Metabolic Acidosis: Determinant of Hospital Mortality of Patients with Aluminum Phosphide Poisoning

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ABSTRACT

Background: Rice Tablet, with the scientific chemical name of aluminum phosphide (ALP), is the most common pesticides and insecticides agent in agriculture, horticulture and is used to protect beans, cereals, and rice. Poisoning with this tablet is associated with a high mortality rate. The aim of this study was to evaluate patients who committed suicide with rice tablets and referred to Sina Hospital, Tabriz, during the years 2011-2015. **Methods:** In a routine data base study that was conducted at Sina

Hospital affiliated to Tabriz University of Medical Sciences, medical records of patients with suicide attempt with rice tablets during the years 2011-2015 were evaluated. During the mentioned period, 90 patients with rice tablet poisoning were admitted to the hospital. The required information was recorded in the check list.

Results: Out of 90 patients, 72 patients (80%) had ALP tablets poisoning. The mean age of subjects was 27.52 ± 0.13 years. In patients with ALP poisoning, the mean of mean arterial pressure (MAP), serum pH, serum bicarbonate, and arterial oxygen saturation between two groups (with or without mortality) were statistically significant (P value<0.001). All variables are related to admission time in the emergency department. To determine the prognostic value of these variables in predicting mortality in patients with ALP poisoning logistic regression was used and only serum bicarbonate can predict mortality with P value=0.011. *Conclusion:* The results of the current study show that the survival of patients with ALP poisoning is associated with MAP, put and serum LCo2, arterial blocd exumption at the time.

pH, and serum HCo3, arterial blood oxygen saturation at the time of admission in the emergency department. Next prospective studies are recommended for more accurate evaluation of the effect of these variables on the patients' survival.

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► Implication for health policy/practice/research/medical education: Metabolic Acidosis: Determinant of Hospital Mortality of Patients with Aluminum Phosphide Poisoning

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1. Introduction:

Suicide refers to a chain of thought and action, in which ideas are changed into action and lead to end his/her life. Para suicide refers to the activities and actions that lead to self-injury but not death. Suicidal thoughts are common among all human beings, so that out of three individuals, one has considered the suicide in their lifetime (1). Suicide is a public health problem and the eighth leading cause of death in adults in some countries. Suicide attempt rate has increased 60% worldwide during last 45 years. Suicide attempt due to its social, economic and psychological consequences imposes many damages on the society (2).

Unintentional poisoning is the fifth leading cause of deaths caused by accidental injuries and 40% cases are caused by drugs. Poisoning prevalence is also very high in Iran (3). Rice tablet, with the scientific chemical and herbal names of aluminum phosphide (ALP) and Banan, respectively is one of the most common pesticides and insecticides agent in agriculture and horticulture and is used to protect beans, cereals and rice (4). Banan or garlic tablet contains garlic extract, salt, starch, and talcum powder and is used as a herbal pesticide to store rice and other grains at home (5). ALP produces phosphine gas, ammonia and carbon dioxide when exposed to water or steam. This chemical is not absorbed dermally and is absorbed orally and through respiratory system. The severity of poisoning is very high through both path. (5, 6).

Taramsari et al. concluded that there is a direct relationship between the consumption time and arrival time to the emergency room, dosage, acid-base status with mortality rate (4) Symptoms of ALP poisoning started a few minutes after consumption and include gastrointestinal symptoms (nausea,

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vomiting, abdominal pain), restlessness, tachycardia, tachypnea, acidosis and hypotension, which eventually leads to multi-organ failure and death within 24-48 hours (7-9).

Cardiovascular impairment is caused by myocardial arrhythmias, damage. and electrocardiogram changes. Acute renal failure and shock are also caused by phosphine (10). Khodabandeh et al. stated that the cardiac arrhythmia is the most common cause of death due to poisoning with rice tablet (6). The most common causes of death by phosphine gas include cardiovascular failure, hypotension, severe acidosis, and acute renal failure (11). Adult respiratory distress syndrome is caused by lung direct contact with phosphine gas (12). According to previous investigations in this regard, since there is no epidemiological study on the situation of patients with rice tablet poisoning in the Tabriz Sina Hospital, in East Azarbaijan Province, Iran, we decided to assess the epidemiology situation of these patients during the last 5 years.

