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Evaluation of blood cortisol and lactate levels as outcome predictors in acute Aluminum phosphide poisoned patients

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Abstract

Background: Aluminum phosphide (ALP) is a highly lethal toxin with mortality rate 70-100%. Death frequently occurs in the first 12 to 24 hours due to cardiac and pulmonary toxicity, lactic acidosis, and adrenal insufficiency altering cortisol level and unfortunately there is no antidote found up till now. There is little data on biomarkers to predict outcome in ALP toxicity and we depend mainly on symptoms which are sometimes misleading. **Aim:** Assess the usefulness of measuring separately blood cortisol and lactate levels in predicting the outcome in Aluminum phosphide intoxicated patients. **Patients and Methods:** A prospective observational study was conducted from first of June 2022 till end of March 2023 on 40 patients of both sexes with acute ALP poisoning admitted to the Poison Control Centre, Ain Shams University Hospitals (PCC-ASUH) with maximum delay time 48 hours. Sociodemographic, intoxication and clinical data were collected for every patient. Investigations included Arterial Blood Gas (ABG) analysis including lactate, and routine lab investigations in addition to blood cortisol, also electrocardiogram (ECG) were done. Outcome was also recorded. **Results:** Blood cortisol and the blood lactate levels were significantly high among the patients who die later on, pH, HCO_3, SaO_2 were significantly reduced in deaths compared with survivors. **Conclusion:** Biochemical abnormalities of hyperlactemia and elevation of blood cortisol level can be used as predictors of mortality in ALP intoxicated patients.

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Key words Aluminum phosphide, lactate, cortisol

Introduction

Aluminum phosphide (ALP) is a well-known pesticide used worldwide as being cheap, it is sold in stores, so it is widely available and used in suicidal attempts with high mortality rate. This usually due to multiorgan failure as cardiogenic shock, hypotension, arrhythmias, metabolic acidosis, pulmonary edema, disseminated intravascular coagulopathy (DIC), hepatic necrosis, renal failure and adrenal insufficiency altering the cortisol level. (Ahmadi et al., 2018)

Toxicity with ALP was increasing over the last years according to Poison Control Centre, Ain Shams University Hospitals (PCC-ASUH) records forty-nine cases were reported in 2019 while 110 cases were in 2020, 148 cases were in 2021 and 182 cases were in 2022 (PCC-ASUH records from 2019 till 2022). In Tanta University Poison Control Center (TUPCC) 193 cases of ALP were reported in 2019, in 2020, 258 ALP cases, in 2021, 280 ALP cases. (TUPCC records 2019 till 2021).

While in Zagazig university hospital (PCCZUH) in 2021, 140 cases of ALP were reported 77% of them died (Hassan & Mwaheb, 2022). The actual number of cases cannot be known because many cases die before reaching the hospital (Mathai & Bhanu, 2010).

Phosphine gas is released when the ALP comes in direct contact with atmospheric moisture or with hydrochloric acid in the stomach which affects the mitochondria causing inhibition of cytochrome C oxidase leading to cellular hypoxia which leads to multi organ failure (Wahab et al., 2008 and Farnaghi et al.,2013).

The adrenal gland insufficiency is affected by the shock or the toxic effect of phosphine gas, which affects the blood cortisol levels and these changes are called “Relative Adrenal Insufficiency” (RAI) or “critical illness-related corticosteroid insufficiency” (CIRCI), It is in the form of change in the secretion, responsiveness, in the protein binding or in the activity of glucocorticoids (Farnaghi et al., 2013).

As for respiration, the Pyruvic acid, under aerobic conditions, is oxidized to acetyl coenzyme which shares in the Krebs cycle producing adenosine triphosphate (ATP); meanwhile in anaerobic conditions it produces lactate in a process called anaerobic glycolysis during fermentation. So, the lactate is considered a marker of hypoxia (Kucherenko et al., 2019).

Aim of the Study

The aim of this study is to assess the usefulness of measuring separately blood cortisol and lactate levels in predicting the outcome in aluminum phosphide acutely poisoned patients.

Patients and Methods

Study design: A prospective observational study was carried out on 40 ALP poisoned patients admitted to the PCC-ASUH with maximum delay time 48 hours from the first of June 2022 till the end of March 2023.

Ethical Considerations: Approval (MS 436/2022) was taken from the Ethical Committee Ain Shams University.

- Approval was taken from PCC-ASUH general director.
- An informed valid consent was taken from the patients' legal guardians and their information was kept anonymous.

Inclusion criteria: All Cases of ALP poisoning admitted to PCC-ASUH with maximum delay time 48 hrs. in the period from the first of June 2022 till the end of March 2023, the diagnosis was based on history of exposure to ALP and by the clinical manifestations of ALP poisoning.

