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Incidence and Outcome of Aluminium Phosphide Poisoning Cases Admitted to the Egyptian National Poisoning Centre

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Abstract

Aluminium Phosphide (ALP) poisoning is one of the major causes of suicidal deaths. It is one of the fatal pesticides. It liberates lethal phosphine gas when it comes in contact either with atmospheric moisture or with hydrochloric acid in the stomach. It causes cellular hypoxia, inhibition of cytochrome c oxidase and formation of highly reactive hydroxyl radicals. The aim of this work was to investigate ALP poisoning-related deaths in the National Egyptian Center of Environmental and Toxicological Research (NECTR), to arouse attention to its use in committing suicide due to its easy availability through the objective data from a sample of acutely poisoned patients admitted to NECTR in Cairo. Management of cases is mainly supportive as there is no specific antidote, causing high mortality rate. Early arrival and proper decontamination, resuscitation, intensive monitoring and supportive therapy may result in good outcome.

Keywords: Aluminium Phosphide (ALP), Blood Lactate Level, Mortality, Phosphine Gas, Prediction

1. Introduction

Aluminium Phosphide (ALP), also known as rice tablet, is widely used all over the world as a fumigant to protect stored grain from pests and rodents[1-3]. It became rapidly one of the most commonly used grain fumigants because of its properties which are considered to be near ideal; it is cheap, toxic to all stages of pests, highly potent, does not affect seed viability, is free from toxic residues and leaves little residue on food grains[4].

ALP is available as 3 gm tablets (trade names: Phostoxin, Bhostoxin, Quickphos, Phostek) releasing 1 g of phosphine gas (PH_3) or as pellets 0.6 g (Quickphos, Alphos, Celphos). The tablets are green, brown or gray and each tablet contains 56% ALP and 44% aluminum carbonate[5].

In the past 25 years ALP poisoning has been the main cause of death in third world countries[4] with an astonishing mortality rate of 40–100%[6] even in high-level specialized hospitals with advanced life-support equipment[7]. Most reports of aluminum phosphide poisoning were suicidal especially in young adults, although accidental poisoning may occur during occupational exposure[8,9]. In Egypt and according to the records of the National Egyptian Centre of environmental and Toxicological Research in Cairo (NECTR), ALP poisoning has emerged as a common suicidal agent.

Upon contact with moisture in the environment or with stomach acidity, ALP undergoes a chemical reaction yielding phosphine gas which is the active pesticidal component[10]. In case of oral intake, the phosphine gas released is absorbed by the gastrointestinal tract with simple diffusion and is mainly excreted by the kidneys and lungs. Phosphine inhibits mitochondrial cytochrome c oxidase and cellular oxygen utilization[11,12]. This rapidly perturbs mitochondrial conformation and inhibits oxidative respiration by 70% leading to severe decrease in mitochondrial membrane potential[12]. As a result, various

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harmful cellular radicals like superoxides and peroxides are generated with subsequent cellular damage by lipid peroxidation[5,13].

The clinical presentation varies according to the route of administration. After inhalation of phosphine gas, patients present with signs of mucous membrane irritation, headache and dizziness in mild cases. Acute respiratory distress syndrome, congestive heart failure and coma may occur in severe cases[14]. On the other hand, ingestion of ALP causes nausea, vomiting, retrosternal and epigastric pain, dyspnea, anxiety, agitation and garlic-odor breath. An early sign of ALP poisoning is severe metabolic acidosis which may occur due to accumulation of lactic acid caused by blockage of oxidative phosphorylation[15]. Hypotension and rapid onset of shock which leads to tissue perfusion failure in the first couple of hours after ingestion due to cardiogenic shock and peripheral circulatory failure; gastrointestinal hemorrhage and ulcerations were also reported[16]. Other cardiovascular complications include cardiac arrhythmias and acute myocardial infarctions. Profound circulatory collapse was believed to be due to the direct effect of PH_3 on the heart cells[17].

