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Evaluation of Various Scoring Systems in Prediction of Acute Aluminum Phosphide (ALP) Poisoning Outcome

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Abstract

Introduction: Aluminum phosphide (Alp) poisoning is a major health problem developing countries because of the high rates of morbidity and mortality even in well-equipped and experienced hospitals..

The aim of this study: Was to evaluate various scoring system (Acute Physiology and Chronic Health Evaluation (APACHE) score, Rapid Emergency Medicine Score (REMS), The Sequential Organ Failure Assessment (SOFA) score) at admission for outcome prediction in acute aluminum phosphide poisoned patients.

Patients and methods: The present study is a cohort study that was carried out on acute Alp poisoned patients at Poison Control Unit, Tanta University Emergency Hospital. It was composed of two periods; one year retrospective (from April 2015 to March 2016) and six months prospective (from April 2016 to September 2016).All admitted patients over 16 years with acute aluminum phosphide poisoning were included in this study. Patients were grouped according to their outcome into survivors and non survivors. From the collected data, APACHE II, SOFA and REMS scores were calculated for every patient.

Results: The present study was carried out on admitted fifty acute Alp poisoned patients. Out of them, survivors represented 44% and 56% were non-survivors. The majority of patients were in the age group 16-20 years, females, student, from rural areas (90%) and most of patients had ingested phosphides intentionally in a median dosage of one tablet. Hypotension, tachypnea, metabolic acidosis, hyperglycemia and higher serum creatinine levels and alanine transaminase (ALT) at admission, were risk factors of mortality from Alp. Non survivors had significantly higher APACHE II, SOFA and REMS score values than survivors. SOFA score had the best AUC (0.989) followed by APACHE II score then REMS score (0.987 and 0.970 respectively). However, no significant differences between AUC values of compared scores could be demonstrated.

Conclusion: The clinical scores (APACHE II, SOFA and REMS) were similar and effective tools for determination of the severity of acute Alp poisoning. However, REMS proved to be more applicable than other scores owing to its simplicity, less time-consuming and effectiveness in emergency situations. Therefore, REMS score is suggested to be used in the emergency situations to predict outcome in Alp poisoned patients.

Keywords | Aluminum phosphide (Alp)**,** prediction, mortality**,** APACHE II score, SOFA score and REMS score.

Introduction

Aluminum phosphide (Alp) is known as "Rice tablet" which is a solid pesticide that rapidly became one of the most commonly used grain fumigants because of its ideal properties; easy application, high efficacy, toxic to all stages of insects, does not affect seed viability, free from toxic residues and leaves little residue on food grains (Bogle et al., 2006 and Wahab et al., 2009).

The majority of intoxicated cases are intentionally while accidental exposure by inhalation of phosphine gas is less commonly recorded (Shadnia et al., 2008).

The fatal dose of aluminum phosphide poisoning is 0.15-0.5 gram (wahab et al., 2009). Mortality rate in various studies ranged from 37-100 %(Goel and Aggarwal, 2007(.

The exact mechanism of action of aluminum phosphide poisoning is still unknown. However, phosphine gas (PH3) is liberated when Alp comes in contact with moisture. Then it is rapidly absorbed causing systemic complications and multi-organ failure through suppression of cytochrome oxidase resulting in histotoxic hypoxia and production of free radicals (Proudfoot, 2009 and Abedini et al., 2014).

Common manifestations of acute Alp poisoning include nausea, vomiting, abdominal pain, acidosis, marked hypotension, tachycardia, arrhythmias, tachypnea dyspnea, agitation, anxiety, and garlic smell on the breath. In addition, pulmonary edema, hepatitis, pericarditis, congestive cardiac failure, acute renal failure, disseminated intravascular coagulation (DIC) and acute gastrointestinal

hemorrhage are occasionally noticed (Moghadamnia, 2012).

Acute Physiology and Chronic Health Evaluation (APACHE II) score was described by Knaus et al in 1985. It is the most frequently used scoring system by physicians because it is reliable, in-expensive and produces accurate results in prediction of the patients' outcomes. However, it includes several blood chemistry variables making it not suitable for quick scoring in the emergency situations (Ratanarat et al., 2005).

Rapid Emergency Medicine Score (REMS) is an attenuated version of APACHE II. It is simple (it does not require invasive or time consuming laboratory values) that allows rapid calculation in emergency conditions (Olsson et al., 2004 and Goodacre et al., 2006).

The Sequential Organ Failure Assessment (SOFA) Score was created in a consensus meeting of the European Society of Intensive Care Medicine in 1994 and further revised in 1996. It determines the extent of a person's organs function or rate of failure (Ferreira et al., 2001).

In the field of clinical toxicology, only few studies had evaluated the efficacy of scoring systems in predicting the outcome of acute aluminum phosphide poisoned patients (Mathai and Bhanu, 2010). So, the aim of this study was to evaluate various scoring system (APACHE II, REMS, SOFA) at admission for outcome prediction in acute aluminum phosphide poisoned patients.

Patients and Methods

Study design

The present study is a cohort study that was carried out on ALP poisoned patients who were admitted at Poison Control Unit, Tanta University Emergency Hospital. It was composed of two periods; one year retrospective (from the start of April 2015 to the end of March 2016) and six months prospective (from the start of April 2016 to the end of September 2016).

The study was carried out following approval of the Medical Research Ethical Committee of Tanta Faculty of Medicine. In retrospective cases, patients' data were collected from patients' files after taking the permission of the head of the poison control unit. In prospective cases, a written informed consent was taken from every patient or his/her guardians. The privacy and confidentiality of patients' data were considered by making code number for every patient.

Patients

Inclusion criteria

All admitted patients over 16 years with acute aluminum phosphide poisoning were included in this study. Diagnosis of acute aluminum phosphide poisoning was based on history of exposure to Alp, the suggestive clinical manifestations (symptoms and sign) and silver nitrate test.