Exclusion criteria: Patients with any of the following conditions were excluded from the study:

1. Co ingestion of other toxins.
2. History of use of steroid.
3. Cardiac, hepatic, endocrine, renal, diabetic, and septic patients.

Data collection: The sociodemographic data and intoxication data were collected. Physical examination was done including general and systemic examination. General examination included: vital data (blood pressure, pulse, respiratory rate, body temperature), conscious level, skin and pupils. Systemic examination included: gastrointestinal examination, cardiovascular examination, respiratory system examination and neurological examination. Outcome was also recorded (as cure, complications or mortality)

Investigations: Five ml of blood was withdrawn from the participants on admission under complete aseptic conditions for assessment of blood cortisol level using ELISA technique (Farnaghi et al., 2013).

Two ml of arterial blood sample was collected on admission on a heparinized syringe and immediately was tested for arterial blood gases (ABG) analysis including blood lactate level.

Another 2 ml of venous blood sample was collected and centrifuged for ten minutes at 5000 rpm. Serum was collected and used immediately for routine laboratory investigations included electrolytes (sodium, potassium), random glucose level, liver function (AST and ALT) and kidney functions (BUN and serum creatinine).

Also, complete blood count (CBC), coagulation profile Prothrombin Time (PT), Partial Thromboplastin Time (PTT), INR, cardiac enzymes, Creatine Kinase-MB (CK-MB), troponin were collected under complete aseptic condition.

Electrocardiogram (ECG) was performed at the time of admission. ECG analysis includes the rate, rhythm, ST\T abnormalities, conduction defects and measurement of P-R, QRS complex and Q-T intervals.

Continuous cardiac monitoring was done once the patient entered the ICU for any ECG changes that may happen.

Statistical analysis: The collected data was revised, coded, tabulated, and introduced to a PC using Statistical package for Social Science Version 25.0.

i. Descriptive statistics: includes Shapiro Wilk's test was used to evaluate normal distribution of continuous data. Mean, standard deviation (± SD), and range was used for parametric numerical data, while median and Interquartile range (IQR) was used for non-parametric numerical data. Also, frequency and percentage of non-numerical data were done.

ii. Analytical statistics: includes Student t test, Mann Whitney Test (U test), Chi-Square test, Fisher's exact test and ROC Curve (receiver operating characteristic) were performed.

- P- value: level of significance was set at:
- P>0.05: Non-significant (NS).
- P< 0.05: Significant (S).
- P<0.01: Highly significant (HS).

Results

After collecting socio-demographic data, intoxication history, physical findings, investigations, treatment received as well as the outcome for all included patients, the data were recorded in a special observation sheet, and then statistically analyzed and presented in tables and graphs.

The median age was 22 years with a range of 13-52 years old, the age group more than 17 years till 25 years old had the highest incidence. It also shows that the females were slightly more affected than males. As regards the residence most of the patients were from rural areas with highest incidence from the Fayoum governorate representing 35% as shown in table (1).

Suicidal mode was the main mode of intoxication occurred in 95%. Majority of the patients (95%) were intoxicated by the oral route. As for the amount of AlP, intoxication by 1 tablet (3g) had the highest incidence. Regarding the delay time more than 2 till 6 hours represented the highest incidence as shown in table (2).

Regarding gastrointestinal system (GIT) manifestations, vomiting had the highest incidence 90%, then abdominal pain, thirst sensation, diarrhea, and nausea. As regard the cardiovascular system manifestations, shock was found in 42.5%, then hypotension was found in 37.5% and hypertension was found in 7.5%. Normal heart rate was found in 60%, then tachycardia was found in 25%, bradycardia was found in 15%. Dyspnea and chest pain had the least incidence 5% each as shown in table (3).

As for the respiratory manifestations, tachypnea was the highest incidence (62.5%), normal respiratory rate and cyanosis represented 20% each and mechanical ventilation (MV) was in 17.5% of patients. As regard neurological manifestations, agitation was in 35%, disturbed conscious level (DCL) was in 30% and no one had convulsions as shown in table (3).

ECG changes in the selected 40 intoxicated patients were shown in table (4) and figure (1).

Correlations between survivors and deaths regarding routine lab investigations and cardiac enzymes were shown in table (5).

There was a high significant difference between survivors and deaths as regard pH, HCO3, SaO2 and lactate while no significant difference was found between them as regard PCO2. The mean among the survivors as regards the lactate was 3.41, while the

mean in the deaths was 10.1 as shown in Table (6).

Table (7) and figure (2) show the ROC curve that lactate blood level can be used as a predictor for death for ALP intoxication at a level of ≥6.25, with 100% sensitivity and 91.4% specificity. There was a significant difference found as regard cortisol blood level, with higher mean levels among deaths. The mean among the survivors was 51.59, while the mean in the deaths was 68.91 as shown in Table (8).