Furthermore, ALP promotes protein denaturation that results in breakdown of integrity of the cell membrane[7]. Focal myocardial necrosis is also one of the signs observed in aluminum phosphide poisoning. This is due to alteration in the ionic permeability of ions such as sodium, magnesium and calcium. Adrenal gland damage, and fluid loss could contribute to profound circulatory collapse[18,19]. Direct corrosive effects of phosphides and phosphine on body tissues had also been reported[20]. Hematemesis due to corrosive lesions of the esophagus and stomach may occur and lead to the development of esophageal stricture[21].

Current medical management is to provide supportive care for almost all cases, until the toxicant has been cleared through the lungs and kidney[22]. Many ALP-poisoned patients deteriorate despite proper supportive treatment. Its free availability on the market and the lack of a proper antidote are regarded as the underlying reasons that accentuate the mortality rate associated with ALP poisoning[23].

The aim of this work was to investigate ALP poisoning-related deaths in a certain period of time through the objective data from a sample of acutely poisoned patients admitted to NECTR, to arouse attention on increased suicidal attempts by ALP due to its easy availability and to evaluate the predictive factors of mortality from acute ALP poisoned cases.

2. Methodology

Over a 6-month period (between January and June, 2018), 21 patients with acute ALP poisoning who were admitted to NECTR were evaluated. Acute ALP-intoxicated patients with no history of co-ingestion of any other drugs were included in the study. Diagnosis of ALP poisoning was based on a definite history of ingestion and clinical manifestations.

Patient history included demographic data, number of tablets ingested, nature of poisoning (suicidal or accidental), time-lapse between ALP consumption and hospital admission, and length of hospital stay. At the time of admission, the presenting complaints, and laboratory data were recorded with full clinical assessment.

Treatment was given to patients according to their presentation; and methods of decontamination done (gastric lavage with sodium bicarbonate), the use of coconut oil, potassium permanganate and activated charcoal were also recorded. Airway protection was done before gastric lavage in some patients. All patients were managed in a medical intensive care unit by supportive approaches because no specific antidote exists for this type of poisoning. Supportive treatment included intravenous (IV) fluids and electrolyte replacement, vasopressors and inotropic drugs, sodium-bicarbonate infusion, magnesium sulfate infusion (1 gm initially, and then 1 gm every 6 hour, intravenously), proton pump inhibitors every 12 hours and N-acetyl cysteine administration; intubation and mechanical ventilation were done when indicated.

On admission and on regular basis, close monitoring of hemodynamic parameters was performed. Laboratory monitoring of arterial blood gases, blood lactate level, and bleeding profile were done and results recorded every 2 hours, liver function tests and kidney function tests were done; electrolytes and random blood sugar were evaluated on admission and repeated when needed.

Patients were compared and categorized into two groups considering the outcome: Survived and non-survived.

3. Statistical Analysis

Data were coded and entered using the statistical package. Statistical Package for the Social Sciences (SPSS) version 25. Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (number) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Mann-Whitney test[24]. For comparing categorical data, chi square ($\chi 2$) test was performed. Exact test was used instead when the expected frequency was less than 5[25]. Correlations between quantitative variables were done using Spearman correlation coefficient[26]. P-value less than 0.05 were considered statistically significant.

4. Results

Twenty-one patients acutely poisoned with ALP were admitted to NECTR in a 6-month period. They were categorized according to the outcome into two groups: Survived and non-survived. Comparison between survived and non-survived ALP-intoxicated cases based on demographic characteristics showed no significant differences between the two groups (Table 1). The majority of patients were young; mean age 20 ± 6.53 years old (range from 9 to 37 years old); unmarried, with male gender predominance (52.4%). Most of the poisoned patients were from El-fayoum governorate (76.2%) which may be due to easy availability of ALP tablets in this area because a high proportion of the population are engaged in farming; and the rest came from Giza (9.5%), Beni sweif (4.8%) and Cairo (9.5%). The incidence was more in students (57.1%) followed by housewives (23.8%) then the unemployed (14.3%) meaning that neither illiteracy nor employment stress were the major factors, but rather it was the social and family factors which motivated these people to commit suicide; 85.7% of poisoned cases were suicidal attempts and only 14.3% were accidental.