Exclusion criteria

- Patients with combined drug ingestion
- Patients less than 16 years (as APACHE score has not been validated for use in children or young people aged less than16 years) (**Knaus et al.,1985)**
- Patients with chronic illness as liver, kidney, heart diseases and active infection.
- Missing data records.
- Referred or transferable patients with previous medical intervention.

Method

All the studied subjects were subjected to the following:

- Complete personal history: name, age, sex, occupation, and residence.
- Toxicological history: alleged mode of poisoning, rout of exposure, amount, delay time and hospital stay.
- Past history of medical diseases
- Complete physical examination (it included vital signs, level of consciousness by Glasgow Coma Scale, examination of central nervous, respiratory, cardiovascular and gastrointestinal systems).
- Laboratory investigations including the arterial blood gases, serum electrolytes (sodium and potassium levels), random blood sugar level, kidney function tests (urea and cratinine), liver function tests (alanine transaminase (ALT), aspartate transaminase (AST) and bilirubin) and complete blood count (hematocrit , platelet and white blood cell count)
- Electrocardiography (ECG) monitoring.
- Plain chest X-ray (Posterior-anterior view).
- Detection of phosphine gas by Silver nitrate test; Five ml of gastric aspirate and 15 ml of water were put in a flask and the mouth of the flask was covered by filter paper impregnated with 0.1N silver nitrate (16.987 gm of silver nitrate in 1L distilled water). The flask was heated at 50oC for 15 to 20 minutes. When phosphine was present, the filter paper turned black (Wahab et al., 2008).

From the collected data, the following scores were calculated for every patient:

APACHE II score was calculated from 12 routine physiologic values; heart rate, mean arterial pressure, body temperature, respiratory rate, oxygenation of arterial blood (PaO2), arterial pH, white blood count, hematocrit value, serum sodium level, serum potassium level, serum creatinine level and Glasgow Coma Scale (GCS). The score for each parameter was assigned from 0 to 4, with 0 being normal and four being the worst value. The sum of these values were added to a mark adjusting for patient age and a mark adjusting for chronic health problems (severe organ insufficiency or immune-compromised patients) to arrive at the APACHE II score which ranged from 0 to 71(Knaus et al., 1985 and Sungurtekin et al., 2006).

Rapid Emergency Medicine Score (REMS) composed of 6 variables; pulse rate, mean arterial pressure, respiratory rate, GCS, peripheral oxygen saturation and age. Age was graded a score from 0 to 6 and the remaining five variables were assigned a score from 0 (normal) to 4 (the worst value) providing a daily score from 0 to 26 (Goodacre et al., 2006).

Sequential Organ Failure Assessment (SOFA) score assessed the function of six organs; respiratory (PO2 divided by FIO2), renal (serum creatinine), hepatic (serum bilirubin), cardiovascular (mean Arterial Pressure and the dose of the administrated vasopressors graded from 2 to 4, hematologic (platelet count), neurologic (Glasgow Coma Score). Each organ was graded from 0 to 4 providing a daily total score from 0 (normal) to 24 (the worst value) point (Vincent et al., 1998 and Jones et al., 2009).

After then, patients were grouped according to their outcome into survivors and non survivors

Statistical analysis

For quantitative data, the Shapiro-Wilk test for normality was performed. For data that were not normally distributed, median and interquartile range (expressed as 25th-75th percentiles) were calculated and Mann-Whitney test was used. For normally distributed data, values were expressed as mean ± standard deviation and Independent samples T test was performed for comparison between two groups. For qualitative data Pearson's Chi square test was used to examine association between two variables. Receiver operation characteristics (ROC) curve analysis was carried out to predict outcome. Areas under ROC curve, sensitivity, and specificity, were calculated. Significance was adopted at $p < 0.05$.

Results

The present study was carried out on fifty acute Alp poisoned patients. Out of them, survivors represented 44% and non-survivors represented 56%.

Table (1) showed that, the majority of patients (64%) were in the age group 16-20 years with a significant association with poor patients' outcome. The highest percentage of patients were females, students and from rural areas.

In the present study, the majority of patients (94%) had ingested phosphides intentionally in a suicidal attempt. The median amount was one tablet. The delay time post ingestion ranged from 0.75 to 14 hours and the median of length of hospital stay was 2 days. There was a significant association between the route of intoxication, delay time, hospital stay and mortality ***(Table 2).***

Table (3) illustrated that, the majority of patients were hypotensive (52%). Tachycardia was detected in 44% of patients while, bradycardia was noticed in 6% of patients and 4%of patients had undetected pulse clinically. Tachypnea was detected in 72% of all patients and in 86% of non survivors. The majority of patients had normal temperature (64%). There was significant association between patients' outcome and each of blood pressure, respiratory rate and temperature.

The majority of patients (68%) had normal level of consciousness**.**12% of cases were presented with agitation**,** 56% with GIT disturbance (vomiting and abdominal pain) and only one case had wheeze.

Table (4) revealed that non survivors had significantly higher level of serum ALT and serum creatinine level than survivors. Th***e*** arterial blood gases (arterial PH, partial oxygen pressure (PO_2), partial carbon dioxide pressure (PCO_2) and bicarbonate level (HCO_3) decreased in non survivors compared to survivors. Serum sodium and random blood sugar were significantly raised in non survivors group when compared to survivors.

In the current study, 54 % of patients had the following types of arrhythmia; sinus tachycardia (36%), bradycardia (6%), atrial fibrillation (4%), ventricular tachycardia (6%) and ventricular fibrillation (2%) with no significant association with patients' outcome **(figure 1).**

Regarding complication, fifteen patients needed mechanical ventilation, four patients were only intubated and Adult Respiratory Distress Syndrome (ARDS) developed in one patient.