Table (9) and figure (3) show the ROC curve that cortisol can be used as a predictor for death from ALP intoxication at a level of ≥28.3, with 100% sensitivity and 45.4% specificity.

Regarding the outcome, the occurrence of complications incidence was 65% among the total studied cases. Survival incidence was 55% and deaths incidence was 45%.

As for the complications that occurred, occurrence of shock had the highest incidence 42.5%, then the elevated cardiac enzymes had incidence 27.5% and the elevated liver enzymes had the least incidence 15%.

Table (1): Distribution of the age, gender, and residence among the selected 40 patients of ALP toxicity:

Socio-demographic data		Total number (n=40)	Percentage
Age (in years)	Range	13-52	
	Median (IQR)	22	
	13-17 years	12	30%
	>17-25 years	16	40%
	more than 25 years	12	30%
Gender	Male	19	47.5%
	Female	21	52.5%
Residence	Fayoum Governorate	14	35%
	Cairo Governorate	13	32.5%
	Qalyubia Governorate	7	17.5%
	Bani Sweif Governorate	5	12.5%
	Sharkeya Governorate	1	2.5%

n: Number, IQR: interquartile ratio

Table (2): Distribution of the mode, route of intoxication, amount of ALP taken and the delay time among the selected 40 patients of ALP toxicity:

		Total number (n=40)	Percentage
Mode of intoxication	Suicidal	38	95%
	Accidental	2	5%
Route of intoxication	Oral	38	95%
	Inhalation	2	5%
Amount of ALP (in tablets)	Less than 1 tablet	12	30%
	1 tablet (3g)	25	62.5%
	More than 1 tablet	3	7.5%
Delay time	0-2 hours	13	32.5%
	>2 hours till 6 hours	23	57.5%
	>6 hours till 24 hours	4	10%

n: Number

Table (3): Distribution of the clinical manifestations that happened among the selected 40 patients of ALP toxicity

Clinical manifestations	Total number (n=40)	Percentage
GIT manifestations		
Nausea	5	12.5%
Vomiting	36	90%
Diarrhea	7	17.5%
Abdominal pain	10	25%
Thirst sensation	9	22.5%
Cardiovascular manifestations		
Hypotension	15	37.5%
Hypertension	3	7.5%
Shock	17	42.5%
Normal heart rate	24	60%
Tachycardia	10	25%
Bradycardia	6	15%
Dyspnea	2	5%
Chest pain	2	5%
Respiratory system manifestations		
Normal respiratory rate	8	20%
Tachypnea	25	62.5%
Bradypnea	0	0%
MV	7	17.5%
Cyanosis	8	20%
Chest crepitations	1	2.5%
Neurological manifestations		
No CNS affection	14	35%
DCL	12	30%
Agitation	14	35%
Convulsions	0	0%

n: Number, MV: Mechanical ventilation, DCL: Disturbed conscious level, CNS: Central nervous system

Table (4): Distribution of the ECG changes among the selected 40 patients of ALP toxicity

ECG changes	Total number (n=40)	Percentage
Normal ECG	24	60%
Sinus tachycardia	10	25%
Sinus bradycardia	6	15%
Wide QRS	1	2.5%
ST segment elevation	1	2.5%
Inverted T wave	1	2.5%
Single extrasystole	4	10%
Ventricular tachycardia	1	2.5%

n: Number

Table (5): Statistical analysis studying the relation between survivors and deaths as regard routine lab investigations and cardiac enzymes:

	Survivors					Deaths					P	Sig
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR			
Na	138.64	2.79	139.0	137.0	140.0	139.28	4.66	138.0	136.0	140.0	0.593*	NS
K	3.90	0.38	3.9	3.6	4.2	3.78	0.28	3.8	3.6	4.0	0.251*	NS
RBS	109.05	33.61	102.0	98.0	120.0	148.11	92.12	123.5	100.0	160.0	0.072*	NS
AST	27.95	32.84	16.0	13.0	28.0	35.89	44.43	13.0	11.0	70.0	0.264**	NS
ALT	19.09	21.58	12.0	9.0	16.0	30.33	29.63	14.5	10.0	65.0	0.314**	NS
BUN	10.18	9.22	8.0	6.0	10.0	8.89	3.25	8.0	6.0	11.0	0.901**	NS
S.Cr	0.82	0.38	0.7	0.5	1.1	0.97	0.33	0.9	0.8	1.2	0.196*	NS
PT	13.19	1.26	12.9	12.2	14.4	14.16	2.72	13.3	12.8	14.0	0.146*	NS
PTT	27.81	5.27	26.5	24.2	30.0	27.12	4.50	26.0	24.0	30.0	0.664*	NS
INR	1.14	0.10	1.1	1.1	1.2	1.18	0.39	1.2	1.1	1.3	0.664*	NS
Hb	13.56	2.10	13.0	12.2	15.0	12.74	1.93	12.2	11.2	15.0	0.333*	NS
Plt	242.68	55.81	234.0	199.0	271.0	337.11	82.38	345.0	300.0	370.0	0.001*	HS
TLCs	10.47	4.30	11.0	7.0	12.0	12.84	6.54	11.0	7.0	17.4	0.178*	NS
CKMB	37.95	61.84	20.0	15.0	29.0	34.11	24.67	25.0	20.0	37.0	0.593*	NS
Troponin	0.11	0.26	0.0	0.0	0.1	0.27	0.96	0.0	0.0	0.0	0.251*	NS