According to the results, Table 1 also shows that twelve patients (57.2%) vomited after intake, the difference between survived and non-survived groups was statistically significant; in our work, delay was 1 hour minimum and 20 hour maximum between poison intake and first symptom; in survived patients the mean was nearly 2 hours and half and in non-survived it was nearly 6 hours; so it was obvious that the period of delay from the time of ingestion until seeking medical advice played an important role in prognosis of these patients. The mean number of tablets ingested varied from less than 3 gm to 6 gm maximum with 57.1% of patients having been poisoned with only one table, the difference between the two groups being statistically significant. The average intensive care unit stay of survivors was 36 hours (35.44 ± 24.1) and in non-survivors was 23 hours (23.33 ± 46.12) (less than one day) with a statistically significant difference between the two groups indicating rapid deterioration due to the severity of ALP poisoning.

Comparison between survived and non-survived patients regarding some laboratory investigations on admission was also shown in Table 1. The investigations done showed significant differences between survived and non-survived groups in prothrombin concentration, hemoglobin and platelets levels; with no significant differences in random blood sugar, urea, creatinine, prothrombin time and white blood cell count.

Various clinical manifestations of patients were represented in Figure 1. Sixteen patients (76.1%) presented with abdominal pain. Seventeen patients (81%) presented with hypotension, and 42.9% presented with tachycardia. Altered sensorium, weakness and anxiety were major findings in seven patients (33.3%). Only four patients (19 %) presented with respiratory distress.

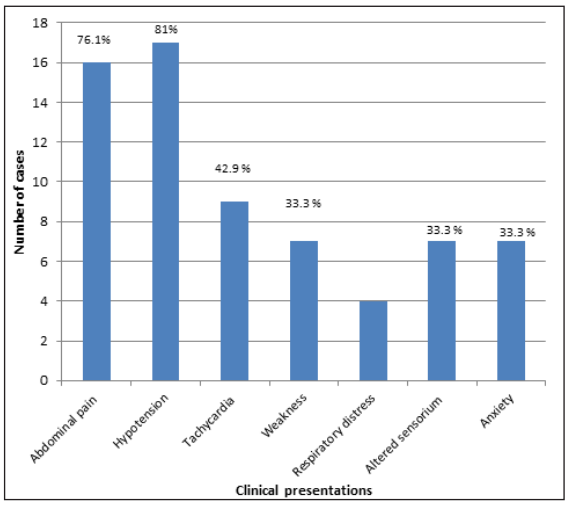


Figure 1. Pattern of clinical presentations.

Regarding blood pressure, Table 2 shows that, on admission, the mean systolic blood pressure was 105.22 ± 18.62 mm Hg in survivors and 81.40 ± 9.52 mm Hg in

Table 1. Comparison of survived and non-survived ALP-intoxicated cases based on demographic, clinical and laboratory findings