Concerning the studied scores (APACHE, SOFA and REMS) in the current study, non survivors had significantly higher APACHE II, SOFA and REMS score values than survivors **(Table5)**.

Table (6) illustrated that, APACHE II score had 92.9 % sensitivity and 90.9% specificity at a cut off value ≥ 9.5. SOFA score ≥ 5.5 can predict the mortality with sensitivity 96.4% and specificity 95.5 %. Furthermore, REMS score≥ 4.5 was predictor of mortality; the sensitivity and specificity was 89.3 % and 95.5 % respectively.

SOFA score had the best AUC (0.989) followed by APACHE II then REMS (0.987 and 0.970 respectively). However, Their AUC values didn't show significant difference **(Figure 2).**

Table (1): The association between socio-demographic data and acute aluminum phosphide poisoned patients' outcome (N=50)

Variables		Outcome						
		Survivor N=22		Non survivors N=28		Total		
		N	%	N	%	N (%)	X^2	P value
Sex	Female	15	68.2	18	64.3	33 (66.0)	0.083	0.773
	Male	7	31.8	10	35.7	17 (34.0)		
Age groups	16-20	9	40.9	23	82.1	32(64.0)	9.511	0.009*
	>20-30	10	45.5	3	10.7	13 (26.0)		
	>30-50	3	13.6	2	7.1	5(10.0)		
Residence	Rural	18	81.8	27	96.4	45 (90.0)	2.922	0.087
	Urban	4	18.2	1	3.6	5(10.0)		
Occupation	House wife	9	40.90	5	17.80	14(28.0)	7.499	0.112
	Student	8	36.4	16	57.1	24 (48.0)		
	Worker	4	18.2	5	17.9	9(18.0)		
	No work	1	4.5	2	7.1	3(6.0)		

**significant at P<0.05, N: numbers, %: percentage, X^2: Chi square test*

Table (2): Association between toxicological data and acute aluminum phosphide patients' outcome (N=50)

Variables		Outcome				Total	Test statistic	P value
		Survivors N=22		Non survivors N=28				
		N	%	N	%	N (%)		
Route	Ingestion	19	86.4	28	100.0	47 (94.0)	X^2 = 4.062	.044*
	Inhalation	3	13.6	0	0.0	3 (6.0)		
Alleged mode of poisoning	Suicidal	21	95.5	26	92.9	47 (94.0)	X^2 =. 00	1
	Accidental	1	4.5	2	7.1	3 (6.0)		
Amount (tablet)	Minimum-maximum	.00-2.00		.00-2.00		0.25-2	Z =-0.820	0.412
	Median	1.00		1.00		1.00		
Delay time(hours)	Unknown	0	0.0	3	10.71	3 (6.00)	Z =-2.164	.030*0
	Minimum-maximum	1.00-14.00		0.75-8.00		0.75-14		
	Median	4.68		2.81		3.00		
Hospital stay (hours)	Minimum-maximum	6.0-72.0		48.0-384.0		6.0-348.0	Z =4.539	P<0.001*
	Median	12.0		48.0		48.00		

**significant at P<0.05, N: numbers, %: percentage, X^2: Chi square test, Z: Mann Whitney test*

Table (3): Association between vital signs and acute aluminum phosphide poisoned patients' outcome (N=50)

		Outcome				Total	X^2	P value
		Survivors N= 22		Non survivors N=28				
		N	%	N	%	N (%)		
Blood pressure	Hypotension	5	22.7	21	75.0	26 (52.0%)	15.615	<0.001*
	Normal	15	68.2	7	25.0	22 (44.0%)		
	Hypertension	2	9.1	0	0.0	2 (4.0%)		
Pulse	Normal	10	45.5	13	46.4	23 (46.0)	0.743	0.863
	Tachycardia	9	40.9	13	46.4	22 (44.0)		
	Bradycardia	2	9.1	1	3.6	3 (6.0)		
	Undetected	1	4.5	1	3.6	2 (4.0)		
Respiratory rate	Tachypnea	12	54.5	24	85.7	36 (72.0)	5.937	0.015*
	Normal	10	45.5	4	14.3	14 (28.0)		
Temperature	Normal	20	90.9	12	42.9	32(64.0)	13.249	0.001*
	Hyperthermia	2	9.1	7	25.0	9 (18.0)		
	Hypothermia	0	0.0	9	32.1	9 (18.0)		

**significant at p <0.05, N: numbers, %: percentage, X^2: Chi square test.*

Table (4): Comparison of laboratory investigations in acute aluminum phosphide poisoned patients (N=50)

Variables			Outcome			
			Survivor N=22	Non survivors N=28	Test statistic	P value
Liver function tests	Serum ALT	Minimum-maximum	5.00-38.00	10.00-85.00	z =-2.086	0.037*
		Median	18.00	25.50		
	Serum AST	Minimum-maximum	10.00-39.00	6.00-90.00	z =-1.429	0.153
		Median	22.50	24.50		
	Serum bilirubin	Minimum-maximum	0.40-1.50	0.40-3.50	z =-1.063-	0.288
		Median	0.70	0.85		
Renal function tests	Blood Urea	Minimum-maximum	21.00-36.00	19.00-47.00	t= -1.881	0.066
		Mean± SD	29.36±5.27	32.86±7.35		
	Serum creatinine	Minimum-maximum	0.60-1.20	0.90-13.00	z =-4.898	<0.001*
		Median	0.85	1.20		
Arterial blood gas	PH	Minimum-maximum	7.20-7.51	7.09-7.46	z =-4.141	<0.001*
		Median	7.43	7.27		
	HCO_3	Mean± SD	16.69±5.87	14.48±6.31	t=1.267	.212
	Po_2	Minimum-maximum	44.00-105.00	11.00-100.00	z =-4.843-	0<.001*
		Median	87.00	30.00		
	Pco_2	Mean± SD	30.90±7.37	23.41±7.17	t = -3.570	.001*
Serum electrolytes	Serum sodium	Mean± SD	138.65±4.10	143.29±4.88	t= 3.645	.001*
	Serum potassium	Minimum-maximum	2.20-5.00	2.20-4.60	z =-.853	.393
		Median	3.00	3.05		
Random blood sugar		Minimum-maximum	79.00-258.00	42.00-288.00	z =-2.317	.021*
		Median	106.00	158.50		

