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Original Research Article

Management of Aluminium Phosphide Poisoning with Antioxidants

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Abstract

Background: The ingestion of Aluminium phosphide leads to considerable oxidative stress. In this study, we assessed the management of Aluminium phosphide poisoning in patients utilizing Glutathione, NAC, and $MgSO_4$.

Methods: This is prospective study included criteria comprised all subjects presenting with Aluminium phosphide poisoning. The treatment protocol involved administering antioxidant NAC, Glutathione, and $MgSO_4$ to all patients. The incidence of secondary complications, such as multiorgan dysfunction syndrome as well as hepatic failure was evaluated.

Results: A total of 30 patients were recruited. An increase was seen from day 1 to day 3 in Total Bilirubin (mean diff: -3.44); albumin (mean diff: -0.086); Globulin (mean diff:-0.103); aspartate aminotransferase (mean diff: -71.86); alanine aminotransferase (mean diff: -59.46) and gamma-glutamyl transferase (mean diff: -20.40) whereas, total leucocyte count, pH and partial pressure of carbon dioxide showed decrease in the mean values from day 1 to day 3. There was an increase in direct Bilirubin, Indirect Bilirubin, ALP, PO_2, and Lactate from day 1 to day 3, but HCO_3 showed a decrease in the values from day 1 to day 3. There was a statistically significant difference from day 3 to discharge with respect to TLC (p=0.001); Total Bilirubin (p=0.001); Albumin(p=0.006); AST (p=0.001); ALT (p=0.001); GGT (p=0.001); pH(p=0.001) and PCO_2(p=0.001).

Conclusion: The administration of N-acetylcysteine, glutathione, and magnesium sulphate as potential antioxidant therapy in Aluminium phosphide poisoning has demonstrated a reduction in the fatal outcome.

Keywords: NAC, Antioxidant, Aluminium phosphide poisoning, Platelet count, Lactate, Bilirubin, HCO_3, PO_2.

Introduction

Pesticide poisoning is a significant global public health concern that contributes significantly to morbidity and mortality rates in India. [1] The utilization of pesticides is widespread, with organochlorines, organophosphate, and ALP (aluminium phosphide) compounds being commonly employed. ALP is a cost-effective and efficient pesticide that does not leave behind any toxic residue and does not negatively impact seed viability. As a result, it has gained significant popularity. Although previously unheard of, ALP has become a prevalent method of suicide among the young adult population in rural areas of northern India since Morocco, Jordan, and Iran. [2,3] ALP is a highly efficacious pesticide that is utilized for both indoor and outdoor purposes in certain developing nations. [4] In Iran, it is commonly referred to as a rice tablet and is primarily employed for safeguarding rice and grains during storage. Numerous studies have indicated that the mortality rates resulting from ALP poisoning can reach as high as 70 to 100%. [5]

The primary mechanisms of toxicity entail the inhibition of cytochrome oxidase c, in addition to oxidative stress. [6,7] The toxicity of ALP is attributed to the presence of phosphine gas (PH3). The primary cause of mortality associated with ALP toxicity is refractory cardiogenic shock. [8] Furthermore, additional factors that contribute to this phenomenon encompass severe refractory metabolic acidosis and severe hypotension. At the cellular level, the inhibition of cytochrome oxidase disrupts cellular respiration, leading to oxidative stress. [1,9-11] To date, there exists no specific antidote for severe aluminium phosphide

poisoning, and the treatment primarily involves addressing the symptoms. A rational approach to manage this cellular dysfunction would involve the use of an agent that can prevent or protect cells from oxidative stress, thereby arresting the progression of cellular damage and its associated manifestations.

Several antioxidants, including melatonin, have been tested in animal models as a means of countering the effects of PH_3. [10] N-acetylcysteine (NAC) functions as an antioxidant and cytoprotective agent by restoring intracellular glutathione levels. Animal studies have demonstrated that NAC plays a protective role in cardiovascular complications by safeguarding cardiac cells against oxidative stress caused by phosphine. [11] A study conducted in Iran has reported that the utilization of NAC provides survival advantages in addition to a decrease in oxidative stress. Hence, we have conducted the impact of Anti-oxidants on the haematological and biochemical parameters of individuals suffering from aluminium phosphide poisoning at different time intervals.