Student t test, **Mann-Whitney test, SD: Standard deviation, IQR: interquartile ratio, Sig: Significance, -P>0.05: Non-significant (NS), -P<0.01: Highly significant (HS).

Table (6): Statistical analysis studying the relation between survivors and deaths as regard ABG:

	Survivors					Deaths					P	Sig
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR			
pH	7.38	.06	7.4	7.3	7.4	7.22	.14	7.2	7.2	7.3	**0.001***	HS
PCO2	34.36	6.93	35.0	28.0	39.0	30.17	9.44	28.5	25.0	37.0	0.113*	NS
HCO3	20.39	4.42	20.4	17.7	23.0	12.51	4.13	12.5	9.6	14.5	**0.001***	HS
SaO2	97.50	1.63	98.0	96.0	99.0	87.17	7.76	86.5	80.0	96.0	**0.001***	HS
Lactate	3.41	2.68	2.4	1.4	5.3	10.19	2.55	10.1	8.7	12.7	**0.001****	HS

Student t test, **Mann-Whitney test, SD: Standard deviation, IQR: interquartile ratio, Sig: Significance, -P>0.05: Non-significant (NS), -P<0.01: Highly significant (HS).

Table (7): Best cutoff point for lactate blood level to predict mortality in ALP intoxicated patients in the current study:

Cutoff level of lactate	Area under curve (CI)	Sensitivity	Specificity	PPV	NPV	p
=>6.25	0.951 (0.832 to 0.994)	94.44	86.36	85.0	95.0	0.001

CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

Table (8): Statistical analysis studying the relation between survivors and deaths as regard cortisol blood level:

	Survivors					Non survivors					P	Sig
	Mean	±SD	Median	IQR		Mean	±SD	Median	IQR			
Cortisol level	51.59	50.27	35.3	15.1	62.8	68.91	38.92	57.6	49.7	68.9	0.03*	S

Mann-Whitney test, SD: Standard deviation, IQR: interquartile ratio, Sig: Significance, -P< 0.05: Significant (S).

Table (9): Best cutoff point for cortisol blood level to predict mortality in ALP intoxicated patients in the current study:

Cutoff level of cortisol	Area under curve (CI)	Sensitivity	Specificity	PPV	NPV	p
=>28.3	0.702 (0.53-0.83)	100.00	45.45	60.0	100.0	0.03

CI: Confidence interval, PPV: Positive predictive value, NPV: Negative predictive value

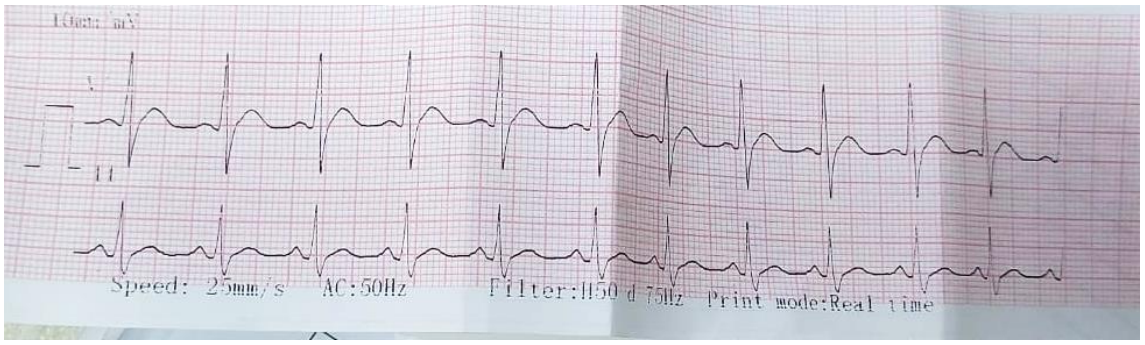

Figure (1): ECG strip showing sinus tachycardia in lead I and II in one of the patients