**significant at p <0.05, N: numbers, %: percentage, X^2: Chi square, z: Mann Whitney test, t: Independent samples T test, SD: standard deviation, ALT: alanine transaminase, AST: aspartate transaminase, Po_2: partial oxygen pressure, Pco_2: partial oxygen pressure, HCO_3: bicarbonate*

Table (5): Comparison of APACHE, SOFA, and REMS scores in acute aluminum phosphide poisoned patients (N=50)

Variables		Outcome				
		Survivor N=22	Non survivors N=28	Total	Test statistic	P value
APACHE	Minimum	0.00	6.00	0.00	z = -5.872	<0.001*
	Maximum	11.00	33.00	33.00		
	Median	3.50	15.00	11.5		
SOFA	Minimum	0.00	4.00	0.00	z =-5.915	<0.001*
	Maximum	7.00	14.00	14.00		
	Median	1.00	9.00	7		
REMS	Minimum	0.00	2.00	0.00	z=-5.689	<0.001*
	Maximum	5.00	18.00	18.00		
	Median	2.00	8.00	5		

*Z: Mann Whitney test, *significant at p<0.05, N: number, APACHE: Acute Physiology and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment, REMS: Rapid Emergency Medicine Score.*

Table (6): The best cut-off values, sensitivity, specificity, and AUC of the applied scoring systems APACHE, SOFA, and REMS

Variables	Cut-off value	Sensitivity %	Specificity %	Accuracy %	ROC- AUC	P value
APACHE score	≥9.5	92.9	90.9	92	0.987	<0.001*
SOFA	≥5.5	96.4	95.5	96	0.989	<0.001*
REMS	≥4.5	89.3	95.5	92	0.970	<0.001*
Pairwise Comparisons	Z	APACHE II vs SOFA = 0.127 APACHE II vs REMS = 1.19 SOFA vs REMS = 0.860				
	P	APACHE II vs SOFA = 0.899 APACHE II vs REMS = 0.231 SOFA vs REMS = 0.390				

**significant at p <0.05, AUC: area under the curve, APACHE: Acute Physiology and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment, REMS: Rapid Emergency Medicine Score*

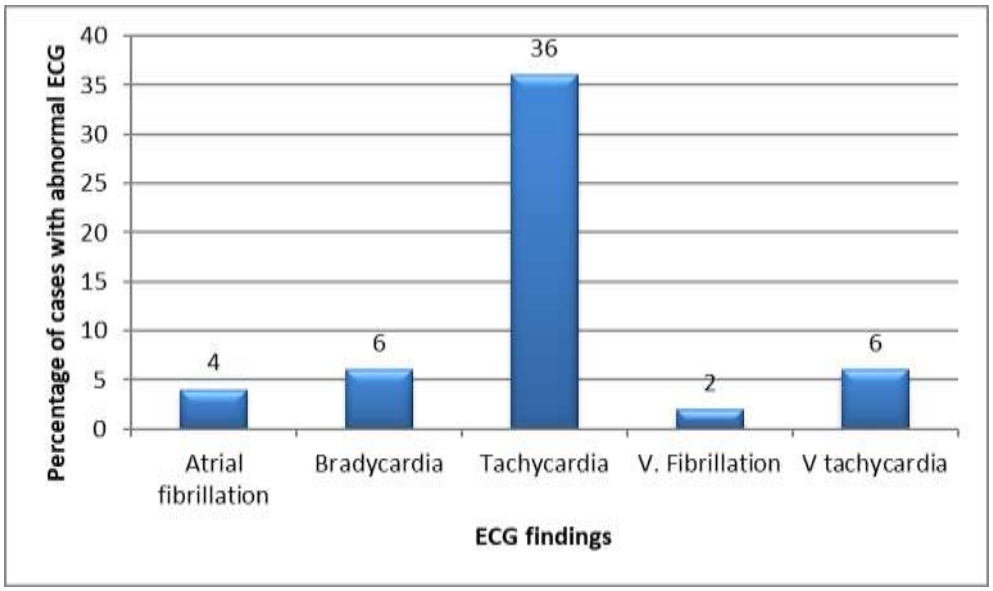

Figure (1): **Bar chart showing ECG changes in acute aluminum phosphide poisoned patients (N=50), v: ventricular.**

