mortality than SAPS II score at admission. The severity of our case was also supported by Shadnia et al [13] who supported SAPS II score as one of the predictors of mortality with mortality of 66.7 % at a mean score of 9.36.

One of the diagnostic hallmarks of cardiac insult in this poisoning is the global LV function [14,15]. It has been reported earlier that cardiac function starts improving by the 5th day [16] with a range lasting up to 10-14 days [17]. Aggressive cardiovascular support during this phase has been suggested to prevent end organ damage due to poor perfusion. It has been mostly done in the form of fluid resuscitation and vasopressor support [2,18,19]. In our case this was successfully provided by early initiation of V-A ECMO as in one earlier reported case [17]. The institution of ECMO in Aluminium Phosphide poisoning can be proposed as an extrapolation of its use in the past in other cardio toxic chemicals [20,21]. Baud et al [20] reported a global survival rate of 79% in their clinical review of literature pertaining to ECMO in cardiotoxic poisonings. They also suggested an algorithm which suggested ECMO as an advanced modality in cardiotoxic poisoning causing multi organ (MOF) failure along with refractory cardiogenic shock. In a clinical review by Johnson et al [21], several case reports from 1989-2012 were reviewed entailing use of ECMO for cardiotoxic poisons like flecainide, tricyclic antidepressants, beta adrenergic receptor antagonists, calcium channel antagonists, digoxin and bupropion. Promising benefit was observed in individual reports and series with the use of ECMO; with a survival of 66% (20 survivors out of total 30) mentioned in the summary. Case reports form the backbone of both reviews as controlled trials in this field are not possible as they would be unethical. Common to both reviews however is the stress on aggressive cardiac support and lack of accurate prognostic markers in cardiotoxic poisonings.

V-A ECMO is a circulatory assist device which uses a centrifugal pump to drive blood out of the venous system and transfuse it into the arterial system thereby providing both Cardiac and

pulmonary support. Circulatory devices are useful in drug induced shock refractory to maximal medical therapy and only when they are used early, before the onset of end organ damage [21] which happens rapidly in severe Aluminium phosphide poisoning. VA-ECMO was chosen over Intra-aortic Balloon Pump (IABP) after reviewing the present literature on IABP in cardiogenic shock [22] and the need for use of ECMO after failure of IABP support in improving cardiac function as mentioned in a case report [17]. Moreover, the complications associated with ECMO like limb ischemia, thrombo and air embolism, bleeding complications, infection risk, thrombocytopenia and hemolysis, are known to occur with IABP also albeit less severe.

ECMO helped us in maintaining good hemodynamic parameters with minimal use of vasopressors and controlled amount of fluids thus limiting the adverse effects of these two; like fluid overload, Acute Respiratory Distress Syndrome (ARDS), end organ damage consequent to high vasopressor usage and more importantly inability to maintain adequate and constant perfusion. One of the probable dilemmas relating to ECMO lie in the criteria for initiation: reversibility of organ dysfunction. There is scarce literature supporting the belief that cardiac insult consequent to this poisoning is reversible. Supporting this scarce literature [16,17], cardiac function in our case started improving after 5 days with near normalization at day 14 prior to discharge.

CONCLUSION

With Aluminium Phosphide, we are facing a deadly toxin with high mortality esp. in the most productive age group. With multiple modalities suggested over the years, no single modality has proven to be successful with conviction. One consensus, though, does exist and that pertains to maintenance of adequate perfusion via aggressive hemodynamic support. With V-A ECMO emerging as an upcoming modality with increasing availability and acceptable risk-benefit ratio, we suggest that it should be further studied as a promising treatment option to tide over the acute phase and act as a "bridge" to recovery of the cardiac function before the onset of multi organ failure (MOF) in a specific subset of patients exhibiting poor prognostic signs like shock refractory to medical therapy, ECG changes including cardiac dysrhythmias, severe metabolic acidosis and adverse APACHE II and SAPS II. However, like in accepted indications of ECMO, the decision should be taken before MOF sets in to improve the effectiveness of this modality.

ACKNOWLEDGEMENTS

I would like to acknowledge the contribution of Dr. Prabhat Dutta, Dr. Akshay, Dr. Sharad Tandon, Dr. Dalip Das and the Critical Care Nursing and support team who worked hard with us on this patient and were instrumental in attaining the desired objective.