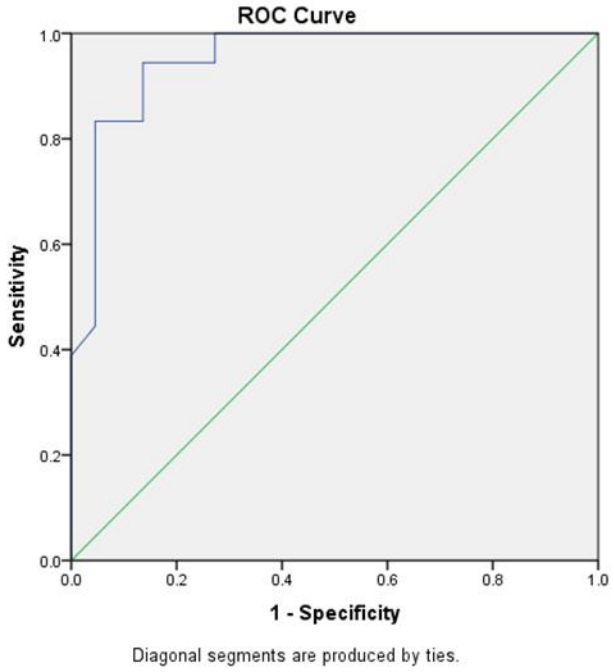

Figure (2): ROC Curve displaying the diagnostic accuracy of lactate blood level to predict deaths in ALP intoxicated patients in the current study

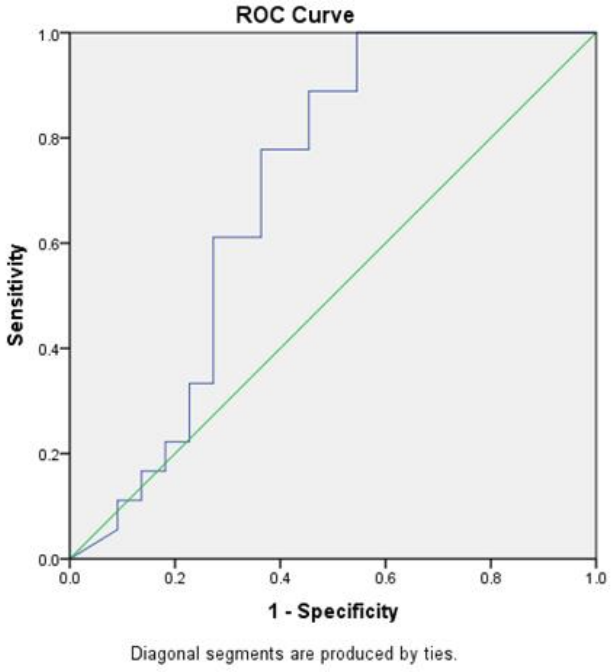

Figure (3): ROC Curve displaying the diagnostic accuracy of cortisol blood level to predict deaths in ALP intoxicated patients in the current study

Discussion

In developing countries, the incidence of AlP poisoning increases due to uncontrolled accessibility and its cheapness. In Egypt, AlP is known as wheat pill and ALP self-poisoning is emerged as major public health problem evidenced by high reported mortality rate. Many patients unfortunately die in spite of intensive care as there is no specific antidote. (Abd Elhakam et al., 2020 and Bogale et al., 2021).

This study aimed to assess the usefulness of measuring separately blood cortisol and lactate levels as predictors for early predicting and estimating the outcome in ALP intoxicated patients.

In the current study, the females with the ALP intoxication had higher incidence 52.5% due to stress that they could not reveal it in a right way. Our result supports previous results by Masoud & Barghash, 2013 and El-Ebiary et al., 2015. On the other hand, Moghadamnia, 2012 reported that the ratio of males to females was 2:1 respectively.

In the present study most of the studied patients were from the rural areas with incidence 67.5%, this was in agreement with Moghadamnia, 2012.

This study found that the commonest mode of intoxication was suicidal in 95% due to social problems. The same result was mentioned by Bogale et al., 2021 who found that most of the patients took ALP for suicidal attempts due to depression and family problems.

Route of intoxication in the current study was mostly through ingestion in 95% of the patients, while the inhalation route was found in only 5% of the patients by an accidental exposure.

The current study is in agreement with several studies, as the oral route was the main route of intoxication in ALP intoxicated patients (Gurjar et al., 2011; Fyala et al., 2020 and Abd-Allah et al., 2022). On the contrary Alnasser et al., 2018 mentioned that in Saudi Arabia, the most common cause of ALP intoxication was accidentally by inhalation when it was

used in fumigation and most of the intoxication had happened in young children.

Most of the patients in the current study ingested one complete tablet (3 g) representing 62.5% of the patients, this incidence was observed also by Masoud & Barghash, 2013. While Alnasser et al., 2018 reported some cases with accidental exposure to ALP with exposure to one tablet up to 8 tablets. In a 70kg individual the lethal dose of ALP reported to be 500mg (Karimani et al., 2018).