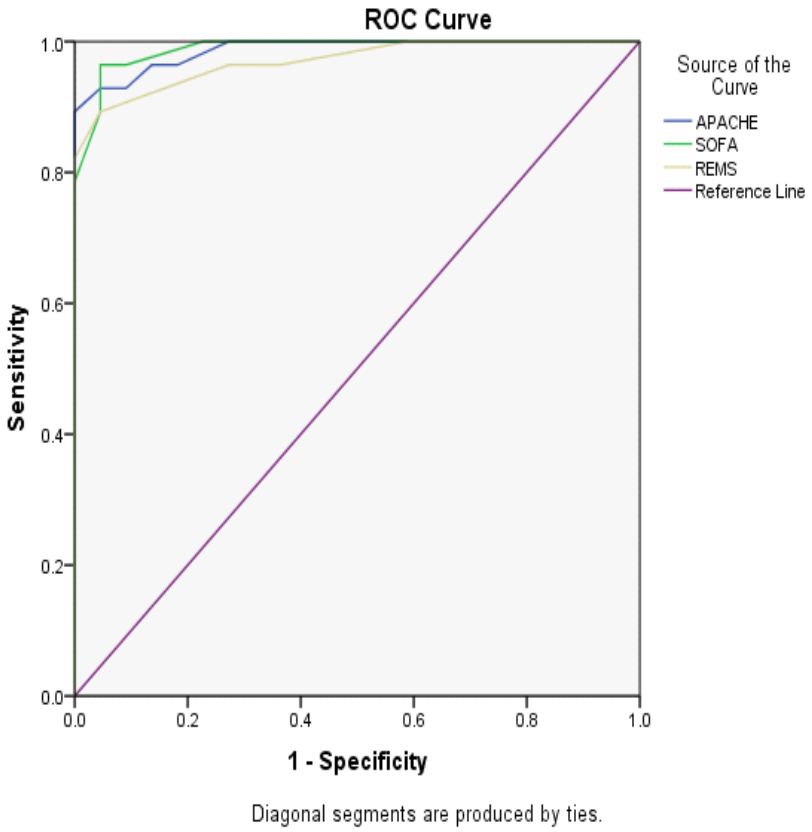

Figure (2): receiver operating characteristics (ROC) curves for prediction of mortality using APACHE, SOFA, and REMS score

Discussion

The present study revealed that 28 patients out of 50 patients died with overall mortality rate of 56%. This finding coincide with Taramsari et al., (2013) in Iran ; and Mathai& Bhanu, (2010) in India who reported that, mortality rates of Alp poisoning were 58.61%and 60% respectively. The high mortality rate could be attributed to extremely toxic property of Alp and absence of a specific antidote.

In the current study, the majority of patients (64%) were in the age group 16-20 years, followed by the age group 20-30 years (26%).This is in agreement with the findings of El-Ebiary et al., (2015) who reported that, 67.50% of Alp poisoned patients were < 20years followed by age group 20-40 years. Moreover, the present study indicates that most of the cases were students (48%); this could be explained by the majority of the studied patients in the present study were younger than 30 years. This is also in agreement with Dash et al., (2005) who reported that the majority of patients in their study were students at school. The high incidence of acute intoxication with Alp in young age groups (10-29 years) could be explained by that younger persons tend to be easily excited, depressed, failure in love, family scolding from parents or teachers, more exposed to failure in education and lack of employment opportunities problems (Kapoor et al., 2006; Khurana et al., 2011 and Chaudhary et al., 2013).

Females of this study represented 66% of the studied patients and 94% of cases were intentionally ingested phosphides in suicidal attempts. This coincides with the findings of Brahim et al., (2013) who reported that, 63.8% of patients intoxicated with Alp were females and 95.7% of cases were suicidal. El Nagger and El Mahdy, (2011) referred this to the high stress in women's life caused by marital disharmony, economic hardship, social problems and scolding from other family members.

The majority of patients (90%) in this study were from rural areas. This is partially in line with the findings of Karamjit et al., (2003) and Kapoor et al., (2006) in India who demonstrated that, 65.12% and 64% of Alp poisoned patients were from rural areas respectively. The high incidence of acute intoxication with Alp in rural areas could be attributed to farming activity in rural areas with easy access to toxic pesticides and lack of awareness about its hazards (El Naggar and El Mahdy, 2011).

The median delay time in this study was 3 hours. This coincides with Wahdan and Elmadah, (2016) in Tanta. The short duration between exposure and arrival to the hospital could be explained by the presence of the Tanta Toxicology Unit in the center of Delta region with easy transportations and many of the cases who attempted suicide did not actually intend to end their lives but they just try to draw attention, gain sympathy from their families, so they rapidly seek medical support.

More than half of patients in the present study were hypotensive (52%), non survivors were more hypotensive than survivors. Teimoory et al., (2013) and

El-Ebiary et al., (2015) reported that hypotension was detected in 92.0% and80% of their cases respectively. Furthermore, Soltaninejad et al., (2012) concluded that systolic blood pressure is a key risk factor for prediction of Alp poisoning mortality at admission to the hospital. The mechanism of shock is multifactorial (myocardial damage, fluid loss and adrenal gland damage) (Proudfoot., 2009). Clinical, biological and electrical observations suggest that, the main cause of hemodynamic failure was myocardial lesion (Siddaiah et al., 2009).

Tachypnea was detected in 72% of all patients. This in accordance with Jaiswal et al., (2009) and El Ebiary et al.,(2015) who found that 100% and 70% of their patients had tachypnea respectively. Tachypnea could be a compensatory response to metabolic acidosis disorder.

The current study revealed significant elevation of serum ALT and serum creatinine in non survivors when compared to survivors. This is in accordance with Mathai & Bhanu, (2010) and Masoud & Barghash, (2013) These effects could be explained by the fact that, phosphine gas cause inhibition of cytochrome oxidase and free radical release that damage various organs especially those with the greatest oxygen requirement (Masoud and Barghash, 2013).

All parameters of ABG were decreased in non survivors than survivors. Mehrpour et al., (2008) and Mostafazadeh et al., (2011) recorded a significant association between metabolic acidosis and mortality. Accumulation of lactic acid that caused by blockage of oxidative phosphorylation and poor tissue perfusion may be the cause of metabolic acidosis (Agarwal et al., 2014). In the present study, partial oxygen pressure (PO_2) was significantly decreased in non survivors when compared to survivors. Accordingly, Wahab et al., (2008) revealed that hypoxia is associated with high mortality rate. Valmas et al., (2008) and Proudfoot, (2009) stated that, phosphine gas inhibits 70% of mitochondrial oxidative respiration by suppression of cytochrome oxidase resulting in histotoxic hypoxia.

