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Original Research Article

Cardiovascular profile of aluminium phosphide poisoning and its clinical significance

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ABSTRACT

Background: Aluminium phosphide is a solid fumigant pesticide and it has currently aroused interest with increasing number of poisoning cases in past three decades. Over the time it has become an effective and widely used medium for suicide and homicide. Aluminium phosphide has highly effective killing power. Death is due to its direct toxic effect over the heart leading to peripheral circulatory failure .Aluminium phosphide poisoning affects the most of the organs. Early symptoms include nausea, vomiting, retrosternal and epigastric pain, dyspnea, anxious, agitation and smell of garlic breath.
Methods: 50 patients, who were admitted in MICU, following consumption of aluminium phosphide tablets were included in the study. Patient's clinical evaluation was done as per standard. PaO_2 was noted with pulse oxymeter. Troponin I, ECG and echo of the patients was done to study the cardiac toxicities and pathological reports were correlated.
Results: Out of 50 cases, ECG was normal in 20 cases and abnormal in 30 cases-sinus tachycardia was most common finding (24%) while heart block was least (4%). On echo, hypokinesia was seen in 40% cases, decreased ejection fraction in 8% cases and normal echo was seen in 12% cases. Serum troponin test was positive in 26%. Out of 50 cases, 19 died and rest 31 cases survived.
Conclusions: $AgNO_3$ test, ECG and pulse oxymetry are bed side, cost effective tools and should be done in all cases. Echocardiography is a useful tool to evaluate cardiac function and cardiac anatomy. Whenever it is available, it must be done in cases of aluminium phosphide poisoning. Serum troponin-I test should be done to assess significant myocardial damage. Thus, proper clinical work out along with relevant investigations and management as per standard protocol may save many more lives.

Keywords: Aluminium phosphide, $AgNO_3$ test, Cardiac toxicity, Serum troponin

INTRODUCTION

Agrochemical poison is a major public health problem in developing countries particularly in setting of low education and poor regulatory frameworks. Aluminium phosphide is a solid fumigant pesticide and it currently aroused interest with increasing number of poisoning cases in past three decades. Due to its increased use for agricultural and non-agricultural purpose, easy availability has increased its misuse to commit suicide. Initially the poisoning was accidental but gradually it became an effective and widely used medium for suicide and homicide. A suicidal, accidental and homicidal poisoning may occur at all times. The choice depends upon its availability, cost and effectiveness. The green revolution in India on one hand opened door for prosperity but had something hidden in it to ruin the human life. Among the large number of poisoning related

deaths in India most of them have been due to aluminium phosphide poisoning (ALP). Aluminium phosphide has highly effective killing power; even half tablet can kill a person in few hours. Death is due to its direct toxic effect over the heart leading to peripheral circulatory failure and hence it has been said to be an "agent for sure death". Death may occur in as early as 1-2 hours, often patients die during shifting from home to MICU wards. Mortality depends upon the number of tablets taken, its freshness, tablet vomited or not and time elapsed between ingestion and hospitalization and treatment and associated disease. The outcome is often fatal as its specific antidote is not available to the best of our knowledge, hence enough medical and paramedical staff, multipara monitor and all emergency medicines, should be readily available.

Aluminium phosphide is reported to be highly toxic when consumed from a freshly opened container and the fatal dose for an average sized individual is 150 to 500 mg. Death is reported to result from profound shock, myocarditis and multiorgan failure.

Since 1992 when aluminium phosphide became freely available in Indian market, it has reportedly overtaken all other forms of poisoning, cases like organophosphorus, barbiturates and zinc phosphide poisoning.

The number of deaths in central India is less but constantly increasing and this has inspired us to carry out the study of cases of aluminium phosphide poisoning, admitted in MICU ward, M. Y. Hospital with special reference to cardiac involvement in the institution.

