International Journal of Advances in Medicine
Nithyapriya TK et al. Int J Adv Med. 2022 Jun;9(6):709-713
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20221356

Original Research Article

Cardiovascular manifestations of acute aluminium phosphide poisoning and their impact on survival

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Received: 12 April 2022
Accepted: 02 May 2022

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ABSTRACT

Background: Aluminium phosphide (AlP) is a common suicidal poison with a high mortality rate due to its cardiovascular impact and lack of antidote. The aim of the study was to describe the electrocardiographic changes and other cardio-vascular manifestations in acute AlP poisoning and evaluate its impact on survival outcomes.
Methods: A prospective cross-sectional study was conducted in a tertiary care hospital including patients who presented with acute AlP ingestion in any form. Patients' vitals and ECG at the time of admission were taken and outcomes of survival were identified. A descriptive study of echocardiography was also done. The clinical parameters were correlated with the survival outcomes.
Results: Fifty patients were included with 30 males and 20 females. The consumption of AlP in tablet form caused more hemodynamic compromise (hypotension and high anion gap metabolic acidosis) as compared to the powder form. ECG changes were seen in 42% of the cases, the most common finding was prolonged QTc interval (26%). The mortality was 30%. Hypotension, bradycardia, and QRS widening were found to be significant predictors of mortality ($p<0.05$). Echocardiography was performed for 10 patients, of which, one had right ventricular dysfunction and two had left ventricular dysfunction.
Conclusions: AlP tablets are more lethal and hemodynamically compromising than AlP powder. Hypotension, bradycardia, and QRS widening are significant predictors of mortality. Direct cardiotoxicity leads to ECG changes, of which, QTc prolongation is the most common.

Keywords: Celphos, AlP, Cardiac poison, Cardiovascular, Survival

INTRODUCTION

The poisoning with AlP, commonly known as celphos, is observed especially in North Western and central parts of India. This is attributable to its widespread use as a fumigant in agricultural and non-agricultural fields. The substance is available as a combination of AlP (56%) with aluminium carbonate which prevents the self-ignition of phosphine with moisture.[1] Hence, it is considered to be highly toxic when ingested from newly opened containers rather than the ones exposed to moisture.[2]

The mortality of AlP poisoning is reported to be as high as 59.3%, owing to the lack of a proper antidote. The lethal dose for a moderately built individual is as low as 150-500 grams.[2] The estimated interval from ingestion to death is reported to vary from 1hr to 2 days.[3] The mechanism of cell injury is due to the release of phosphine gas from AlP which is cytotoxic and causes free radical-mediated injury. Phosphine is believed to cause injury both by a specific inhibitory effect on mitochondrial cytochrome-c oxidase and by inhibiting cellular enzymes by its reducing effect.

Hydroxyl radicals cause lipid peroxidation and protein denaturation. When phosphine gas is inhaled, it affects the kidney, lungs, liver, and gastrointestinal tract as well, in addition to its major effect on the cardiovascular system.[3] Phosphine gas, having a high vapor pressure, easily permeates porous materials. It causes a direct toxic effect on cardiac myocytes and causes circulatory collapse.

Cardiovascular manifestations of AlP poisoning are reported as tachycardia, bradycardia, pulmonary edema, raised JVP, decreased heart sounds, and an S3 gallop. Electrocardiographic (ECG) changes are varied including ST-T changes, arrhythmias, LV dysfunction, bundle branch blocks, and QTc prolongation.[4,5]

Although the pathway of cellular damage by AlP leading to hemodynamic instability and death has been known for a long time, the early changes in ECG and the hemodynamic parameters at admission which may predict mortality and which may help prioritize intervention remains unknown. We have conducted a prospective cross-sectional study to describe the early ECG changes and cardiovascular manifestations of acute AlP poisoning and evaluate their impact on survival outcomes.

METHODS

A cross-sectional study was conducted at KPS institute of medicine, GSVM medical college, Kanpur from December 2019 to October 2021. Patients in the age group 15 years to 60 years, who have ingested AlP in any form, attended the medicine Outpatient department or were admitted to the medicine ward during the study period were included in the study. We excluded patients who had a history of cardiac diseases, had undergone any cardiac surgery, had electrolyte imbalances leading to cardiac dysfunction which included hypokalaemia (<3.5 mEq/l), hyperkalaemia (>5.5 meq/l), hypocalcaemia (<8.5 mg/dl), hypercalcaemia (>10.5 mg/dl) and hypomagnesemia (<1.46 mg/dl), had also ingested other poisons affecting cardiovascular systems such as cyanide, atropine, and digoxin, had severe hypothyroidism (serum TSH >20 mIU/l), or had severe anaemia (Haemoglobin less than 7 g/dl). Written informed consent was taken from the patients or their guardians before inclusion in the study. The study received ethical clearance from institute ethics committee (EC/BMHR/2021/93).