The current study observed that the delay time was mostly from 2 to 6 hours, and this was due to the long distance between the rural areas they came from and our PCC. Similar result was found by Beyranvand et al., 2019. However, the delay time observed by Bhalla et al., 2017 was found to be 3 hours only.

In the present study, the hospital stay time was 24 till 48 hours with the highest incidence 47.5%. Hosseinian et al. (2011) was in accordance with the current study.

Regarding GIT symptoms, vomiting was the most common symptom with incidence 90%, Bogale et al., 2021 and Abdelhamid et al., 2023 were in agreement with the current study as vomiting could be due to irritation of the gastric mucosa by phosphine gas. While Elabdeen et al., 2020 mentioned that the GIT symptoms were representing 56% only. Thirst sensation was found in the ALP intoxicated patients in this study with incidence 22.5% and this could be due to severe vomiting and dehydration.

In the current study most of the patients had normal heart rate with incidence 60%, while 25% had tachycardia and only 15% had bradycardia, and this was reported by Abdelhamid et al., 2023. While Garg, 2020 found that tachycardia represented by palpitation was a common complaint in ALP intoxicated patients.

This study found that, 42.5% of patients had shock, 37.5% had hypotension. Also, Farnaghi et al., 2013 reported that shock and hypotension are common manifestations of ALP toxicity as it causes low perfusion to vital organs leading to hepatic, renal failure and adrenal damage.

Hypotension could be due to fluid loss, dehydration, peripheral vasodilatation and due to the effect of the adrenal glands and the intractable shock could be due to myocardial injury and also due to adrenal gland insufficiency (Changal et al., 2017).

In this study, chest pain and dyspnea were the least cardiovascular symptoms seen. On the other hand, Garg, 2020 found that chest pain and dyspnea were the most common cardiovascular symptoms found and the most common cause of death in acutely poisoned patients with ALP.

Twelve lead ECG was found normal in 60% of the intoxicated patients, while sinus tachycardia was found in 25% of the patients, sinus bradycardia was found in 15% of the patients and the single extra systole was found in 10% of the patients, as for the wide QRS, ST segment elevation, inverted T wave, ventricular tachycardia, were found each in only 2.5% of the patients.

The current study supported Soltaninejad et al., 2012, who found that 55% of the studied patients had sinus rhythm while only 45% of them had dysrhythmia.

On the other hand, El-Ebiary et al., 2015 mentioned that normal ECG was observed in only 20% of the patients while the ST segment was found elevated in 20% of the patients. While, Garg, 2020 mentioned that the supraventricular tachycardia was found in half of the patients and the ventricular tachycardia was found in 40% of the studied patients.

Regarding respiratory system, tachypnea was seen as the main symptom with incidence 62.5%, normal respiratory rate was found in 20% and no one had bradypnea and this was also reported by Singh et al., 2014 and Saif et al., 2015. In contrast, Elabdeen et al., 2020 observed that the tachypnea was only found in 38% of the patients while 62% were seen with normal respiratory rate on admission.

Coarse crepitation was found in this study in only 1 patient with incidence 2.5%. On the contrary, Hashemi-Domeneh et al., 2016 mentioned that chest crepitation was a common respiratory symptom because pulmonary edema was reported frequently.

In the current study, 20% of the patients had cyanosis and 17.5% were mechanically ventilated on admission. This result was in accordance with Hashemi-Domeneh et al., 2016. On the other hand, Shadnia et al., 2010 found that about 60% of ALP studied patients had cyanosis.

In the current study, 35% of the patients came with agitation and 30% had DCL, no one had convulsions also Hashemi-Domeneh et al., 2016 mentioned the same result.

In our study, serum electrolytes (sodium and potassium) were within the normal range in the survivors and the deaths, and no significant difference was found between the survivors and deaths as regards serum sodium and potassium. El-Ebiary et al., 2015; Beyranvand et al., 2019 and Elabdeen et al., 2020 were in accordance with the current study

In this study no significant difference was found between survivors and deaths regarding RBS. The same result was reported by Abd Elghany et al., 2018.

However, Sharma et al., 2018 found that a significantly higher difference was found between the survivors and deaths as regard RBS, and Mehrpour et al., 2008 suggested that hyperglycemia can be used as a prognostic factor for mortality in acute intoxication by ALP.

In the current study, regarding the liver function tests (AST and ALT) and kidney function tests (BUN and serum creatinine) were within the normal range on admission for both survivors and deaths and this result was also mentioned by Beyranvand et al., 2019 and Elabdeen et al., 2020.

However, El-Ebiary et al., 2015 found that ALT was elevated in 55% of the patients. On the other hand, Mathai & Bhanu, 2010 and Masoud & Barghash, 2013 found that there was an acute kidney injury in acute ALP intoxicated patients.