2. Materials and Methods:

This study was a routine data base study, which as conducted in Sina hospital in Tabriz Medical Sciences University, Tabriz, north west of Iran. In this study, the medical records of patients attempted suicide with rice tablets during the years 2011-2015 were evaluated. Inclusion criteria included all medical records of patients with suicidal attempt with rice tablets who referred to Sina hospital during the last 5 years, and the exclusion criterion was incomplete medical record. Sampling was done in a full-census manner. During the period mentioned above, 90 patients with rice tablet poisoning were admitted to the hospital. All ethical criteria were observed in this study and the of patients information all remained confidential. After visiting hospital archive ward and using HIS software, the medical records of patients with rice tablet poisoning were extracted.

The records were reviewed and required information, including age, sex, type of tablets (Banan/ALP), manner of consumption (alone, dissolved in water,

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breaking, water drinking after taking the the time interval tablet), of tablet consumption till referral to the emergency room, initial vital signs and symptoms of patient, initial laboratory findings, duration of hospital stay and outcome were recorded corresponding the in checklist. The patients were first divided into two groups based on the type of tablet (ALP and Banan) and the intended variables between the two groups were evaluated. Finally, patients in ALP group were divided into two groups based on the outcome of hospitalization (with and without mortality) and the research variables were evaluated in these two groups.

17.0. To describe the data, descriptive deviation, analysis (Mean±standard and percentage) frequency was used. Normality of data distribution was evaluated using Kolmogorov - Smirnov test. Chisquare test and T test were used to compare qualitative quantitative and data. respectively. Logistic regression was used to determine the prognostic value of variables in predicting mortality rate in patients. The significance level of P value of 0.05% was considered while comparing groups.

3. Results:

ALP and Banan poisonings were reported in 72 (80%) and 18 (20%) patients out of total patients, respectively. Also, male and female

The recorded data were entered into SPSS

Variables	Aluminum Phosphide	Banan	P value
Age (years)	28.78±11.75	28.94±16.615	0.961
Male/Female	46/26 (1.76)	9/9 (1)	0.294
Live place			1.0
• Urban	64 (88%)	16 (88%)	
• Rural	8 (12%)	2 (12%)	
Ingestion time (hour before referring)	5.89±7.15	4.55±4.903	0.350
Ingestion type			< 0.001
Complete	7 (9.7%)	4 (22.2%)	
Broken tablet	12 (16.7%)	10 (55.6%)	
• Dissolved in water before	13 (18.1%)	4 (22.2%)	
ingestion			
• Drinking water after ingestion	40 (55.6%)	0 (0%)	
Level of consciousness			< 0.001
• Alert	23 (31.9%)	18 (100%)	
• Lethargic	25 (34.7%)	0 (0%)	
Obtundation	11 (15.3%)	0 (0%)	
Stupor	3 (4.2%)	0 (0%)	
• Coma	10 (13.9%)	0 (0%)	
ICU admission	19 (26.4%)	0 (0%)	0.01
Intubation	41 (56.9%)	0 (0%)	< 0.001
Nausea	51 (70.8%)	13 (72.2%)	1.000
Vomiting	53 (73.6%)	11 (61.1%)	0.384
Lab finding			
• With blood cell (mm ³)	11434.72±3669.10	7827.70±2837.52	< 0.001
• Hemoglobin (g/L)	13.86 ± 2.10	13.49±1.84	0.504
• Creatinine (mg/dl)	0.98±0.32	0.94±0.28	0.584
• Urea (mmol/L)	26.60±10.31	20.72±4.47	0.021
• pH	7.28 ± 0.16	7.37±0.11	0.038
• Paco ₂ (mmHg)	34.79±10.78	38.26±6.45	0.195
 Hco₃ (mmol/L) 	17.94±6.23	23.16±4.12	0.001
Vital sign			
• MAP (mmHg)	72.35±23.01	84.6±9.94	0.030
 Respiratory rate (per minute) 	20.02 ± 5.62	17.7±3.02	0.106
 Heart rate (beat per minute) 	94.64±16.72	88.6±11.65	0.153
 Hear rate (beat per limitute) O₂ Sat (percent) 	92.86±6.33	95±3.55	0.172

Table 1: Demographic status and vital signs in patients with ALP and Banan poisonings