Demographic Characteristics		Total No.		Survived		Non-survived		
		No.	%	No.	%	No.	%	p value
Gender	Male	11	52.40%	5	55.60%	6	50.00%	1
	Female	10	47.60%	4	44.40%	6	50.00%	
Age	Mean ± SD	20 ± 6.53		19.33 ± 6.78		20.5 ± 6.59		0.602
Residence	Giza	2	9.50%	0	0.00%	2	16.70%	0.735
	El fayoum	16	76.20%	8	88.90%	8	66.70%	
	Cairo	2	9.50%	1	11.10%	1	8.30%	
	Benis weif	1	4.80%	0	0.00%	1	8.30%	
Occupation	Student	12	57.10%	5	55.60%	7	58.30%	0.906
	Unemployed	3	14.30%	2	22.20%	1	8.30%	
	House wife	5	23.80%	2	22.20%	3	25.00%	
	Carpenter	1	4.80%	0	0.00%	1	8.30%	
Cause	Suicide	18	85.70%	7	77.80%	11	91.70%	0.553
	Accidental	3	14.30%	2	22.20%	1	8.30%	
Clinical and Laboratory Parameters								
Vomiting after intake	yes	12	57.20%	9	75%	3	25%	< 0.001*
	no	9	42.90%	0	0%	9	100%	
Period of delay (in hours)	Mean ± SD	4.48 ± 5.19		2.56 ± 2.07		5.92 ± 6.37		0.169
Number of tablets	Mean ± SD	0.99 ± 0.49		0.81 ± 0.53		1.12 ± 0.43		0.018*
Period of hospital stay (in hours)	Mean ± SD	28.52 ± 37.95		35.44 ± 24.10		23.33 ± 46.12		0.013*
RBS (70–120 mg %)	Mean ± SD	121.38 ± 38.41		126.44 ± 38.00		117.58 ± 39.95		0.219
Urea (15–50mg/dl)	Mean ± SD	34.24 ±7.44		32.78 ± 8.26		35.33 ± 6.92		0.972
Creatinine (0.5–1.5 mg/dl)	Mean ± SD	1.04 ± 0.28		1.02 ± 0.36		1.06 ± 0.23		0.554
PT	Mean ± SD	17.91 ± 11.39		14.83 ± 2.73		20.23 ± 14.73		0.058
PC %	Mean ± SD	65.9 ± 23.48		75.56 ± 20.64		58.67 ± 23.64		0.028*
INR	Mean ± SD	2.59 ± 3.52		1.37 ± 0.45		3.51 ± 4.49		0.648
Hb	Mean ± SD	12.38 ± 2.37		12.28 ± 1.41		12.44 ± 2.89		0.024*
WBC	Mean ± SD	13.92 ± 6.26		9.85 ± 2.85		16.24 ± 6.62		0.788
PLT	Mean ± SD	239.64 ± 83.24		239.5 ± 38.52		239.71 ± 103.96		0.006*

SD: Standard Deviation, No.: Number of subjects, *Significant at p value ≤ 0.05

non-survivors with no statistically significant difference between the two groups. However, a statistically significant difference was observed in both systolic and diastolic blood pressure between survived and non-survived 4 and 8 hours after admission indicating progressive deterioration in blood pressure which by the time became unresponsive to medical treatment.

Table 2. Comparison between survived and non-survived patients regarding blood pressure

	SBP			DBP		
	Survived	Non survived	p value	Survived	Non survived	p value
on admission	105.22 ± 18.62	81.4 ± 9.52	0.133	60.56 ± 13.57	50.5 ± 9.56	0.182
after 2 hours	101.11 ± 20.28	86.2 ± 17.45	0.34	62.22 ± 14.81	53.5 ± 15.99	0.436
after 4 hours	101.33 ± 14.22	93.78 ± 17.93	0.014*	65.56 ± 10.14	59.44 ± 17.82	0.029*
after 8 hours	103.75 ± 9.16	81.43 ± 16.76	0.012*	61.25 ± 9.91	46.29 ± 13.03	0.012*
on following days	107.5 ± 7.07	70 ± 0	0.095	66.25 ± 7.44	40 ± 0	0.382

SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure

Regarding serum lactate levels, Figure 2 shows comparison between survived and non-survived groups in serum lactate levels at different time intervals. Results revealed that there was a statistically significant difference between the two groups in serum lactate level on admission and after 2 hours. Figure 2 also shows progressive deterioration in lactic acidosis in non-survived patients. Results of the study showed positive correlation between blood lactate level and different parameters of blood gases after 2 and 6 hours from admission between survived and non-survived patients in Table 3. The various treatment strategies used in patients and their effects on the outcome were collected in Table 4. Gastric lavage was performed in 8 patients who came within 2 hours of toxin intake (38.1%); while 13 (61.9%) didn't have gastric lavage due to late presentation and from them 8 patients died (66.7%) indicating the importance of rapid hospital transfer and rapid decontamination. Gastric lavage was done with sodium bicarbonate in 6 patients and in 2 patients with water done outside the center.