Materials & Methods

This was a prospective study conducted in the Emergency Medical unit of S. S. Institute of Medical Sciences & Research Centre, Davangere, over a period of 1 year. All patients who presented to the Emergency Outpatient Department with a suspected history of ALP ingestion were screened, and those who presented with shock were deemed eligible for enrollment in the study. Written informed consent was obtained from the next to kin of the patient. Patients with uncertain ALP or zinc phosphide consumption, patients who had ingested ALP in combination with other drugs or alcohol, and those with a history of NAC allergy were excluded. Our emergency unit evaluated and included 30 ALP (Aluminium Phosphide) poisoning cases in the study. Vital signs and demographic variables were recorded. All participants received consistent levels of supportive care, which included gastric decontamination using a combination of coconut oil and potassium permanganate. NAC therapy was administered to all subjects at the same dose recommended for paracetamol poisoning, after dissolving in normal saline. A total of 150 mg/kg of NAC (N-acetylcysteine) was intravenously administered over 1 hour after being diluted in 200 ml of normal saline. This was followed by an infusion of 50 mg/kg in 500 ml of normal saline over 4 hours, and subsequently, an infusion of 100 mg/kg in 500 ml over 16 hours. $MgSO_4$ (4g) injection, I.V. in 100 ml normal saline, and inotropes were started if indicated. $MgSO_4$(1g) injection, I.V. in 100 ml normal saline was given in case of cardiac arrhythmias (SOS). An intravenous administration of 600 mg of Glutathione in 100 ml of normal saline was carried out once daily for a duration of three days. The patients were duly monitored for the development of complications or improvement in their clinical state through the regular monitoring of vital signs, renal function tests, and liver function tests. The vital signs of the patients were documented on day 1, day 3, and the day of their discharge. The outcome measures studied were secondary complications such as hepatic failure, and multiorgan dysfunction syndrome.

Statistical Analysis

Data was entered in the Microsoft Excel spreadsheet. Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation/median, and Interquartile range (based on data distribution) for quantitative variables. Inferential statistical methods, such as the Paired t-test or Wilcoxon sign test (depending on the distribution of the data), were utilized to compare laboratory parameters at different time intervals (Day 1 vs. Day 3; Day 3 vs. Discharge) and the level of significance is set at 5%.

Results

During the study period, a total of 30 patients who had suffered from ALP poisoning due to oral consumption were admitted. The data from all 30 patients were analyzed in the study because every patient was alive and therefore eligible for inclusion in the study. Data was subjected to the Normalcy test (Shapiro-Wilk test). Direct Bilirubin (DB), Indirect Bilirubin (IB), Alkaline phosphatase (ALP), Partial pressure of oxygen (PO_2), Lactate, and Bicarbonate (HCO_3) showed both normal and skewed distribution. Hence, both parametric (Paired sample t-test) and non-parametric tests (Wilcoxon sign) tests were applied.

A mean increase was seen from day 1 to day 3 in Haemoglobin (Hb) (mean diff: -0.076); Platelet count (PC) (mean diff: 0.04); PCV (mean diff: -0.403); Total Bilirubin (TB) (mean diff: -3.44); albumin (mean diff: -0.086); Globulin (mean diff: -0.103); aspartate aminotransferase (AST) (mean diff: -71.86); alanine aminotransferase (ALT) (mean diff: -59.46) and gamma-glutamyl transferase (GGT) (mean diff: -20.40) whereas, total leucocyte count (TLC), pH and partial pressure of carbon dioxide (PCO_2) showed decrease in the mean values from day 1 to day 3. A statistically significant difference was observed from day 1 to day 3 with respect to TLC (p=0.001); PC(p=0.046); PCV(p=0.023); Total Bilirubin (p=0.001); Albumin(p=0.035); AST (p=0.001); ALT (p=0.001); GGT (p=0.001); pH(p=0.001); PCO_2(p=0.001). [Table 1]

Table 1: Comparison of the changes in the mean lab parameters from day 1 to day 3 using Paired t-test