Variables		With mortality	Without mortality	P value
Age		30.93±12.95	25.94±9.39	0.074
Male/Female		28/13 (68%)	18/13 (58%)	0.459
	hour before referring)	5.87±5.36	3.47 ± 2.95	0.104
Ingestion type				
•	Complete	5 (12%)	2 (6%)	
•	Broken tablet	9 (22%)	3 (10%)	0.254
•	Dissolved in water before ingestion	5 (12%)	8 (26%)	
•	Drinking water after ingestion	22 (54%)	18 (58%)	
Level of conscio	6			
•	Alert	9 (22%)	14 (45.2%)	
•	Lethargic	13 (31.7%)	12 (38.7%)	
•	Obtundation	7 (17.1%)	4 (12.9%)	0.025
•	Stupor	2 (4.9%)	1 (3.2%)	
•	Coma	10 (24.4%)	0 (0%)	
	Connu			
ICU admission		17 (41%)	2 (6%)	0.001
Intubation		38 (93%)	3 (10%)	< 0.001
Nausea		22 (53.7%)	29 (93.5%)	< 0.001
Vomiting		25 (61%)	28 (90.3%)	0.007
Lab finding		20 (01/0)	20 (301270)	0.007
•	With blood cell (mm3)	12748.78±3933.83	9696.77±2397.15	< 0.001
•	Hemoglobin (g/L)		14.17±2.06	0.272
•	Creatinine (mg/dl)	13.62±2.12	0.86 ± 0.23	0.005
•	Urea (mmol/L)	1.07 ± 0.35	24.19±8.01	0.085
•	pH	28.41±11.51	7.37±0.11	< 0.001
•	1	7.22 ± 0.17	35.84±8.01	0.475
	Paco2 (mmHg)	33.99± 12.51	22.22±4.61	< 0.001
•	Hco3 (mmol/L)	14.70 ± 5.28		
Vital sign				
•	MAP (mmHg)	64.27±26.47	83.03±10.59	< 0.001
•	Respiratory rate (per minute)	20.90±6.34	18.87±4.33	0.130
•	Heart rate (beat per minute)	97.58±18.44	90.74±13.46	0.086
•	O2 Sat (percent)	90.39±7.33	96.12±1.98	< 0.001
Treatment	02 Sat (percent)			
1 Toutinent	NaHco ₃	34 (83%)	21 (68%)	0.166
•	MgSo ₄	37 (90%)	25 (81%)	0.310
•		17 (41%)	18 (58%)	0.234
•	Vitamin E	18 (44%)	8 (26%)	0.234
•	N-Acetyl Cysteine	5 (12%)	2 (6%)	0.691
•	GIK	33 (80%)	23 (74%)	0.576
•	Calcium Gluconate	33 (0070)	23 (11/0)	0.570

Table 2: Demographic status and vital signs of patients with and without mortality

patients accounted for 55 (61.1%) and 35 (38.9%) of participants. The mean age of patients was 28.81 ± 12.76 . Also, urban and rural patients accounted for 80 (88.9%) and 10 patients (11.1%), respectively. In terms of manner of taking the tablets, the frequency of methods used was follows: 11 patients (12.2%) complete form of tablets, 17 patients (18.9%) dissolved in water, 40 patients (44.4%) drinking water after taking

the tablets and 22 patients (24.4%) broken tablets.

The average length of stay in hospital was 3.42 ± 2.71 days and the minimum and maximum length of stay was 1 and 15 days, respectively. Average length of stay in the ICU was just 0.75 ± 2.23 days, and the minimum and maximum length of stay was 0 and 12 days, respectively. A total of 45.6% (41 patients) of the participants had a need for intubation, the average duration of which

Table 3: Results of logistic regression inpredictive value of variables in determiningthe mortality

Variable	Beta	P value
MAP	0.002	0.924
РН	0.212	0.116
HCO3	1.743	0.558
O ₂ sat	0.191	0.011

was 0.90 ± 1.75 days, and the minimum and maximum duration was 0 and 9 days, respectively, and the mean consumption time till referred to emergency department was 4.81 ± 5.41 hours (mode=2.00 hours). The minimum and maximum duration was obtained 0.50 and 24 hours.

Table 1 shows the demographic status and vital signs in patients with ALP and Banan poisonings. Patients with ALP poisoning were divided into two groups with and without mortality based on their outcome during the hospital admission and discharge time. The variables were compared in the two groups. The incidence of shock (mean pressure (MAP)<65mmHg), arterial metabolic acidosis (pH<7.35 or Hco3<24mmol/L) and hypoxemia (O2sat<92% in room air) in patients in the first moments of the emergency department visits, was 20.8% (n =15), 81.9% (n = 59) and 27.8% (n =20), respectively. Table 2 shows the demographic status and vital signs in patients with and without mortality.