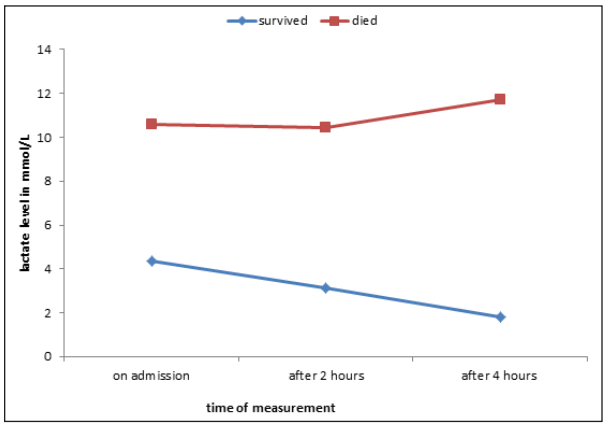


Figure 2. Comparison between survived and non-survived patients regarding serum lactate level.

Eight patients (38.1%) received vasopressors (noradrenaline infusion) to raise their blood pressure; unfortunately, seven (87.5%) died as their first presentation was severe persistent hypotension not responding to fluid replacement or vasopressors.

Table 3. Correlation between lactate level and different parameters of blood gases

Lactate level / ABG parameters			On admission	After 2 hours	After 6 hours
pH	On admission	Correlation Coefficient	–.774-	–.566-	–.500-
		P value	< 0.001*	0.009	0.035
		N	21	20	18
	After 2 hours	Correlation Coefficient	–.559-	–.808-	–.801-
		P value	0.01*	< 0.001*	< 0.001*
		N	20	20	18
	After 6 hours	Correlation Coefficient	–.080-	–.483-	–.627-
		P value	0.752	0.042*	0.005*
		N	18	18	18

HCO_3	**On admission**	**Correlation Coefficient**	−.728	−.690	−.711
		P value	< 0.001*	0.001*	0.001*
		N	21	20	18
	After 2 hours	**Correlation Coefficient**	−.630	−.806	−.769
		P value	0.003*	< 0.001*	< 0.001*
		N	20	20	18
	After 6 hours	**Correlation Coefficient**	−.370	−.611	−.682
		P value	0.13	0.007*	0.002*
		N	18	18	18

Table 4. Various treatment strategies used in patients and their effects on outcome

		All patients	%	Survived		Non-survived		p value
				Number	% within survival	Number	% within died	
Gastric lavage	**With $NaHCO_3$**	6	28.60%	4	44.40%	2	16.66%	0.673
	With water	2	9.50%			2	16.66%	
	No	13	61.90%	5	55.60%	8	66.70%	
Noradrenaline administration	**Yes**	8	38.10%	1	11.10%	7	58.30%	0.067
	No	13	61.90%	8	88.90%	5	41.70%	
N-acetyl cysteine	**Yes**	7	33.30%	5	55.60%	2	16.70%	0.159
	No	14	66.70%	4	44.40%	10	83.30%	
Oral k permanganate	**Yes**	3	14.30%	1	11.10%	2	16.70%	1
	No	18	85.70%	8	88.90%	10	83.30%	
Oral coconut oil	**Yes**	3	14.30%	1	11.10%	2	16.70%	1
	No	18	85.70%	8	88.90%	10	83.30%	
Oral $NaHCO_3$	**Yes**	11	52.40%	6	66.70%	5	41.70%	0.387
	No	10	47.60%	3	33.30%	7	58.30%	
Plasma infusion	**Yes**	3	14.30%	1	11.10%	2	16.70%	1
	No	18	85.70%	8	88.90%	10	83.30%	
Use of ventilator	**Yes**	6	28.60%	0	0.00%	6	50.00%	0.019*
	No	15	71.40%	9	100.00%	6	50.00%	