Regarding serum electrolytes, serum sodium was significantly increased in non survivors group compared to survivors which is agreement with the findings of Shadnia et al., (2010),

This study revealed that non-survivors had a statistically significant increase in random blood sugar (the median was 158.50 mg/dl) when compared with survivors. In accordance with that, Mehrpour et al., (2008) stated that, Alp poisoned patients with glucose levels greater than 140 mg/dl at admission were at high risk of mortality. Suggested mechanisms for this hyperglycemia include impaired oxidative phosphorylation and glucose utilization with involvement of the adrenal axis and/or pancreas (Singh et al., 2006 and Verma et al., 2007). However, previous study by Mehrpour et al., (2008) reported that hypoglycemia in aluminum phosphide poisoning is a rare finding and it is dangerous. Hypoglycemia might be due to impairment of glycogenolysis and gluconeogenesis secondary to adrenal gland damage and decrease circulating cortisol level (Chugh et al., 2000). Moreover, Mathai&Bhanu, (2010) and Masoud&Barghash, (2013) did not find any significant association between random blood sugar and mortality.

Various scoring systems have been developed during the last few decades to evaluate the severity of illness and to predict patients' outcome (Kelly et al., 2002).

APACHE II score is a general mortality prediction model in critically ill patients (Strand and Flaatten, 2008). Non survivors of the present study had significantly higher APACHE II score values at admission than survivors (medians = 15 vs 3.5 respectively). The ability of APACHE II to predict patients who died was 92.9 % and patients who survived was 90.9% at $\geq$ 9.5 cut off value. In line with this, Mathai and Bhanu, (2010) found that, survivors of Alp poisoned patients had significantly lower score than non-survivors (8.64 ± 5.27 vs 14.56 ± 6.66, respectively).Moreover, Hajouji et al., (2006) revealed that APACHE II was positively correlated with poor outcome in Alp poisoned patients.

In the current study, REMS score had higher values in non survivors when compared to survivors (median was 8.0 vs. 2.00 respectively), with a sensitivity and specificity, 89.3 % and 95.5 % respectively at a cut off value $\geq$ 4.5. No other studies evaluated the use of REMS as a predictor of outcome in Alp poisoned patients.

Other previous studies by Olsson et al., (2004), Cattermole et al., (2009) and El-Sarnagawy and Hafez, (2017) reported that REMS was a good predictor of bad outcome in ICU admitted patients, long term mortality in patients attending non-surgical emergency department and the need of mechanical ventilation in drug-overdosed patients with disturbed conscious level respectively.

Regarding SOFA score, it was developed as a tool for assessment of organ failure. The present study revealed that SOFA score showed higher value in non survivors than survivors with median of 9.00 vs 1.00 respectively with 96.4 % sensitivity and 95.5 % specificity at a cut off value $\geq$5.5. To the best of author's knowledge, no previous studies evaluated the use of the SOFA as a predictor of outcome in Alp poisoned patients. Vosylius et al., (2004) and Halim et al., (2009) demonstrated that, SOFA score was significantly higher in non- survivors than survivors in surgical &intensive care patients and in patients with severe sepsis respectively.

The current study demonstrates that, SOFA score had the best A UC (0.989) followed by APACHE II score then REMS score (0.987 and 0.970 respectively. However, no significant differences between AUC values of compared scores. APACHE II and SOFA includes several blood chemistry variables. Subsequently, they are not suitable for quick evaluation in the emergency conditions. On contrary, REMS score is a simple clinical score (neither requires any laboratory parameters nor any staff training and extra skills).

Conclusion

Aluminum phosphide is a remarkably toxic compound with a high mortality rate reached in the current study to 56%.The presence of hypotension, tachypnea, metabolic acidosis, hyperglycemia and higher serum creatinine and ALT levels at admission, were risk factors of mortality from Alp poisoning. The clinical scores (APACHE II, Sofa and REMS) were similar and effective tools for determination of the severity of acute Alp poisoning. However, REMS proved to be more applicable than other scores owing to its simplicity, less time-consuming and effectiveness in emergency situations. Therefore, REMS is suggested to be used in the emergency situations to predict outcome in Alp poisoned patients.

Reference

Abedini M, Fatehi F, and Tabrizi N (2014): Ischemic stroke as a rare manifestation of aluminum phosphide poisoning: a case report. Acta Medica Iranica. 52(12): 947-949.

Agarwal A, Robo R, Jain N, Gutch M, et al., (2014): Oxidative stress determined through the levels of antioxidant enzymes and the effect of N-acetyl cysteine in aluminum phosphide poisoning. Indian J Crit. Care Med. 18(10); 666 -671.

Bogle RG, Theron P, Brooks P et al., (2006): Aluminum phosphide poisoning. Emerge Med J. 23 (1):e3.

BrahimB, Abderrahim EB , Nawfal N et al., (2013): Statistics of acute aluminum phosphide poisoning in Fez, Morocco. J. Life. Sci. 7(11): 1159-1164

Cattermole GN, Mak SKP, Liow CHE et al., (2009): Derivation of a prognostic score for identifying critically ill patients in an emergency department resuscitation room. Resuscitation. 80: 1000–1005.

Chaudhary S, Momin SG. Vora DH et al., (2013): An Epidemiological study of fatal aluminum phosphide poisoning at Rajkot. IOSR- JP. 3 (1): 17-23.

Chugh SN, Kishore K, Aggarwal N et al., (2000): Hypoglycemia in acute aluminum phosphide poisoning. J Assoc Physicians India. 48:855–856.

Dash SK, Raju AS, Mohanty MK et al., (2005): Socio-demographic profile of poisoning cases. Journal of Indian Aca Forensic Medicine. 27 (3):0971 -0973.