According to R. Katria, Amitra et al the exact cause of ECG changes and circulatory collapse in ALP poisoning is not known.[1]

It has been postulated that elemental phosphorus acts as a general protoplasmal poisoning interfering with the enzyme system.[2] In inhibits incorporation of the aminoacids into myocardial proteins and this metabolic effect may be responsible for cardiac dysfunction. A direct toxic effect of phosphorus over myocardium contractibility and lowering of systemic vascular resistance which is unresponsive to adrenergic agent.[3] The most important factor for cardiac involvement appears to be systemic toxic effect of phosphine gas as it is known that it causes non-competitive inhibition of cytochrome oxidase in the mitochondria in experimental animals.[4]

The mechanism of death from ALP appears to be myocarditis, as evidenced by cardiogenic shock and ECG abnormalities in all those who ultimately died. ECG abnormalities appeared before a substantial fall in blood pressure in number of cases, even in those cases where conduction blocks or bradyarrhythmia appeared. G.S. Wander, Arora S et al found acute pericarditis in ALP poisoning.[5]

The various ECG changes observed were ST-T wave changes (elevation/depression), supraventricular tachycardia with conduction defects, atrial fibrillation, A-V dissociation and LBBB.[6]

According to Nagar KS et al, it would be logical to presume these changes were due to deleterious effects of poisoning on myocardium.[7] ST-T changes do not fit into the distribution area of any specific coronary artery, hence appear to be due to focal myocardial damage as a result of this poison. The reversibility of ECG changes denote that although the effect is focal yet it is due to some reversible factors such a change in trans-membrane action potential as a result of ionic disturbances brought on by focal myocardial involvement.

Sepaha GC et al found increased SGOT levels suggesting myocardial necrosis abnormalities in X-ray chest 45% patients who had frank pulmonary edema. Other biochemical alterations are decreased serum bicarbonate and serum cholinesterase and increased blood urea, serum creatinine, bilirubin, SGPT.[8]

Bajaj R. et al has described aluminium phosphide toxicity early as well as late. Early toxicity (1st 24 hours) includes severe acidosis, hypokalemia, and severe peripheral circulatory shock. Most important late toxicity (after 24 hours) was ARDS.[9]

No specific treatment is known. Depending upon the presenting signs attention must be given to maintain the blood pressure or control of pulmonary edema. The use of oxygen should be started early. If the pulmonary edema persists or recur steroid therapy or uses of ACTH are indicated because of their value in pulmonary edema caused by oxides of nitrogen.[10] Most of the patients did not respond to dopamine infusion to combat the shock. Hemodialysis was given to one patient who developed acute renal failure and the patient survived.[11]

Laha NN et al have supported use of magnesium sulphate. Early induction of vomiting with injection magnesium sulphate (1 ampoule of 20%, 2 ml 6 hours) led to good prognosis and mortality is reduced from previous 100% to 37%.[11,12]

Treatment was mainly with hydrocortisone. Injection digoxin was used if no arrhythmias were there. This regimen helped in reducing mortality from previous 100% to 37%. The treatment also included routine measure like gastric lavage, I.V. dopamine drip, I.V. lasix, antibiotics and sodium bicarbonate.

This study was conducted in MICU ward, department of medicine, M. Y. Hospital, Indore, India from May 2015 to October 2015. The aim of the study was to register 50 cases of aluminium phosphide poisoning admitted in MICU ward as per selection criteria, to perform detailed clinical work up and relevant investigations in these cases (as per proforma) and put them on standard treatment

protocol. Also to find out various co-morbidities particularly cardiovascular involvement in these cases and finds their significance.

METHODS

Observational and non-interventional study was conducted in department of medicine, M. Y. Hospital, Indore, Madhya Pradesh, India on 50 enrolled patients who were admitted in MICU, following consumption of aluminium phosphide tablets.

50 patients, who fulfilled the inclusion criteria and having none of the exclusion criteria and who/their relatives gave consent to participate in this study were included in the study.

Inclusion criteria

- 50 patients with history of exposure to aluminium phosphide poisoning
- Age and gender of patients age 15 years to70 years, both male and female patients
- Patients who were willing to undergo this study their written and informed consent was taken.