Table 5. Risk of death in relation to certain parameters

		All patients	%	Survived		Non-survived		p value
				No.	%	No.	%	
Gastric lavage	Yes	8	38.10%	4	44.40%	4	33.30%	0.673
	No	13	61.90%	5	55.60%	8	66.70%	
Vomiting after ingestion	Yes	12	57.20%	**9**	**75%**	**3**	**25%**	0.001*
	No	9	42.90%	**0**	**0%**	**9**	**100%**	
No. of tablets		0.99 ± 0.49		0.81 ± 0.53		1.12 ± 0.43		0.018*
Period of delay (in hours)		4.48 ± 5.19		2.56 ± 2.07		5.92 ± 6.37		0.169

pH level on admission		7.27 ± 0.16		7.37 ± 0.06		7.19 ± 0.18		<0.001*
Serum lactate level on admission		7.94 ± 5.14		4.38 ± 2.79		10.61 ± 4.93		<0.001*
Use of ventilator	Yes	6	28.60%	0	0.00%	6	100.00%	0.019*
	No	15	71.40%	9	60.00%	6	40.00%	

Three patients (14.3%) received oral coconut oil, only one survived due to early administration. Three patients (14.3%) received oral dilute K permanganate solution. Oral N- acetyl cysteine was given to 7 patients; of whom 5 survived (71.4%) due to early administration indicating the importance of the use of antioxidants. Six patients were intubated and mechanically ventilated but no one was saved. Three patients received plasma infusion due to bleeding diathesis but two of them died.

Table 5 shows that the risk of death increased in relation to certain parameters, the absence of vomiting, the lower the pH, the higher blood lactate level on admission and the need for ventilator use. All these results showed statistically significant differences between the survived and non-survived groups. Eleven patients (91.7%) died due to shock and severe hypotension and one patient (8.3%) developed several complications due to prolonged hospital stay.

Among survived patients, six (28.6%) were discharged against medical advice (mostly due to financial problems) and three (14.3%) improved and were discharged, they presented mainly with bleeding diathesis with little effect on blood pressure. Two of the survived did immediate gastric lavage with sodium bicarbonate solution and one vomited immediately several times meaning that rapid gastric decontamination had good prognostic value. They received N-acetyl cysteine 600 mg IV (first initial loading dose 150 mg/kg in 200 ml over one hour, then 50 mg/kg in 500 ml over the next 4 hours then the last infusion was 100 mg/kg in one liter over the next 16 hours). One of them, received packed plasma shortly after admission and the other two improved on antifibrinolytic agent (tranexamic acid: 10–15 mg/kg IV over 20 minutes, then 1 mg/kg/hour continuous infusion for 6–10 hours).

5. Discussion

The incidence of ALP poisoning in Egypt is increasing steadily. Recently, NECTR has witnessed an increased incidence of suicidal attempts by ALP which becomes a major clinical problem due to its high toxicity, difficulties in management of patients and high mortality rates. In our study, the mortality rate was 57.1%; of the total of 21 cases, eleven patients (91.70%) died due to sudden cardiac arrest caused by severe hypotension resistant to medical treatment despite massive fluid replacement and vasopressors administration, and the remaining patient (8.3%) died after prolonged hospital stay due to Acute Respiratory Distress Syndrome (ARDS).

Several postulated causes of intractable hypotension was described in researchers' studies. Intractable shock caused by ALP poisoning might be due to arrhythmia, conduction disturbance and myocardial damage[27]. Moreover, the peripheral circulatory failure, owing to widespread small vessel injury, leads to peripheral vasodilatation and shock. Also, fluid loss due to excessive vomiting, could contribute to shock. Another added factor is the direct toxic effects of PH_3 on the adrenal cortex accompanied by decreased cortisol levels.