El-Ebiary AE, Elgazzar FM, Soliman MA et al. (2015): predictors of prognosis in acute aluminum phohphide poisoning .Mansoura J. Forensic Med. Clin. Toxicol. Vol. XXIII (2):13-26.

El Naggar AM and El Mahdy NM (2011*):* Zinc phosphide toxicity with a trial of tranexamic acid in its management. J Adv Res. 2: 149-156.

El-Sarnagawy GN and Hafez AS (2017): Comparison of different scores as predictors of mechanical ventilation in drug overdose patients. Hum ExpToxicol. 36 (6): 1–8.

Ferreira FL, Bota DP, Bross A et al., (2001): Serial evaluation of the SOFA scores to predict outcome in critically ill patients. JAMA. 286:1754-1758.

Goel A and Aggarwal P (2007): Pesticide poisoning.Natl Med J India. 20(4): 182-191.

Goodacre S, Turner J and Nicholl J (2006): Prediction of mortality among emergency medical admissions. Emerg Med J. 23 (5):372-375.

Hajouji IM, Oualili L, Abidi K et al., (2006): Severity factors of aluminum phosphide poisoning (Phostoxin). Ann Fr Anesth Reanim.25:382-385.

Halim DA, Tri Murni W and Redjeki IS (2009): Comparison of Apache II, SOFA, and Modified SOFA scores in predicting mortality of surgical patients in intensive care unit at Dr. Hasan Sadik in general hospital. Crit Care & Shock. 12:157-169.

Jaiswal S, Verma RK and Tewari N (2009): Aluminum phosphide poisoning: Effect of correction of severe metabolic acidosis on patient outcome. Indian J Crit Care Med. 13:21– 24.

Jones AE, Trzeciak S and Kline JA (2009): The Sequential Organ Failure Assessment score for predicting outcome in patients with severe sepsis and evidence of hypo-perfusion at the time of emergency department presentation. Crit Care Med. 37(5): 1649-1654.

Kapoor AK, Sinha US, Singh AK et al., (2006): An Epidemiological study of aluminum phosphide poisoning at Allahabad. *IJFMT.* 4 (1): 1970-1973.

Karamjit S, Oberoi SS and Bhullar DS (2003): Poisoning trends in the Malwa region of Punjab. J Punjab Acad Forensic Med Toxicol. 3: 26–29.

Kelly A, Nicholl J and Turner J (2002): Determining the most effective level of TRISS-derived probability of survival for use as an audit filter. Emerg Med J. 14:146–152.

Khurana P, Dalal JS, Multani AS and Tejpal HR (2011): The study of aluminum phosphide poisoning in a tertiary care hospital, Amritsar. Journal of Indian Academy of Forensic. 33 (4):330-334.

Knaus WA, Draper EA, Wagner DP et al., (1985): APACHE II: A severity of disease classification system. Crit Care Med. 13:818–829.

Louriz M, Dendane T, Abidi K et al., (2009): Prognostic factors of acute aluminum phosphide poisoning. Indian J Med Sci. 63(6):227-234.

Masoud RA and Barghash SS (2013): Laboratory prognostic potential for acute aluminum phosphide poisoning. AAM J. 11: 213-234.

Mathai A and Bhanu MS (2010): Acute aluminum phosphide poisoning Can we predict mortality? Indian J Anaesth. 54:302-307.

Mehrpour O, Alfred S, Shadnia S et al., (2008): Hyperglycemia in acute aluminum phosphide

poisoning as a potential prognostic factor. Hum Exptoxicol. 27(7):591- 595.

Moghadamnia AA (2012): An update on toxicology of aluminum phosphide. Daru. 20(1):25.

Mostafazadeh B, Pajoumand A, Farzaneh E et al., (2011): Blood levels of methemoglobin in patients with aluminum phosphide poisoning and its correlation with patient's outcome. J Med Toxicol. 7:40-43

Olsson T, Terent A and Lind L (2004): Rapid Emergency Medicine Score can predict long-term mortality in nonsurgical emergency department patients. ACAD EMERG MED. 11:1008-1013.

Proudfoot AT (2009): Aluminum and zinc phosphide poisoning. ClinToxicol (Phila). 47(2):89-100.

Ratanarat R, Thanakittiwirun M and Thongyoo S (2005): Prediction of mortality by using the standard scoring systems in a medical intensive care unit in Thailand. J Med Assoc Thai. 88:949–955.

Shadnia S, Mehrpour O and Abdollahi M (2008): Un-intentional poisoning by phosphine released from aluminum phosphide. Hum ExpToxicol. 27:87-89.

Shadnia S, Mehrpour O and Soltaninejad K (2010): A simplified acute physiology score in the prediction of acute aluminum phosphide poisoning outcome. Indian J Med Sci. 64 (12):532-539.

Siddaiah L, Adhyapak S and Jaydev S (2009): Intra-aortic balloon pump in toxic myocarditis due to aluminum phosphide poisoning. J. Med. Toxicol. 5:80-83.

Singh S, Bhalla A, Verma SK et al., (2006): *Cytochrome-c oxidase inhibition in 26 aluminum phosphide poisoned patients. Clin. Toxicol*. (Phila). 44(2):155-158.

Soltaninejad K, Beyranvand MR, Momenzadeh SA et al., (2012): Electrocardiographic findings and cardiac manifestations in acute aluminum phosphide poisoning. J. Forensic Legal Med. 19:291-293.

Strand K and Flaatten H (2008): Severity scoring in the ICU: A review. Acta Anaesthesiol Scand. 52:467–478.

Sungurtekin H, Gurses E and Balci C (2006): Evaluation of several clinical scoring tools in organophosphate poisoned patients. Clinical Toxicology. 44:121–126.