Parameters	Time interval	N	Minimum	Maximum	Mean	S. D	Mean diff	p-value
Hb	Day 1	30	9.6	15.4	12.1	1.3	-0.076	0.274
	Day 3	30	9.4	14.8	12.2	1.3		
TLC	Day 1	30	14873.0	21560.0	18181.7	1841.9	3778.3	0.001*
	Day 3	30	12200.0	16897.0	14403.4	1270.7		
PC	Day 1	30	1.7	4.6	2.8	0.7	0.04	0.046*
	Day 3	30	1.7	4.5	2.9	0.8		
PCV	Day 1	30	33.0	40.4	36.4	1.8	-0.403	0.023*
	Day 3	30	33.5	41.0	36.8	1.7		
TB	Day 1	30	1.5	2.4	1.9	0.3	-3.44	0.001*
	Day 3	30	3.8	7.0	5.4	0.7		
ALB	Day 1	30	2.5	3.6	3.0	0.3	-0.086	0.035*
	Day 3	30	2.5	3.6	3.1	0.4		
GLB	Day 1	30	2.4	3.6	3.1	0.3	-0.103	0.055
	Day 3	30	2.2	3.9	3.2	0.4		
AST	Day 1	30	118.0	180.0	141.4	14.0	-71.86	0.001*
	Day 3	30	178.0	246.0	213.2	18.9		
ALT	Day 1	30	128.0	166.0	145.8	10.5	-59.46	0.001*
	Day 3	30	186.0	232.0	205.3	12.2		
GGT	Day 1	30	78.0	95.0	85.9	4.6	-20.40	0.001*
	Day 3	30	99.0	118.0	106.3	4.5		
pH	Day 1	30	7.3	7.5	7.4	0.0	0.17	0.001*
	Day 3	30	7.2	7.3	7.2	0.0		
PCO_2	Day 1	30	31.0	45.0	39.8	3.6	14.46	0.001*
	Day 3	30	19.0	31.0	25.3	3.5		

*Significant

There was an increase in DB, IB, ALP, PO_2, and Lactate from day 1 to day 3, but HCO_3 showed a decrease in the values from day 1 to day 3. A statistically significant difference was found from day 1 to day 3 with Direct Bilirubin, Indirect Bilirubin, ALP, PO_2, Lactate, and HCO_3 (p=0.001). [Table 2]

Table 2: Comparison of the changes in the lab parameters from day 1 to day 3 using the Wilcoxon sign test

Parameters	Time interval	Minimum	Maximum	Median	IQR	p value
DB	Day 1	0.9	1.8	1.20	0.4	0.001*
	Day 3	2.5	5.0	3.35	0.9	
IB	Day 1	0.4	1.1	0.70	0.3	0.001*
	Day 3	1.2	2.5	1.95	0.7	
ALP	Day 1	146.0	186.0	176.00	11.5	0.001*
	Day 3	176.0	257.0	230.00	25.3	
PO_2	Day 1	60.0	83.0	78.00	7.0	0.001*
	Day 3	82.0	92.0	86.00	4.0	
Lactate	Day 1	0.8	2.1	1.40	0.4	0.001*
	Day 3	2.4	4.1	2.75	0.4	
HCO_3	Day 1	20.0	26.0	23.00	2.3	0.001*
	Day 3	12.0	18.0	15.00	3.0	

*Significant

There was a mean increase seen from day 3 to discharge in pH (mean diff: 0.171) and PCO_2 (mean diff: 13.46); whereas Hb (mean diff: 0.0067); TLC (mean diff: 3609.7); PC (mean diff: 0.02); PCV (mean diff: 0.186); Total Bilirubin (mean diff: 3.606); Albumin (mean diff: 0.13); Globulin (mean diff: 0.046; AST (mean diff: 118.5); ALT (mean diff:108.73) and GGT (mean diff: 15.10) showed decrease in the mean values from day 3 to Discharge. There was a statistically significant difference from day 3 to discharge with respect to TLC (p=0.001); Total Bilirubin (p=0.001); Albumin(p=0.006); AST (p=0.001); ALT

(p=0.001); GGT (p=0.001); pH(p=0.001) and PCO_2(p=0.001). [Table 3]

Table 3: Comparison of the changes in the mean lab parameters from day 3 to discharge using a paired t-test