Marashi and colleagues[28] proposed that insufficiency in vascular wall integrity could explain everything that happens after absorption of phosphine gas. They claimed that the main problem was massive intravascular fluid loss causing refractory hypovolemic shock which leads to multiorgan failure. Also, Moghadamnia[5] , Mehrpour and colleagues[7] stated that ALP causes hypotension resistant to medical treatment, persistent metabolic acidosis and Multiple Organ Failure (MOF) due to lipid peroxidation. The refractory hypotension does not respond to massive crystalloid administration and vasoactive substances[29]. In this context, refractory metabolic acidosis may be a reflection of organ hypoperfusion[30].

Recent studies stated that ALP-induced toxic myocarditis caused severe hemodynamic changes that eventually lead to hypotension which was resistant to fluid therapy and inotropes and was considered the main cause of death in patients with ALP poisoning[31,32].

Results of this study showed that more poisonings occurred in younger adults in El Fayoum governorate; this

could be explained by the higher stress and psychological burden and depression in these people due to worsening of the socio-economic conditions, scolding from other family members and stresses of failure in social life or education or lack of employment opportunities. In addition, a large proportion of the population was engaged in farming where overcrowding and easy access to toxic pesticides play an important role in rural areas. The high incidence of ALP poisoning in rural areas was also reported in the majority of toxicology centers[6,33,34].

Intentional oral intake of ALP in our study accounted for 85.7% of cases. Similarly, Shadnia and colleagues[35] reported that self-poisoning was observed in 93% of cases. They also stated that all deaths occurred in the first 24 h due to arrhythmia. Most of our non-survived patients lost their lives in the first 24 hours (23.33 ± 46.12 hours) with a significant difference between survived and non-survived. Similarly, in Iran and India the cause of poisoning was mainly suicidal[5].

It has been suggested in various studies that there was an association between the absence of gastrointestinal symptoms such as nausea and vomiting and severity of ALP poisoning[3,8]. Similarly, in the present study, absence of nausea and vomiting was higher in patients who lost their lives (57.2%) while survived patients vomited several times indicating the importance of rapid gastric decontamination.

Regarding serum lactate level, hyperlactatemia is defined as the serum lactate level of ≥ 2 mol/L[36]. Hyperlactatemia in ALP toxicity is a result of both energy insufficiency and oxidative stress, with possible interaction with mitochondrial electron transport chain and the inhibition of cytochrome c oxidase leading to metabolic acidosis and increased lactate production[37,38]. Serum lactate levels have been used as a prognostic factor in critically ill patients[39,40]. In accordance, our results revealed that all patients had hyperlactatemia on admission, in the survived the mean was 4.38 ± 2.79 and in the non-survived the mean was 10.61 ± 4.93 (figure 2) with highly significant difference between survived and non-survived patients which carried bad prognostic outcome. In the survived the level improved on subsequent measurements while in the non-survived the levels continued to rise. In correlation with different parameters of Arterial Blood Gases (ABG), Table 3 showed strong correlation between serum lactate level and pH and HCO_3 levels on admission and after 2 and 6 hours. In concordance, Erfantalab and colleagues[41] examined patients with ALP poisoning admitted to the Medical Toxicology Intensive Care unit in Iran, they found that poisoned patients had higher levels of blood lactate within the first hours post-ingestion. They stated that blood lactate level within the 8 to 16 hours post-ingestion could be successfully used as a prognostic sign in acute ALP poisoning. Also, their results showed significant correlation between blood lactate levels and pH at 6 to 22 hours post-ingestion. For each point increase in serum lactate level, the chance of death increased by 13% in poisoned patients[42].

Determination of predictive factors of mortality on admission may allow more intensive monitoring and treatment that may improve patients' outcome. Accordingly, to predict the medical outcome and the risk of mortality among acute ALP poisoned patients, several authors tried to develop certain criteria by using some independent variables.

Louriz and colleagues[37] found a correlation between mortality in acute ALP poisoning, shock and altered consciousness.

Sulaj and colleagues[43] reported that the dose of ALP ingested, the interval between ingestion, the beginning of treatment, and the depth of coma were the predictors of mortality in poisoned patients. Erfantalab and colleagues[41] demonstrated that certain factors such as blood pressure, heart rate, blood pH and serum bicarbonate levels were significantly different between people who died due to acute ALP poisoning and those who survived; findings which coincide with our results.