The clinico-demographical details were noted in the study proforma which included the name, age, sex, address, the form of AlP ingested, the duration of ingestion, and vitals at the time of the first presentation including blood pressure (BP), pulse rate, respiratory rate, blood oxygen saturation (SpO_2), temperature, and random blood sugars (RBS). All the patients underwent ECG at the time of the first presentation. The ECG was assessed for rhythm, QRS widening, ST-T changes, and corrected QT (QTc) interval. An Echocardiography (ECHO) was done in patients with ECG changes, once the patients were hemodynamically stable. The ECHO was descriptively analysed for left ventricle (LV) dysfunction with left ventricle ejection fraction (LVEF) and right ventricle (RV) dysfunction with Tricuspid annular plane systolic excursion (TAPSE) and RV fractional area change. RV fractional area >35 % and TAPSE >18 mm considered to be normal. The survival outcomes in the study population were noted and correlated with ECG changes and hemodynamic parameters at the time of admission.

Statistical analysis

Statistical analysis was done using Stata/MP 16 (StataCorp LLC, Texas, USA). Descriptive statistics were used in the form of mean ± standard deviation, median, and absolute frequency. The Chi-square test was used for non-parametric distribution and the students' t-test was used for parametric distribution. Spearman and Pearson correlation coefficients were used, where appropriate. A $p<0.05$ was considered statistically significant.

RESULTS

Sixty-three patients of acute AlP poisoning presented to the institute during the study period, of which 13 patients were excluded from the study. The study included 50 patients. The mean age of the study population was 29.8 years with a range of 18 years to 55 years. Table 1 describes the clinico-demographical factors and outcomes in the study population.

Table 1: Descriptive details of clinico-demographical factors.

Demographical variables	Frequency (%)
Gender	
Male	30 (60)
Female	20 (40)
Celphos formulation	
Tablet	25 (50)
Powder	25 (50)
Pulse rate (per min)	
Bradycardia (<60)	5 (10)
Normal (60-100)	17 (34)
Tachycardia (>100)	28 (56)
Blood pressure	
Hypotension	27 (54)
Normotension	23 (46)
Saturation (SpO_2)	
Less than 95%	18 (36)
More than or equal to 95%	32 (64)
Random blood sugar (mg/dl)	
Less than 70	7 (14)
70 to 200	36 (72)
Greater than 200	7 (14)
Haematocrit (%)	
Less than 42	36 (72)
42 to 54	12 (24)
More than 54	2 (4)
Total leucocyte count (per cm^3)	
Less than 4000	2 (4)
4000 to 10000	12 (24)
More than 10000	36 (72)
Outcome	
Expired	15 (30)
Alive	31 (62)
Abscond	4 (8)

In the study population, 50% (25/50) of patients took AlP in the form of tablets with a mean of 2.4 tablets (range 0.5 to 9). The patients who consumed AlP in the form of tablets were found to have significantly high hemodynamic instability in the form of hypotension (p=0.02), metabolic acidosis (p=0.019), and ECG changes (p=0.002) than those who consumed it in powder form. The patients who expired due to consumption of AlP tablets (9 patients) consumed a mean of 3.67 tablets as compared to those who survived who consumed a mean of 1.64 tablets. This difference was found to be statistically significant (p=0.001). Of the 23 patients who presented after consumption of AlP in powder form, 6 patients (26%) expired.

The mean systolic BP in patients was 92 +/- 35 mm Hg and the mean diastolic BP was 57±29 mm Hg. Twenty-one patients (42%) had some form of ECG changes at the time of presentation (Figures 1 and 2). Table 2 summarizes the various ECG changes observed. The prolonged QTc interval was the most common finding, seen in 13 patients.