REFERENCES

1. Kumar A, Pathak A, Verma A, Kumar S. Accidental inhalational poisoning by multiple pesticides of organophosphorus group in an aged person; an uncommon occurrence. *J Forensic Med Toxicol.* 2012; 29: 78 – 83.
2. A Wahab, MS Zaheer, S Wahab, RA Khan. Acute aluminium phosphide poisoning: an update. *Hong Kong Journal of Emergency Medicine.* 2008; 15: 152-155.
3. Sudakin DL. Occupational exposure to aluminium phosphide and phosphine gas? A suspected case report and review of the literature. *Hum Exp Toxicol.* 2005; 24: 27–33.
4. Chugh SN, Ram S, Sharma A, Arora BB, Saini AS, Malhotra KC. Adrenocortical involvement in aluminium phosphide poisoning. See comment in PubMed Commons below *Indian J Med Res.* 1989; 90: 289-294.
5. Chugh SN, Dushyant, Ram S, Arora B, Malhotra KC. Incidence & outcome of aluminium phosphide poisoning in a hospital study. See comment in PubMed Commons below *Indian J Med Res.* 1991; 94: 232-235.
6. Wahab A, Rabbani MU, Wahab S, Khan RA. Spontaneous self-ignition in a case of acute aluminium phosphide poisoning. See comment in PubMed Commons below *Am J Emerg Med.* 2009; 27: 752.
7. Moghadamnia AA. An update on toxicology of aluminum phosphide. See comment in PubMed Commons below *Daru.* 2012; 20: 25.
8. Tripathi SK, Gautam CS, Sharma PL. Clinical pharmacology of aluminium phosphide poisoning. *Ind J Pharmacol.* 1992; 24: 134–137.
9. Ashok Kumar Jain, Manish Nigam, SD Garg, BP Dubey, A Arora. Aluminium phosphide poisoning autopsy findings. *Journal of Indian Academy of Forensic Medicine.* 2005; 27: 35-39.
10. Arora B, Punia RS, Kalra R, Chugh SN, Arora DR. Histopathological changes in aluminium phosphide poisoning. See comment in PubMed Commons below *J Indian Med Assoc.* 1995; 93: 380-381.
11. Chugh SN, Chugh K, Ram S, Malhotra KC. Electrocardiographic abnormalities in aluminium phosphide poisoning with special reference to its incidence, pathogenesis, mortality and histopathology. See comment in PubMed Commons below *J Indian Med Assoc.* 1991; 89: 32-35.
12. Mathai A, Bhanu MS. Acute aluminium phosphide poisoning: Can we predict mortality? See comment in PubMed Commons below *Indian J Anaesth.* 2010; 54: 302-307.
13. Hosseinian A, Pakravan N, Rafiei A, Feyzbakhsh SM. Aluminum phosphide poisoning known as rice tablet: A common toxicity in North Iran. See comment in PubMed Commons below *Indian J Med Sci.* 2011; 65: 143-150.
14. Shadnia S, Mehrpour O, Soltaninejad K. A simplified acute physiology score in the prediction of acute aluminum phosphide poisoning outcome. *Indian J Med Sci.* 2010; 64: 532-539.
15. Bogle RG, Theron P, Brooks P, Dargan PI, Redhead J. Aluminium phosphide poisoning. *Emerg Med J.* 2006; 23: 3.
16. Bhasin P, Mital HS, Mitra A. An echocardiographic study in aluminium phosphide poisoning. *J AssocPhys India.* 1991; 39: 851.
17. Gupta MS, Malik A, Sharma VK. Cardiovascular manifestations in aluminium phosphide poisoning with special reference to echocardiographic changes. *J AssocPhys India.* 1995; 43: 773–774, 779–780.
18. Elabbassi W, Chowdhury MA, Fachtartz AA. Severe reversible myocardial injury associated with aluminium phosphide toxicity: A case report and review of literature. See comment in PubMed Commons below *J Saudi Heart Assoc.* 2014; 26: 216-221.
19. S.RanjanBajpai. Aluminium Phosphide Poisoning: Management and Prevention: review paper. *Journal of Indian Academy of Forensic Medicine.* 2010; 32: 352-354.
20. Alok Kumar, CV Singh, Seema Dayal, VK Gupta, Suraj Kumar, ArchanaVerma. Acute Severe Suicidal Poisoning by Celphos Powder a Rare Case Report from Rural India. *Journal of Indian Academy of Forensic Medicine.* 2013; 35: 275-278.
21. Frédéric J Baud, Bruno Megarbane, Nicolas eye, Pascal Leprince. Clinical review: Aggressive management and extracorporeal support for drug-induced cardiotoxicity. *Critical Care.* 2007; 11: 207
22. Johnson NJ, Gaieski DF, Allen SR, Perrone J, DeRoos F. A review of emergency cardiopulmonary bypass for severe poisoning by cardiotoxic drugs. See comment in PubMed Commons below *J Med Toxicol.* 2013; 9: 54-60.

Cite this article

Chauhan M, Dewan S, Attawar S, Kamat S, Kumar V, et al. (2015) Successful Treatment of Cardiotoxicity of Aluminium Phosphide Poisoning with Extracorporeal Membrane Oxygenation (ECMO): A Case report. *J Pharmacol Clin Toxicol* 3(4):1056.