Exclusion criteria

- Pre-existing cardiac, respiratory, hepatic, metabolic or renal disorder, multisystem disease
- Concomitant exposure to another poison
- Prisoners and orphans were not included
- Non-willing/uncooperative patient were not included.

Mean, standard deviation, probability and coefficient of correlation was done by SPSS20.0 statistical software.

Methodology

All the patients and/or his/her legally acceptable representative were provided complete information regarding the aims and objectives, procedure of the study. A written Informed consent was taken from each patient or the relative.

Patient's clinical evaluation was done as per standard (proforma) wherein details like exposure to aluminium phosphide tablets, symptoms, physical examination and relevant investigations- Hb%, CBC, urine- routine and microscopic exam, liver function test, renal function test, random blood glucose, serum electrolytes, ECG (12 lead standard ECG), X-ray chest PA view, 2-D echo doppler were done. $Pa0_2$ was noted with pulse oxymeter.

Pathological reports were done with help of pathology department, M. G. M. Medical College and M. Y. Hospital, Indore, Madhya Pradesh, India. A complete psychiatric evaluation of patients was done after recovery from acute illness wherever it was feasible.

Complications were labeled as below

- Shock, if systolic BP < 90 mmHg
- ARF, if serum creatinine > 2 mg/dL
- Hepatitis, if serum bilirubin > 2 mg/dL or SGPT > 120 U/L
- Respiratory failure, if SpO2 < 60 mmHg.

RESULTS

50 patients were enrolled in the study, 32 were male and 18 were females. 15 cases (30%) were in age group 21-30 years, Another 15 cases (30%) were in age group 31-40 years. Thus, maximum 30 cases (60%) belonged to age group 21-40 years (Table 1).

Table 1: Distribution of cases of celphos poisoning in various age groups (n=50).

Age (years)	No. of cases	Percentage
15-20	11	22%
21-30	15	30%
31-40	15	30%
41-50	7	14%
51-60	0	0%
61-70	2	4%

Table 2: Distribution of cases as per status of systemic blood pressure (normal/hypotension/shock/ hypertension (n = 50).

B. P. Normal				Shock (BP < 90 mmHg with cold extremities			
Male		Female		Male		Female	
No.	%	No.	%	No.	%	No.	%
4	8	2	4%	12	24%	4	8%

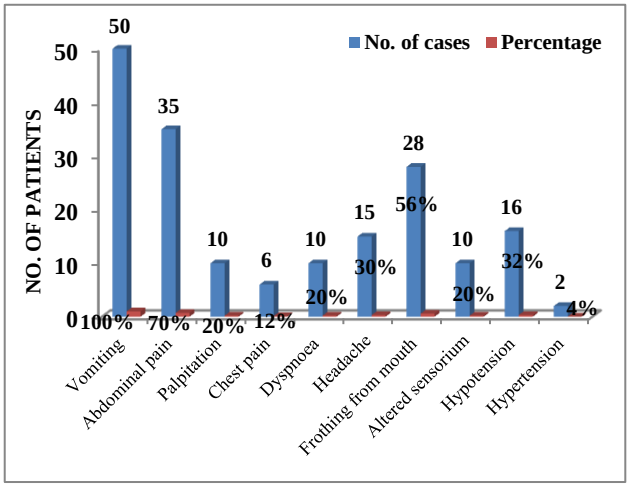


Figure 1: Pattern of clinical presentation in 50 cases of celphos poisoning (n = 50).

Vomiting (l00% cases) and abdominal pain (70% cases) were most common symptoms. While palpitation,

dyspnoea, altered sensorium were seen in 20% cases (Figure 1).

BP was normal in 6 cases only (Table 2). Only 2 cases (4%) had systemic hypertension. On digital pulse oximetry 31 cases (62%) had normal PaO_2; (95-I 00%) while 19 cases (38%) had PaO_2 < 95%. Silver nitrate strip test was positive in 46 cases (92%) while test with $AgNo_3$ on gastric lavage sample was positive in 47 cases (92%).

ECG was abnormal in 30 cases out of 50; sinus tachycardia was seen in l2 cases while heart block was seen only in 2 cases (Figure 2, 4-8). TLC (4000-l2000/mm^3) was raised in 30 cases (60%). Serum troponin I test was positive in 26%cases (Table 3).