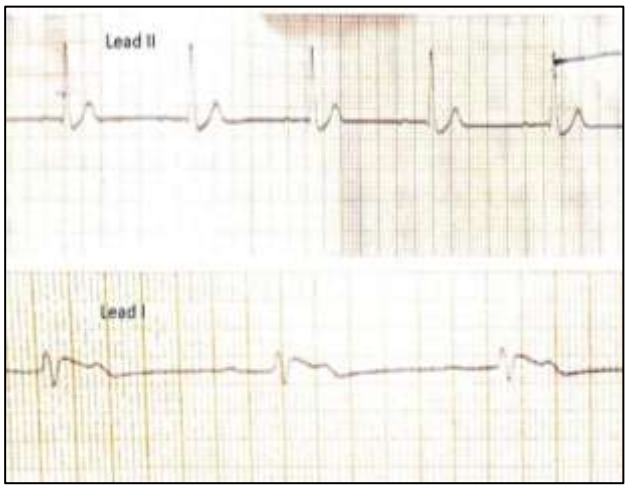

Figure 1: ECG of a patient with acute AlP poisoning with junctional bradycardia with a rate of 45/min.

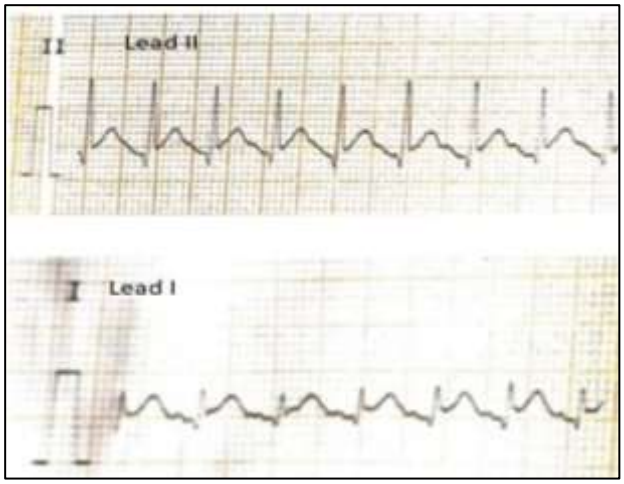

Figure 2: ECG of a patient with acute AlP poisoning with narrow complex tachycardia.

An echocardiography was done in 10 out of 21 patients with ECG Changes. Two patients had an LVEF <55% while others had normal LV function. Only one patient had a TAPSE of 16 mm and RV fractional area change of 33%, suggesting RV dysfunction.

Fifteen patients (30%) expired due to AlP poisoning. The mean duration after ingestion of AlP to expiry was 22.1 hrs with a range of 2 hrs to 72 hrs.

Table 2: Summary of electrocardiographic (ECG) changes observed at presentation in acute aluminium phosphide poisoning and their correlation with survival outcomes.

Variables	N (%)	Survival outcomes*		P value
		Expired	Alive	
ECG changes				
No	29 (58)	6	21	0.07
Yes	21 (42)	9	10	
Rhythm abnormality				
No	47 (94)	13	30	0.24
Yes	3 (3)	2	1	
ST depression				
No	48 (96)	15	29	0.45
Yes	2 (4)	0	2	
ST elevation				
No	40 (80)	13	25	0.47
Yes	10 (20)	2	6	
QRS widening				
No	47 (94)	12	31	0.03
Yes	3 (6)	3	0	
QTc interval				
Normal	37 (74)	8	25	0.054
Prolonged	13 (26)	7	6	

*Excluding 4 patients in whom survival outcomes are not known.

Table 3: Correlation between various clinical parameters and mortality in patients of acute AlP poisoning.

Clinical parameters	Survival outcomes*		P value
	Expired	Alive	
Hypotension	14	10	<0.001
Bradycardia	5	1	0.03
Tachycardia	6	20	0.1
Hypoglycemia	2	3	0.3
Hyperglycemia	4	3	0.14
ECG changes			
Prolonged QTc	7	6	0.054
QRS widening	3	0	**0.03**
ST elevation	2	6	0.47
ST depression	0	2	0.45
Abnormal rhythm	2	1	0.24

Table 3 summarizes the correlation values between various hemodynamic parameters and ECG changes with mortality. Bradycardia and hypotension at presentation were significant predictors of mortality in patients with

acute AlP poisoning. Of various ECG changes, widening of QRS interval was a significant predictor of mortality.