Parameters	Time interval	N	Minimum	Maximum	Mean	S. D	Mean diff	p value
Hb	Day 3	30	9.4	14.8	12.15	1.28	0.0067	0.926
	Discharge	30	10.1	15.0	12.14	1.24		
TLC	Day 3	30	12200.0	16897.0	14403.37	1270.74	3609.7	0.001*
	Discharge	30	9647.0	11746.0	10793.67	547.87		
PC	Day 3	30	1.68	4.50	2.89	0.75	0.02	0.373
	Discharge	30	2	4	2.87	0.69		
PCV	Day 3	30	33.5	41.0	36.78	1.69	0.186	0.311
	Discharge	30	33.0	40.2	36.59	1.84		
TB	Day 3	30	3.8	7.0	5.36	0.74	3.606	0.001*
	Discharge	30	1.0	2.2	1.76	0.28		
ALB	Day 3	30	2.5	3.6	3.06	0.37	0.13	0.006*
	Discharge	30	2.2	3.6	2.93	0.37		
GLB	Day 3	30	2.2	3.9	3.15	0.40	0.046	0.528
	Discharge	30	2.2	4.2	3.11	0.44		
AST	Day 3	30	178.0	246.0	213.23	18.93	118.5	0.001*
	Discharge	30	76.0	108.0	94.73	8.33		
ALT	Day 3	30	186.0	232.0	205.27	12.19	108.73	0.001*
	Discharge	30	82.0	110.0	96.53	6.38		
GGT	Day 3	30	99.0	118.0	106.27	4.46	15.10	0.001*
	Discharge	30	79.0	102.0	91.17	4.53		
pH	Day 3	30	7.16	7.26	7.22	0.03	0.171	0.001*
	Discharge	30	7.33	7.45	7.39	0.03		
PCO_2	Day 3	30	19.0	31.0	25.33	3.51	13.46	0.001*
	Discharge	30	34.0	45.0	38.80	2.93		

*Significant

An increase in PO_2 and HCO_3 from day 3 to discharge but Direct Bilirubin, Indirect Bilirubin, ALP, and Lactate showed a decrease from day 3 to discharge. There was a statistically significant difference from day 3 to discharge with respect to Direct Bilirubin, Indirect Bilirubin, ALP, PO_2, Lactate, and HCO_3 (p=0.001). [Table 4]

Table 4: Comparison of the changes in the lab parameters from day 3 to discharge using the Wilcoxon sign test

Parameters	Time inter-val	Minimum	Maximum	Median	IQR	p value
DB	Day 3	2.5	5.0	3.35	0.9	0.001*
	Discharge	0.4	1.4	1.10	0.2	
IB	Day 3	1.2	2.5	1.95	0.7	0.001*
	Discharge	0.4	0.9	0.65	0.2	
ALP	Day 3	176.0	257.0	230.00	25.3	0.001*
	Discharge	88.0	126.0	109.50	16.0	
PO_2	Day 3	82.0	92.0	86.00	4.0	0.001*
	Discharge	90.0	98.0	94.00	2.0	
Lactate	Day 3	2.4	4.1	2.75	0.4	0.001*
	Discharge	0.8	1.4	1.20	0.3	
HCO_3	Day 3	12.0	18.0	15.00	3.0	0.001*
	Discharge	21.0	26.0	24.00	3.0	

*Significant

Discussion

Aluminium phosphide poisoning has always been a big headache and menace for intensivists throughout the world probably due to the non-availability of its antidote and 100% mortality which does not encourage the physicians to try wholeheartedly to salvage the patients. This study

assessed the impact of antioxidants on laboratory parameters at different time intervals in patients suffering from Aluminium phosphide poisoning. The study group comprised 30 patients and most patients exhibited symptoms such as discomfort, vomiting, and a burning sensation in the chest. These findings align with prior research indicating that vomiting and abdominal pain are the most prevalent symptoms. [1,2,12,13] Vomiting, and abdominal pain may be attributed to the localized impact of aluminium phosphide on the gastric mucosa. [1]

Most patients presented themselves at our medical facility within 6 hours after ingestion, a finding that agrees with the observations made by Louriz et al. and Shadnia et al. [13,14] Early reporting after ingestion may suggest either an increased awareness concerning the probable fatality of this toxin or an early referral to a tertiary medical facility from the outskirts. A very high mortality rate was seen, particularly among patients who presented themselves within 6 hours of ingestion.[15]This denotes the rapid action of poison and the early onset of tissue hypoxia, which may be accountable for mortality despite the timely implementation of supportive measures. [1]