Table 3: Distribution of 50 cases of celphos poisoning according to status of S. troponin-I test (n = 50).

S.troponin-i test positive (> 0.10ng/ml)				S.troponin test negative (<0.01 ng/ml)			
Male		Female		Male		Female	
No.	%	No.	%	No.	%	No.	%
9	18%	4	8%	23	46%	14	28%

Table 4: Distribution of cases of celphos poisoning according to arterial blood gas analysis (ABG) (n = 50).

ABG	Value			
	Normal		Abnormal	
	No.	%	No.	%
PH(7.38-7.44)	17	34%	33	66%
PCo_2 (31-42 mmHg)	19	38%	31	62%
PO_2(85-95 mmHg)	20	40%	30	60%
Bicarbonate (24-26 mmol/lit)	6	12%	44	88%

Table 5: Echocardiography findings in celphos poisoning cases.

Abnormal (n = 24)	No. of cases	Percentage
Hypokinesia (global)	20	40%
Decreased ejection fraction	4	8%
Pericardial effusion	0	0%
Normal (n = 6)	6	12%

*Whenever feasible; Those who died in 24 hours or absconded Echo could not be done; Hence ECHO study could be done in 30 cases only; **Commonly observed abnormal findings on Echo.

Arterial blood gas analysis: most common abnormality was acidosis in 44 cases (Table 4).

Out of 50 cases, echocardiography could be done in 30 cases (60%). Most important echo finding was: hypokinesia (global) in 40% cases (Table 5). Only 6% cases had raised blood urea and 8% cases had raised serum creatinine.

Out of total 50 cases. 19 died (l5 male and 4 female). Rest 31 cases, who survived (I 7 were male and I4 were female) (Figure 3).

Table 6: Correlation between pH value and ecg abnormality.

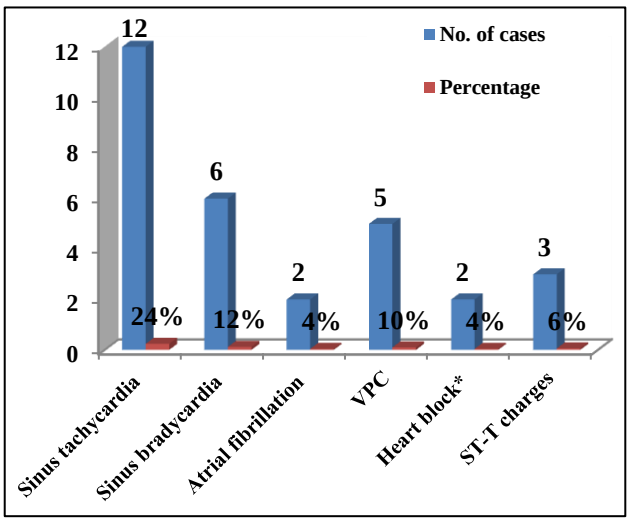
Crosstab (P^H value and ECG)				
		ECG		Total
		-	+	
P^H	1.00	7	9	16
	2.00	3	24	27
Total		**10**	**33**	**43**

Table 7: Correlation between HCO_3- value and ECG abnormality.

Crosstab (HCO_3)				
		ECG		Total
		-	+	
HCO_3	1.00	0	2	2
	2.00	10	31	41
Total		**10**	**33**	**43**

Table 8: Correlation between trop-I and ECG abnormality.

ECG TROP-I Cross tabulation				
		TROP-I		Total
		-	+	
ECG	1.00	25	13	38
	2.00	12	0	12
Total		**37**	**13**	**50**



*Included cases with complete heart block, 1st or 2nd degree heart block and bundle branch block cases.

Figure 2: Various ECG changes seen in patients of celphos poisoning (n = 50).