Taramsari MR, Badsar A, Shafaghi A, Namakin MN, Ebrahimi H and Karkan MF (2013): Alteration in liver enzymes in aluminum phosphide poisoning, a retrospective study. Iranian J Toxicol. 7 (21): 854-857.

Taramsari MR, Ourangpour R, Zarkami T et al., (2006): Survey patients poisoned with aluminum phosphide (rice tablet). JGUMS. 14(56):42-47.

Teimoory M, Aghabiglooie A and Shadinia S (2013): Determining clinical symptoms of getting poisoned by aluminum phosphide in comparison with getting poisoned by zinc phosphide, in relation with patients of Loqman hospital. Journal of Basic and Applied Scientific Research. 3 (8): 410-417.

Valmas N, Zuryn S and Ebert PR (2008): Mitochondrial uncouplers act synergistically with the fumigant phosphine to disrupt mitochondrial membrane potential and cause cell death. Toxicology. 252:33–39.

Verma SK, Ahmad S and Shirazi N (2007): Acute pancreatitis: a lesser-known complication of aluminum phosphide poisoning. Hum. Exp. Toxicol. 26(12): 979-981.

Vincent JL, De Mendonca A, Cantraine F et al., (1998): Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med. 26:1793-1800

Vosylius S, Sipylaite J and Ivaskevicius J (2004): Sequential Organ Failure Assessment Score as the determinant of outcome for patients with severe sepsis. Croat Med J.45:715-720.

Wahab A, Rabbani MU, Wahab S et al., (2009): Spontaneous self-ignition in a case of acute aluminum phosphide poisoning. Am. J. Emerg. Me. 27(6): 752.e5-6.

Wahab A, Zaheer MS, Wahab S et al., (2008): Acute aluminum phosphide poisoning: an update. Hong Kong J Emerg Med. 15(3): 152-155.

Wahdan AA and Elmadah EI (2016): Methemoglobinemia and intra-vascular hemolysis; unusual presentations of metal phosphides poisoning. Ain Shams Journal of Forensic Medicine and Clinical Toxicology. 26:129-139.

الملخص العربى

تقييم أنظمة قياسية مختلفة للتنبؤ بنتائج التسمم الحاد بفوسفيد الألمونيوم

سها على عبد الغنى و منى محمد حشمت و مرفت مندى عريبى وغاده نبيل السرنجاوى ١

المفدمه : يعد التسمم بفوسفيد الألومنيوم (Alp) مشكلة صحية كبيرة في البلدان النامية بسبب إرتفاع معدل المرض والوفيات حتى في المستشفيات المجهزه جيدا وذات الخبرة العالية.

الهدف من البحث :كان الهدف من الدراسة هو تقييم أنظمة قياسية مختلفة) مقياس أباتشى 2 ومقياس السوفا ومقياس الريمس (عند دخول المستشفى للتنبؤ بنتائج مرضى التسمم الحاد بفوسفيد الألومنيوم.

المرضى وطرق البحث: هي دراسة حشدية مراقبة تم إجراؤها على المرضى المصابين بالتسمم الحاد بفوسفيد الألومنيوم بوحدة علاج التسمم بمستشفى الطوارئ الجامعى بجامعة طنطا لمدة سنة إستعادية (من إبريل 2015 إلى مارس 2016) ولمدة ستة أشهرمستقبلية (من إبريل 2016إلى سبتمبر 2016). إشتملت الدراسه على كل المرضى المصابين بالتسمم الحاد بفوسفيد الالومنيوم الذين تتجاوز اعمارهم 16عاما ،حيث تم تقسيم المرضى وفقا لمصائرهم إما الناجين أو غير الناجين. وقد تم حساب أباتشى 2والريمس والسوفا لكل مريض.

النتائج: أجريت هذه الدراسة على خمسين مريضا مصابا بالتسمم الحاد بفوسفيد الألومنيوم ، مثل الناجون 44٪ ، بينما مثل غير الناجون 56٪ .فى الدراسه الحاليه .كانت غالبية المرضى في الفئة العمرية من 20-16سنة ، إناث ، طلاب، من المناطق الريفية(90٪) ، كما أن معظم المرضى تناولوا فوسفيد الالومنيوم بقصد الإنتحار ، وقد بلغت متوسط كمية التعرض لقرص واحد . وكانت عومل الخطر للوفيات من التسمم الحاد بفوسفيد الالومنيوم (عند دخول المستشفى) هى: إنخفاض ضغط الدم، ضيق التنفس، حموضة الدم الايضيه ، إرتفاع السكر في الدم وإرتفاع مستويات الكرياتينين في الدم ووظائف الكبد (الألانين ترانسامينيز).كان هناك إرتفاعا ذو دلالة إحصائية فى مقياس الأباتشي 2والريمس والسوفا فى غير الناجين مقارنة بالناجين.

وفد أظهر مقياس السوفا أفضل منطقه تحت المنحنى (0.989) يليه مقياس الأباتشي الثاني ثم مقياس الريمس (0.987و 0.970 على التوالي) .ومع ذلك لم يكن هناك فرقا ذو دلالة إحصائية بين تلك القيم .

الخلاصه: بالرغم من تماثل الأنظمه الإكلينيكيه (أباتشي الثاني، سوفا و ريمس) كأدوات فى تحديد شدة التسمم بفوسفيد الألومنيوم فإن نظام الريمس يعد قابلا للتطبيق أكثر بين الأنظمة الأخرى لسهولة تطبيقه ولقلة إستهلاكه للوقت وفاعليته فى الحالات الطارئة .لذلك يقترح إستخدام نظام الريمس فى الحالات الطارئه لتوقع نتائج التسمم الحاد بفوسفيد الألومونيوم .

الكلمات المفتاحيه إ:فوسفيد الألومنيوم ،التنبؤ، الوفاة، مقياس الاباتشى الثانى ، مقياس السوفا ومقياس الريمس.

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