The coagulation profile (PT, PTT, INR) in this study showed no significant difference between the

survivors and deaths. Abd Elhakam et al., 2020 was in agreement with our study. However, Majidi et al., 2021 found a significant difference in the PT and INR between survivors and deaths of ALP poisoned patients.

Considering the CBC, it was found normal in all the patients on admission and there was no significant difference between the survivors and deaths as regarding hemoglobin and total leucocytic count, but for the platelets there was a significant difference between them. Eric et al., 2021 was in accordance with the present study.

The CKMB and the troponin in the current study showed no significant difference between the survivors and deaths on admission. However, El-Ebiary et al., 2015 was against the current study who found a significant difference between the survivors and deaths as regard the troponin, as it was positive in 40% of the patients due to cardiovascular changes.

In the current study, normal ABG was found in the survivors with normal pH, PCO2 level, and HCO3 level, On the other hand, most of the deaths had severe metabolic acidosis since admission which was refractory to many treatment modalities like volume expansion and sodium bicarbonate. A high significant difference was found between survivors and deaths as regard pH, HCO3. While no significant difference was found between them as regard PCO2.

The current study supported Dadpour et al., 2016 who found that all the survived patients had normal ABG on admission. Many studies were in accordance with our study as mentioned by Shadnia et al., 2009 and Farzaneh et al., 2018, that the pH and HCo3 levels were good prognostic tools for mortality in patients acutely intoxicated with ALP.

In this study, a high significant difference was found between the survivors and deaths, as regards the oxygen saturation as it was found with normal levels in the survivors. While the oxygen saturation was found to be low in the non survivors and this supported many other studies (El-Ebiary et al., 2015; Beyranvand et al., 2019 and Elabdeen et al., 2020).

Proudfoot, 2009 explained hypoxia from phosphine gas, which disrupts mitochondrial morphology, prevent about 70% of mitochondrial oxidative respiration, and leads to marked defect in mitochondrial membrane potential, hence inhibition of cytochrome oxidase.

Regarding blood lactate level in this study, a high significant difference was found between the survivors and deaths as the survivors had median lactate level 2.4 mmol/L which improved and became normal with appropriate treatment, while the deaths had median lactate level on admission 10.1 mmol/L and unfortunately, they deteriorated rapidly.

The present study supported Abd Elhakam et al., 2020 who mentioned that there was a significant difference between the survivors and deaths as regard the lactate level, as it was found significantly high in the deaths. This could be due to inhibition of the cellular respiration and damage of the mitochondria by the inhibition of the cytochrome C oxidase and so inhibition of the ATP production.

Lactate elevation may be caused by increased production, decreased clearance, or both. Contributing factors include: hypoperfusion due to macro- and/or microcirculatory dysfunction, mitochondrial dysfunction. Liver dysfunction may contribute to both increased production and decreased clearance (Andersen et al.,2013).

In the current study a cut off value for the blood lactate level was determined by the ROC curve at a level of ≥6.25 mmol/L with 100% sensitivity and 91.4% specificity and so the lactate blood level can be used as a predictor for death for the acute ALP intoxicated patients.

Abd Elhakam et al., 2020 found the same results and mentioned that the lactate level can be used as a prognostic factor for the severity of ALP intoxicated patients.

In the current study a significant difference between the survivors and deaths was found as regard cortisol blood level, with higher mean levels among non survivors.

Similarly, Chugh et al., 1989 studied the effect of ALP on adrenal cortex and found that 20 out of 30 patients with ALP poisoning had elevated blood cortisol level. However, Farnaghi et al., 2013 found that there was no significant difference between fatal and non-fatal cases regarding the cortisol blood level.

Adrenal cortex changes could be attributed to shock or toxic effect of phosphine gas. Adrenal gland damage may decrease or increase blood cortisol concentration. There are few reports about blood cortisol levels in ALP toxicity and the optimal range of blood cortisol in ALP poisoning has not yet been identified. Histopathologic examination of adrenal cortex following ALP toxicity revealed hemorrhage, necrosis, and lipid depletion (Farnaghi et al., 2013).

However, alteration in cortisol metabolism may be due to changes in secretion, protein binding, responsiveness, and glucocorticoids activity this is called "critical illness-related corticosteroid insufficiency" (CIRCI) (Venkatesh & Cohen, 2011).

Cortisol blood level was found to be a predictor for mortality in this study, the median level for the survivors was found 35.3 ug/dl while the median in deaths was found 57.6 ug/dl and a cut off value was determined by the ROC curve ≥28.3 ug/dl, with 100% sensitivity and 45.4% specificity. So, it can be used as a stress marker to predict the outcome of the acutely intoxicated ALP patients.

On the contrary, Masoud & Barghash, 2013 mentioned that the cut off value of the cortisol was <29.1 µg/dL with sensitivity 88.89% and specificity 100% and so cortisol level was observed to decrease with severity, and they explained this due to the severe adrenocortical insufficiency.