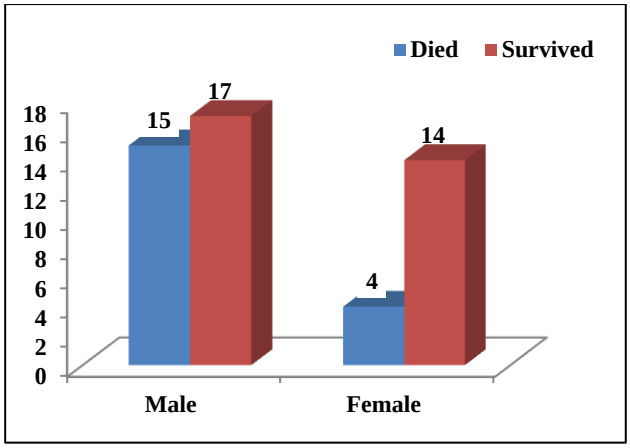


Figure 3: Outcome of patients of celphos poisoning in 50 patients.

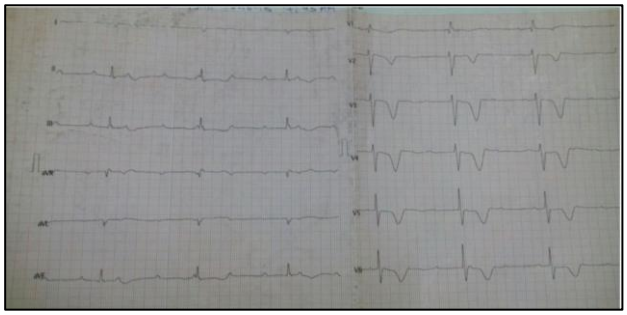


Figure 4: AV dissociation, complete heart block, T inversion from V2- V6, RBBB (rSR' pattern inV1).

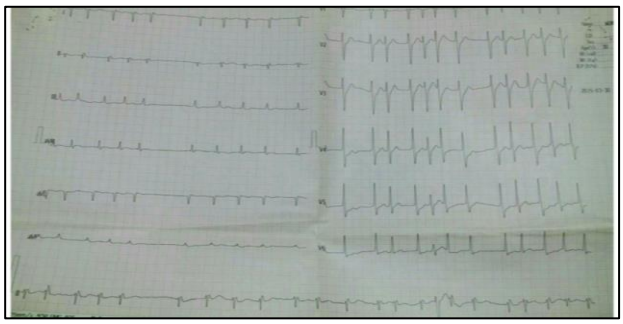


Figure 5: Varying R-R interval, atrial fibrillation with fast VR.

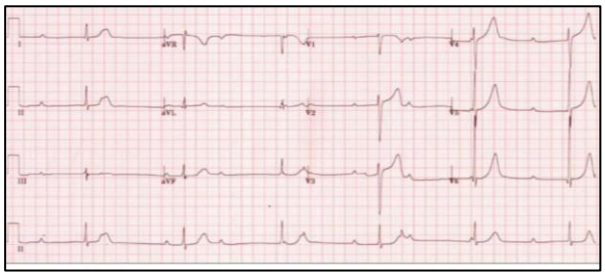


Figure 6: Complete heart block.

DISCUSSION

Several studies have been done in India as well as abroad on celphos poisoning. Various workers have studied clinically as well as by performing various investigations. Since the population varies from area to area, clinical presentation as well as outcome of the cases may be different. Even the compound aluminum phosphide may vary in amount whether tablet is fresh or exposed to air, vomiting, reaching to hospital in time and associated co-morbidity. Various studies have been done in this country and abroad in this direction have been reviewed by us. Sepaha GC et al studied 20 cases of celphos poisoning in M. Y. Hospital, Indore.[8] Raman et al, Singh S et al, Nagar KS, Ram A et al, Laha NN et al, Wander GS, Arora S et al and Chugh SN have studied aluminium phosphide poisoning cases in Central India and other parts of the country.[5,7,11-16]

ln present study 60% patients were in age group 21-40 years and 64% were male. There is no correlation between sex and ECG findings (p = 0.639). Mode of presentation has not changed significantly with passage of time. Commonest symptom being vomiting noted in 50 cases (l00%), abdominal pain in 35 cases (70%), headache in 15 cases (30%), palpitation in 10 cases (20%), dyspnoea in l0 cases (20%), 28 cases (56%) had frothing from mouth, I6 eases (32%) had hypotension and altered sensorium in I0 eases (20%) which were similar to the findings in study of Laha NN et al.[12] On arterial blood gas analysis, pH was abnormal in 66% cases, PCO_2 was abnormal in 62% cases, PO_2 was abnormal in 60% cases and bicarbonate was abnormal in 84% cases.