In our study, like previous research, lower levels of hemoglobin (Hb), packed cell volume (PCV), platelet count (PC), and higher total leukocyte count (TLC) at presentation were found to be relatedto poor outcomes. This suggests that severe myocardial depression at presentation is an indicator of poor prognosis in patients with ALP poisoning. All patients in our study group were considered comparable in terms of severity as they all had "severe poisoning," which was characterized by the presence of circulatory shock. The mean levels of PC, PCV, total bilirubin (TB), albumin (ALB), globulin (GLB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT) were significantly improved from day 1 to day 3. Similarly, the pH and partial pressure of carbon dioxide (PCO_2) levels decreased significantly from day 1 to day 3 in the current research study. There is no evidence to suggest that ALP is a direct nephrotoxic agent. In this context, acute kidney injury is accountable to be secondary to severe myocardial depression, leading to prolonged hypoperfusion, which is manifested by elevated levels of serum creatinine. Most of the cases studied presented with metabolic acidosis (pH 6.9-7.34) mostly due to lactic acid accumulation caused by histotoxic hypoxia and poor tissue perfusion. This agrees with Jaiswal *et al*., who reported that all ALP-intoxicated patients presented with severe metabolic acidosis. [16] Moreover, about 33 cases (55%) presented with sinus tachycardia. According to Gurjar *et al*., the analysis of temporal correlation in electrocardiogram alterations in ALP poisoning has revealed that within the first 3 to 6 hours, there is a prevailing occurrence of sinus tachycardia. [17]

The present investigation comprised patients who had already developed shock, whereas certain studies incorporated normotensive as well as hypotensive patients in their study cohort. [18] It was demonstrated that administering antioxidant pretreatment, in conjunction with post-treatment, resulted in a reduction of oxidative stress on the tissues, thereby enhancing the survival rate. [19] Comparable results have been documented by Tehrani et al. in a prospective investigation. In this study, the administration of antioxidants in substantial quantities led to the mitigation of oxidative stress, thereby yielding noteworthy survival advantages. [12] The findings are consistent with our study. Antioxidants may play a significant role in reducing oxidative stress. However, further investigation is required utilizing an alternative regimen, whereby the highest dosage of antioxidants is administered within the initial 3-to-6-hour period. The absence of an established clinical scoring system to classify the severity of poisoning may pose a challenge in comparing studies, as the severity of the ailment may vary.

The administration of medical intervention for cardiogenic shock, which is recognized as a primary contributor to mortality in cases of ALP poisoning, has the potential to decrease the associated fatality rate. [5,8] The management of cardiogenic shock in certain treatments involves the utilization of IABP (Intra-aortic Balloon Pump), glucagon, and digoxin. [8,20] In the present study, it was observed that our patients experienced respiratory distress. However, following the administration of antioxidant treatment, there was a significant improvement in the partial pressure of carbon dioxide and partial pressure of oxygen in arterial blood. Erfantalab [21] has shown evidence that specific factors, including heart rate, blood pressure, blood pH, and levels of serum bicarbonate, exhibit significant differences between individuals who succumbed to acute ALP poisoning and those who survived after ingesting ALP tablets. Similarly, Shadnia et al. [14] have reported a statistically significant variance in HCO3and blood pH between individuals who perished due to acute ALP poisoning and those who survived. [22] In our investigation, it was observed that the levels of HCO3 showed a statistically significant decrease from day 1 to day 3. This phenomenon can be attributed to the pathological effects of phosphine on various organs, which results in the generation of free radicals and damaging different body tissues by inhibiting cytochrome oxidase. The correlation of these factors with mortality in patients suffering from acute ALP poisoning is noteworthy. The

impairment is notably more severe in organs with high perfusion rates, which necessitate substantial quantities of oxygen, such as the brain, heart, and kidneys. [13]