Complications occurred in 65% of the patients. These complications included occurrence of shock had the highest incidence 42.5%, elevated cardiac enzymes in 27.5%, and elevated liver enzymes represented 15%.

On the other hand, El-Ebiary et al., 2015 mentioned that elevated cardiac enzymes were positive in 40% of the patients while AST, and ALT were

elevated in 37.5%, and 55% of the patients respectively Rahbar et al., 2013 mentioned that elevated liver enzymes were found in 31.7% of the patients. And Sharma et al., 2018 mentioned that 100% of the patients had shock.

In the present study, the outcome of the 40 intoxicated patients by ALP was as follows 55% survived and they were discharged while the deaths represented 45%, similar result was reported by El-Sarnagawy, 2017 who found the mortality rate of 44.7%. D'Abrantes et al., 2021 also found that the mortality rate represented 40%.

While Jain et al., 2010 observed that the mortality rate was 71%. El-Ebiary et al., 2015, found that the mortality rate was 67.5%.

The cardiovascular toxicity was found to be the most common cause of death in the current study, this supported (Mehrpour et al., 2019 and Sahoo et al., 2020) who found that toxic myocarditis, hypotension, intractable shock, brady or tachy arrhythmias, congestive heart failure were the common cause of death.

Conclusion

This study clarified that biochemical abnormalities of hyperlactemia, and elevation of blood cortisol level were found significantly more among deaths and thus careful monitoring of blood lactate and cortisol levels provide important predictors for early estimation of the outcome in acute ALP intoxicated patients.

Recommendations

This study highlights that careful monitoring of blood lactate and cortisol levels provide important predictors for early estimation of the outcome in acute ALP intoxicated patients.

Raising the awareness about proper usage and hazards among people handling ALP due to its lethal effects.

Restrict ALP sale and distribution to prevent further deaths as it must be sold under restricted conditions for the farmers under the supervision of the agricultural ministry.

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تقييم مستويات الكورتيزول و اللاكتات في الدم كمؤشرات للنتائج في مرضي السمية الحادة بفوسفيد الألومنيوم

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الملخص العربي

المقدمة: فوسفيد الألومنيوم هو سم قاتل للغاية و تبلغ معدلات الوفيات به 70-100٪ و تحدث الو**فيات** في أول 12 إلى 24 ساعة بسبب التأثير السام على القلب والرئة، و**حمضي**ة الدم ، بالإضافة إلى قصور الغدة الكظرية التي تغير مستوى الكورتيزول فى الدم. المشكلة الرئيسية هي أنه لا يوجد ترياق متاح لعلاج سمية فوسفيد الألومنيوم حتى الآن. هناك القليل من البيانات حول المؤشرات التى تتنبأ بنتائج السمية بفوسفيد الألومنيوم و نعتمد بشكل أساسي على الأعراض التي تكون مضللة في بعض الأحيان.

الهدف من البحث: هدفت هذه الدراسة إلى تقييم قياس مستويات الكورتيزول واللاكتات في الدم بشكل منفصل كمنبئات للتنبؤ المبكر بالنتائج لدى المرضى المتسممين بفوسفيد الألومنيوم.

طريقة البحث: تم إجراء دراسة مستقبلية رصدية في الفترة من الأول من يونيو 2022 حتى نهاية مارس 2023 على 40 مريضًا من كلا الجنسين تم دخولهم إلى مركزالسموم بمستشفيات جامعة عين شمس مصابين بتسمم حاد بـفوسفيد الألومنيوم والذين جاءوا بأقصى وقت تأخير 48 ساعة. تم جمع البيانات الاجتماعية والديموغرافية والتسمم والبيانات الإكلنيكية لكل مريض. وشملت الفحوصات تحليل غازات الدم الشرياني بما في ذلك اللاكتات، وإجراء فحوصات مخبرية روتينية بالإضافة إلى الكورتيزول في الدم، كما تم إجراء رسم القلب لجميع المرضى. وكذلك تم تسجيل نتائج المرضى كالتالى (تحسن , مضاعفات أو وفاة).

نتائج البحث: كانت مستويات الكورتيزول واللاكتات في الدم مرتفعة بشكل ملحوظ ،كما كان هناك نقص فى أكسجين الدم و حمضية الدم و نقص مستوى البيكربونات فى الدم بشكل ملحوظ فى الحالات التي انتهت بالوفاة و كانت النتائج لها دلالة إحصائية.

الإستنتاج: أن ارتفاع الاكتات فى الدم وكذلك ارتفاع مستوى الكورتيزول في الدم بشكل ملحوظ بين الحالات التي انتهت بالوفاة ، وبالتالي من الممكن استخدامهما كمتنبئين للوفيات لدى مرضى السمية الحادة بفوسفيد الألومنيوم و توصى هذه الدراسة بهما.

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