DISCUSSION

AlP is a widely used fumigant in the agricultural field and is a major suicidal poison in India. The mortality rates in AlP poisoning have been reported to be as high as 77.2% with an estimated interval from ingestion of poison to death ranging from 3 hrs to 1-2 days.[6,7] The high mortality is reportedly due to rapid hemodynamic compromise and the unavailability of an antidote. Similar to the previously reported data on mortality rates, we found that 30% of the patients presenting with AlP poisoning expired. The mean duration from ingestion of AlP to death in our study was 22 hrs with a range of 2 hrs to 72 hrs. The small window available for any life-saving intervention in this population generates the need to identify early predictors of mortality. Cardiac toxicity and resultant hemodynamic compromise are the major cause of mortality, but deaths due to adult respiratory distress syndrome, liver failure, gastrointestinal ulcerations and bleeding have been reported.[3] Although neurologic manifestations rare, ischemic stroke as delayed manifestation has reported.[8]

We found that the consumption of tablets leads to higher mortality as compared to the powder form. This is in agreement with the previously reported data that the consumption of AlP from unopened containers is more lethal as compared to open powder form.[2,3] A study conducted by Chugh et al showed that 60% of the study population who took AlP as tablets developed hypotension and 10% developed ECG changes , while those who consumed it as powder neither developed any systemic upset nor had mortality.[6] The findings of our study also suggest that tablet formulation leads to significantly higher ECG changes and hypotension as compared to powder form. Our findings differed in that consumption of AlP in powder form also leads to mortality in 26% of the cases. The difference may be because of the change in the amount of AlP in the powder form over time, as the study conducted by Chugh et al dates back to the 1990s.

Cardiotoxicity in acute AlP poisoning is present in the form of myocarditis, arrhythmias, and conduction disturbances, with ECG changes depicting toxic myocarditis, electrolyte disturbances, and ischemia. ECG changes may present as ST-segment changes and rhythm abnormalities but are usually temporary and revert to normal once the patient is asymptomatic.[4] Some studies do suggest the persistence of ECG changes.[9] Previous studies on ECG changes in AlP poisoning have found that 45% of the study population had dysrhythmia, 45% had ST elevation, 35% had prolonged QTc interval, and 20% had bundle branch blocks.[5] In our study, ECG changes were seen in 42% of the cases with prolonged QTc interval as the most common finding. Since we had excluded patients with electrolyte abnormalities, the ECG changes in our study could be attributed to the direct cardiovascular effects of AlP. In addition, we found that QRS widening was a significant predictor of mortality. Elgazzar et al have evaluated ECG and ECHO changes in 90 patients with AlP poisoning.[10] They found that ECG changes were significantly different in survivors and non-survivors. They also found that the survivors had a higher mean LVEF than non-survivors (50.86±6.30% vs. 26.52±7.64%, respectively, $p<0.001$) and a lower percentage of global LV hypokinesia (4.8% vs. 94.2%, $p<0.001$). Although all patients in our study who presented with QRS widening expired and ECG changes were higher in non-survivors than survivors (47.4% vs 22.2%, respectively), overall, ECG changes did not differ significantly between survivors and non-survivors. This may be attributed to the small sample size of our study. Echocardiography could only be done in a limited number of patients in our study and showed LV dysfunction in 20% of the patients.

The mortality in acute AlP poisoning had been associated in earlier studies with the increased serum creatinine concentration, low pH and low serum bicarbonate levels, need for mechanical ventilation, need for vasoactive drugs, low acute physiology and chronic health evaluation (APACHE) score, Glasgow coma scale (GCS)<13, and a low systolic BP.[2,4,11] In our study, we found that mortality is significantly associated with bradycardia and hypotension at the time of presentation. There was no significant association between mortality with tachycardia and changes in blood sugar levels.

Our study is limited by the inherent limitations of a cross-sectional study. The sample size of our study is also low, as the study was interrupted by the COVID-19 pandemic. We did not evaluate the trend of ECG changes in the patients throughout their management. Also, ECHO could not be done in a significant number of patients due to logistic issues.

CONCLUSION

AlP is a commonly used suicidal poison that is highly fatal due to its direct cardiotoxic effect. The consumption of tablet form is more lethal and hemodynamically compromising than powder. Hypotension, bradycardia, and QRS widening are significant predictors of mortality. Direct cardiotoxicity leads to ECG changes, of which, QTc prolongation is the most common. This may lead to rhythm disturbances later on leading to hemodynamic compromise. A study is required to evaluate interventions aimed at preventing mortality in such patients.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Nithyapriya TK, Giri R, Sachan M, Khan AM. Cardiovascular manifestations of acute aluminium phosphide poisoning and their impact on survival. Int J Adv Med 2022;9:709-13.