The utilization of blood lactate levels as a prognostic indicator in patients who are critically ill has been observed. [23] Lactate has been studied for prognostic purposes in patients who have been poisoned by acetaminophen, metformin, beta-blockers, cyanide,paraquat, and carbon monoxide. [24] The condition of hyperlactatemia is characterized by a serum lactate level of ≥2 mmol/L. [25] Generally, the mechanisms underlying hyperlactatemia, which include hypoperfusion, result in cellular hypoxia, heightened activity of Na^+/K^+–ATPase under normoxia conditions, elevated levels of pyruvate and lactate due to increased anaerobic glycolysis, reduced lactate clearance, muscle hyperactivity resulting from seizures, and impaired electron transfer as well as oxidative phosphorylation. [26] The assessment of blood lactate concentration is commonly employed in the identification and treatment of individuals exhibiting indications and manifestations of sepsis or shock and serves as an indicator of tissue hypoperfusion. [27] The blood lactate level has been documented as an inadequate prognostic indicator for predicting mortality in patients admitted to the hospital and intensive care unit. [28] The prognostic significance of blood lactate levels has been investigated in the context of drug and chemical poisoning. [29] The occurrence of hyperlactatemia in ALP toxicity is attributed to a combination of inadequate energy supply and oxidative stress. This may potentially interact with the mitochondrial electron transport chain and impede cytochrome c, ultimately resulting in metabolic acidosis and heightened production of lactate. [30] In our study, it was observed that patients who were poisoned with Aluminium Phosphide exhibited elevated levels of blood lactate during the initial hour following ingestion. However, subsequent treatment with antioxidants resulted in a significant reduction in lactate levels. There was a significant decrease in bilirubin levels and ALP in antioxidant-treated patients.

The present study was limited by the small sample size under investigation and the data collection process was confined to a single care centre. Therefore, attempts to generalize the findings to other settings should be made with caution. For enhancing predictive accuracy, larger data sets, more sophisticated modeling, novel biomarkers, and more advanced data collection methods are recommended in the conduction of future studies.

Conclusion

The current investigation suggests that the timely administration of substantial quantities of NAC, Glutathione, and $MgSO_4$, in conjunction with appropriate supportive care, has a cutting edge over relying solely on supportive treatment for the outcome of such highly lethal poisonings.

References

1. Singh S, Bhalla A, Verma SK, Kaur A, Gill K. Cytochrome-c oxidase inhibition in 26 aluminium phosphide poisoned patients. Clin Toxicol (Phila) 2006;44:155-8.
2. Moghadamnia AA, Abdollahi M. An epidemiological study of poisoning in northern Islamic Republic of Iran. East Mediterr Health J 2002 ;8:88-94.
3. Akkaoui M, Achour S, Abidi K, Himdi B, Madani A, Zeggwagh AA, *et al*. Reversible myocardial injury associated with aluminum phosphide poisoning. Clin toxicol 2007;45:72 8-31.
4. Mehrpour O, Singh S. Rice tablet poisoning: a major concern in Iranian population. Hum Exp Toxicol 2010;29:701-2.
5. Mehrpour O, Jafarzadeh M, Abdollahi M. A systematic review of aluminium phosphide poisoning. Arh Hig Rada Toksikol 2012;63:61 -73.
6. Mehrpour O, Keyler D, Shadnia S. Comment on aluminium and zinc phosphide poisoning. Clin Toxicol (Phila. 2009;47:838-9; author reply 839.
7. Mehrpour O, Abdollahi M, Sharifi MD. Oxidative stress and hyperglycaemia in aluminium phosphide poisoning. J Res Med Sci 2014;19: 196.
8. Mehrpour O, Amouzeshi A, Dadpour B, Oghabian Z, Zamani N, Amini S, *et al*. Successful treatment of cardiogenic shock with an intraaortic balloon pump following aluminium phosphide poisoning. Arh Hig Rada Toksikol 2014;65:121-6.
9. Anand R, Kumari P, Kaushal A, Bal A, Wani WY, Sunkaria A, *et al*. Effect of acute aluminium phosphide exposure on rats: A biochemical and histological correlation. Toxicol Lett 2012;215:62-9.
10. Anand R, Sharma DR, Verma D, Bhalla A, Gill KD, Singh S. Mitochondrial electron transport chain complexes, catalase and markers of oxidative stress in platelets of patients with severe aluminium phosphide poisoning. Hum Exp Toxicol 2013;32:807-16.
11. Shakeri S, Mehrpour O. Aluminum phosphide poisoning in animals. Int J Med Toxicol Forensic Med. 2014;5:81-97.
12. Tehrani H, Halvaie Z, Shadnia S, Soltaninejad K, Abdollahi M. Protective effects of N-acetyl cysteine on aluminium phosphide-induced oxidative stress in acute human poisoning. Clin Toxicol (Phila) 2013;51:23-8.