There is a significant difference between PH level and ECG finding (p = 0.014) however no significant difference found between HCO3 level and ECG finding (p = 0.425) (Table 6 and Table 7). Findings of this study correlates well with Chugh SN et al, who on blood gas analysis showed acidosis (pH less than 7.3), hypoxaemia (PO_2 Less than 50 mmHg) and hypocarbia (PCO_2 less than 37 mmHg) and bicarbonate (less than 19 mEq/Lit.).[15]

In present study blood urea (10-50 mg/dl) was raised in 3 cases (6%) and serum creatinine (0.8-1.6 mg/dl in 4 cases (8%) only which slightly differ from Singh S et al who found increased blood urea, serum creatinine, bilirubin and transaminase in half of pt. out of 11.[11] ECG was abnormal in 30 cases out of 50. Various ECG Changes recorded were: sinus tachycardia in l2 cases (24%), sinus bradycardia in 6 cases (l2%), ventricular premature beat in 5 cases (l0%) and heart block was seen in 2 cases (4%) which correlated well with findings of Raman R et al according to whom most consistent ECG finding was ST-T abnormality in the form of ST segment inversion/depression, S. tachycardia, SVT, complete heart block with idiojunctional rhythm, idioventricular rhythm, LBBB, 2nd degree morbitz type II A.V block.[13]

Out of 50 cases, echocardiography could be done in 30 cases (60%). Commonly observed important Echo findings were: hypokinesia (global) in 20 cases (40%). Decreased ejection traction in 4 cases (8%) and normal echo in 6 cases (12%) which are really important findings. Serum troponin-I test was done in all cases. However it was positive in 26% cases (indicating significant myocardial damage). There is significant difference between ECG finding and troponin-I ($p = 0.019$) while There is no significant difference between age group and Troponin-I level ($p = 0.573$) (Table 8).

Out of total 50 cases. 19 died (38%). Rest 31 cases, who survived (61 %). Mortality rate was low in our study than reported by various workers. Singh S et al 73% mortality, Sepaha GC et al 85% mortality, Siwach SB et al 70% mortality, Ram A et al, 72.72% mortality and Chugh SM et al who reported 66% mortality in their studies.[8,11,14,15] The correlations were all statistically significant with 'p' values less than 0.05

CONCLUSION

Though times have changed but presentation and mortality depends on number of tablets consumed, whether tablet is fresh or exposed to air, vomited or not and delay in getting hospitalized at some center with facilities for proper treatment may determine the outcome. Mode of presentation has not changed significantly with passage of time.

Pulse oximetry is a bed side, cost effective tool and should be done in all cases. Silver nitrate test is economical and handy test which can be done bedside. This test was done as breath test as well as in gastric lavage sample. Hence it should be done in all cases. ECG should be done in all the cases to find out exact cardiac abnormality, so that proper treatment can be instituted in time. Echocardiography is a useful tool to evaluate cardiac function and cardiac anatomy. Whenever and wherever it is available, it must be done in cases of aluminium phosphide poisoning to supplement ECG.

Arterial blood gas analysis another useful test, though it is relatively costlier and not available in peripheral centres but should be done at all tertiary care centres and district hospitals. Renal function test and serum troponin-I test can be done to know baseline level of S. creatinine and urea, so as to assess magnesium sulphate toxicity and management of myocardial infarction if suspected. Thus, it was concluded that proper clinical work out along with relevant investigations as mentioned in our proforma and management as per standard protocol may save many more lives. Still larger studies are required in this direction at various centres in this direction.

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Ethical approval: The study was approved by the institutional ethics committee

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