So, based on our results; we suggested a four-variable risk-prediction nomogram including SBP, serum lactate level, prothrombin concentration and serum HCO_3 levels to be used as a prognostic tool to predict mortality in ALP-poisoned patients. Similarly, Farzaneh and colleagues[44] developed a four-variable risk-prediction formula including SBP, GCS, urinary output (UOP) and serum HCO_3 to provide quick and simple analysis that could identify high-risk patients and predict the risk of mortality.

So, physicians could apply this nomogram to detect cases of acute poisoning at risk of death during a patient's stay in the ICU, to enhance patient management to reduce mortality risk, and to detect those patients who appeared well at first but may then progress towards a fatal outcome. Accordingly, the mortality risk could be estimated and calculated numerically. This developed tool is a basic chart which through the use of some

independent variables, is able to provide a numerical estimation of the rate of death in patients with ALP poisoning. In addition, the developed nomogram is easy to use as all its required factors are readily and routinely gathered in the medical care setting, requiring only five minutes for measuring and determining the risk of death in ALP-poisoned patients.

Regarding management in our patients, unfortunately, there is no standard protocol for the management of ALP poisoning in the textbooks and reference databases.

Thus, treatment depended on the physician who admitted and managed the patients. In this study, gastric decontamination was performed in patients who presented within 2 hours of ALP ingestion using sodium bicarbonate or potassium permanganate solutions. In different parts of the world, many decontamination procedures were used to decrease the absorption of consumed ALP. Some advocate gastric lavage with potassium permanganate (1:10 000) immediately after admission, to be repeated two or three times followed by a slurry of activated charcoal (approximately 100 g) given through a nasogastric tube[45]. Some authors considered gastric lavage should probably be avoided after ingestion of phosphides as it might increase the rate of disintegration and increased their toxicity[19]. Some authors had also suggested that vegetable oil might decrease the release of PH_3 from ALP[46,47]. Solutions composed of water should not be used for gastric decontamination after acute ALP poisoning[48]. Instead, using vegetable oils for gastric lavage or castor oil to inhibit greater PH_3 release as well as stimulation of luminal evacuation could be practical.

In this study, three patients received coconut oil (14.3%), which is believed to form a protective layer on the gastric mucosa, thereby preventing the absorption of phosphine gas. Also, it helps in diluting the hydrochloric acid (HCl) and again inhibiting the breakdown of phosphide from the pellet in addition to its non-miscibility with fat[47]. Others received potassium permanganate (14.3%), some received vasopressors (38.1%) with no significant difference between survived and non-survived in clinical outcome. In this study, seven patients (33.3%) received N-Acetyl Cysteine (NAC) on admission, five of them survived; so, this might indicate the importance of using antioxidants in patients' management, as oxidative stress is one of the main mechanisms of ALP toxicity. NAC is an important antioxidant and a cytoprotective agent that replenishes intracellular glutathione.

6. Conclusions and Recommendations

Owing to the rapidly increasing number of deaths and suicides due to ingestion of aluminium phosphide, the need of the hour is the development of a specific antidote capable of counteracting the action of PH_3 molecules, thus preventing the free radical-mediated cellular and mitochondrial injury, the factors associated with the high mortality rate.

Based on the results of this study, on admission, the presence of metabolic acidosis and severe hypotension could be used as alarming predictive factors of mortality from acute ALP poisoning. Early management of these risk factors via intensive hemodynamic monitoring and proper supportive care might improve patients' outcome. A better outcome could also be achieved with early arrival, prompt diagnosis and rapid decontamination.

In addition to this, public awareness and easy availability of ALP become the two most important issues to act upon. Regulatory action to ban highly hazardous pesticides, particularly ALP and substitution with safer agents is necessary. Strict measures, both at the administrative as well as the legislative levels are required to strategically modify and restrict the supply of ALP especially in rural areas.

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8. References

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