As Table 2 shows, there was a statistically significant relationship between MAP, pH, HCO3, creatinine, white blood cell (WBC), O2 saturation variables and level of consciousness in ALP poisoned patients with and without mortality. Logistic regression was used to determine the prognostic value of these variables in predicting mortality in patients with ALP poisoning. Table 3 shows the result of this analysis.

$$Probability = \frac{\exp(\beta + \beta_x x_1)}{1 + \exp(\beta + \beta_x x_1)}$$

$$Probability of mortality = \frac{\exp(-36.79 + 0.19 H co3)}{1 + \exp(-36.79 + 0.19 H co3)}$$

4. Discussion:

In this retrospective study, the medical records of 90 patients who had attempted suicide using rice tablets between 2011 and 2015 were examined. A total of 72 patients attempted suicide using ALP tablets. According to the results of the present study on outcomes in these patients, there was an association between the survival of patients with hypotension, acidosis, loss of consciousness, and hypoxia on admission to the hospital. Among the variables listed, serum bicarbonate can predict the hospital mortality in patients with ALP poisoning.

Suicide is considered as one of the most important public health problems and it considered as the top 10 causes of death in some communities (13). ALP, which is called rice tablet, is used to protect rice from pests. Occupational rodents and and accidental poisonings with this tablet are rare and most poisonings occur due to suicide attempts (14, 15). Damage caused by phosphine gas that is produced by ALP is likely to occur at the cellular level and leads to inhibition of Cytochrome C oxidase protein in mitochondria, disrupts cellular metabolism and eventually leads to multiorgan damage (16, 17). Phosphine gas also leads to inhibition of protein synthesis and enzyme activity, especially in mitochondria of heart and lungs cells (5).

Etemadi-Aleagha et al., in a study that was carried out by during 8 years in Tehran, showed increased incidence of ALP poisoning over the years 2006 to 2013 (18). The prevalence of suicide attempts with ALP tablets was higher in men (46/26), which was consistent with other studies (19). Taramsari et al. (2006), in a study on 116 patients with ALP poisoning, showed that 78.4% of patients had gastrointestinal symptoms and there was a significant relationship between the mortality rate and presence of acidosis, hypotension and arterial oxygen saturation (4). It has been suggested in various studies that there is an association between the absence of gastrointestinal symptoms such as nausea and vomiting severity of ALP poisoning (10, 14). In the present study, the prevalence of nausea and vomiting was lower in patients with mortality and this difference was statistically significant between the two groups of patients who died and survived.

The shock mechanism is not clear in these patients and the hypotension incidence of in these patients is 76-100%. Several factors, myocardial injury, including coronary vasodilatation and fluid loss have been proposed as causes of shock. Some studies indicated that left ventricular dysfunction caused by ALP poisoning will be improved after several days (20). A total of 20.8% of studied patients experienced hypotension and shock at the arrival time to the emergency department. Steroids were used to treat shock in some studies that leads to a reduction in the dose of dopamine used. But the mechanism of steroids' effect in these patients is unknown. Hypoxia is caused in these patients in the field of inhibition of oxidative phosphorylation caused by ALP, which ultimately leads to circulatory failure and organ perfusion (21). The incidence of hypoxia in our studied patients was 27.8%.

Consistent with the results of other studies metabolic acidosis was the most common acid-base disorder in patients studied in the present study (10, 14). In a study on 102 cases of poisoning with ALP in two years, Hosseinian et al. (2011) concluded that the presence of acidosis and hepatic dysfunction is related to the mortality rate (14). The results of their study are similar to the results of the current study. 81.9% of patients in the emergency department had metabolic acidosis.

Overall, the mortality rate caused by taking 500 mg ALP tablets has been reported about 30-100%. High serum level of phosphine is associated with an increased risk of mortality (22). Some studies reported a mortality rate of 40-80% (23, 24). In the previous studies in Iran, the mortality rate ALP poisoning has been reported 23-58% (14, 25). In the

present study, the mortality rate was 56.9%. Higher mortality rates were reported when fresh tablets were used compared with powdered or expired tablets, which could be due to hydrolysis of tablets in the moist air and lower levels of phosphine gas (26).

A limitation of our study was its retrospective nature and we could not evaluate other variables required due to defects in documentation of some medical records of patients.

5. Conclusion:

The results of the current study show that the serum bicarbonate level at the moment of arrival to the emergency department can predict the mortality in patients' with ALP poisoning. Next prospective studies are recommended for more accurate evaluation of the impact of this variable on the survival of patients. Also, due to the high mortality rates caused by rice tablet poisoning (ALP) and lack of specific antidote, the best treatment is prevention. In the prevention of accidental poisonings, especially in children, it is very important to raise families' level of awareness and closely monitor the production and distribution of these compounds.

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