13. Louriz M, Dendane T, Abidi K, Madani N, Abouqal R, Zeggwagh AA. Prognostic factors of acute aluminum phosphide poisoning. Indian J Med Sci 2009;63:227-34.
14. Shadnia S, Mehrpour O, Abdollahi M. Unintentional poisoning by phosphine released from aluminum phosphide. Hum Exp Toxicol 2008;27:87-9.
15. Bhalla A, Jyothinath P, Singh S. Antioxidant therapy in patients with severe aluminum phosphide poisoning: a pilot study. Indian J Crit Care Med 2017;21:836-40.
16. Jaiswal S, Verma RK, Tewari N. Aluminum phosphide poisoning: effect of correction of severe metabolic acidosis on patient outcome. Indian J Crit Care Med 2009;13:21-4.
17. Gurjar M, Baronia AK, Azim A, Sharma K. Managing aluminum phosphide poisonings. J Emerg Trauma Shock 2011;4:378-84.
18. Katira R, Elhence GP, Mehrotra ML, Srivastava SS, Mitra A, Agarwala R, *et al*. A study of aluminum phosphide (ALP) poisoning with special reference to electrocardiographic changes. J Assoc Physicians India 1990;38:47 1-3.
19. Azad A, Lall SB, Mittra S. Effect of N-acetylcysteine and L-NAME on aluminium phosphide induced cardiovascular toxicity in rats. Acta Pharmacol Sin 2001;22:298-304.
20. Oghabian Z, Mehrpour O. Treatment of aluminum phosphide poisoning with a combination of intravenous glucagon, digoxin and antioxidant agents. Sultan Qaboos Univ Med J 2016; 16:e352-5.
21. Erfantalab P, Soltaninejad K, Shadnia S, Zamani N, Hassanian-Moghaddam H, Mahdavinejad A, *et al*. Trend of blood lactate level in acute aluminum phosphide poisoning. World J Emerg Med 2017;8:116-20.
22. Shadnia S, Sasanian G, Allami P, Hosseini A, Ranjbar A, Amini-Shirazi N, *et al*. A retrospective 7-years study of al phosphide poisoning in Tehran: opportunities for prevention. Hum Exp Toxicol 2009;28:209-13.
23. Fall PJ, Szerlip HM. Lactic acidosis: from sour milk to septic shock. J Intensive Care Med 2005;20:255-71.
24. Inoue S, Saito T, Tsuji T, Tamura K, Ohama S, Morita S. Lactate as a prognostic factor in carbon monoxide poisoning: a case report. Hum Exp Toxicol 2011;30:836-43.
25. Gunnerson KJ. Clinical review: the meaning of acid–base abnormalities in the intensive care unit – epidemiology. Crit Care 2005;9:508-16.
26. Hulme J, Sherwood N. Severe lactic acidosis following alcohol related generalized seizures. Anaesthesia 2004;59:1228-30.
27. 38Kompanje EJ, Jansen TC, van der Hoven B, Bakker J. The first demonstration of lactic acid in human blood in shock by Johann Joseph Scherer (1814-1869) in January 1843. Intensive Care Med 2007;33:1967-71.
28. Rishu AH, Khan R, Al-Dorzi HM, Tamim HM, Al-Qahtani S, Al-Ghamdi G, *et al*. Even mild hyperlactatemia is associated with increased mortality in critically ill patients. Crit Care 2013;17: R197.
29. Manini AF, Kumar A, Olsen D, Vlahov D, Hoffman RS. Utility of serum lactate to predict drug-overdose fatality. Clin Toxicol (Phila) 20 10;48:730-6.
30. Anand R, Sharma DR, Verma D, Bhalla A, Gill KD, Singh S. Mitochondrial electron transport chain complexes, catalase and markers of oxidative stress in platelets of patients with severe aluminum phosphide poisoning. Hum Exp Toxicol 2013;32(8):807-16.