Trend of blood lactate level in acute aluminum phosphide poisoning

Peyman Erfantalab¹, Kambiz Soltaninejad², Shahin Shadnia¹, Nasim Zamani¹, Hossein Hassanian-Moghaddam¹, Arezou Mahdavinejad¹, Behrooz Hashemi Damaneh¹

¹ Toxicological Research Center, Excellent Center of Clinical Toxicology, Department of Clinical Toxicology, Loghman Hakim Hospital, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
² Department of Forensic Toxicology, Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran

Corresponding Author: Shahin Shadnia, Email: shahin1380@yahoo.com

BACKGROUND: Aluminum phosphide (AlP) poisoning is common in the developing countries. There is no specific antidote for the treatment of acute AlP poisoning. Early diagnosis of poisoning and outcome predictors may facilitate treatment decisions. The objective of this study was to determine the trend of blood lactate level in acute AlP poisoning to evaluate its role as a prognostic factor.

METHODS: This was a prospective study on acute AlP intoxicated patients during one year. Demographic data, clinical and laboratory data on admission, and outcome were recorded in a self-made questionnaire. Blood lactate levels were analyzed every two hours for 24 hours.

RESULTS: Thirty-nine (27 male, 12 female) patients were included in the study. The mortality rate was 38.5%. The mean blood pressure, pulse rate, blood pH and serum bicarbonate level were significantly different between the survivors and non-survivors groups. Blood lactate level was significantly higher in the non-survivors group during 8 to 16 hours post ingestion.

CONCLUSION: Blood lactate level could be used as an index of severity of acute AlP poisoning.

KEY WORDS: Aluminum phosphide; Poisoning; Blood lactate; Prognostic factor

INTRODUCTION

Aluminum phosphide (AlP) is a fumigant that has been used to protect stored grains.¹ It is a common cause of intentional poisoning with high mortality in developing countries.²,³ AlP is known as "rice tablet" in Iran and marketed in 3 g tablets under brand name of Phostoxin®, which contain 56%.²

Severe intoxication cases may present with various degrees of metabolic acidosis with signs and symptoms like tachypnea, hyperpnea, tachycardia, hypotension, decreased mental status, and multisystem organ failure.¹

Studies using Glasgow Coma Scale (GCS), electrocardiogram (ECG), blood glucose level and scoring systems like Acute Physiology and Chronic Health Evaluation (APACHE) and Simplified Acute Physiology Score (SAPS) have attempted to predict mortality in acute AlP poisoning. The data regarding their utility are inconsistent.⁴⁻⁷

Blood lactate levels have been used as a prognostic factor in critically ill patients.⁸,⁹ Lactate has also been studied for prognostication in patients with poisoning from metformin, acetaminophen, beta blockers, carbon monoxide, cyanide and paraquat.¹⁰⁻¹⁶

The aim of this study is to determine the prognostic utility of blood lactate in acute poisoned patients admitted to the Medical Toxicology Intensive Care Unit (MTICU).

METHODS

This is a prospective study of patients with acute AlP poisoning admitted to the MTICU between March 2014 and March 2015. The diagnosis was based on the history
of exposure and positive silver nitrate test on stomach content and exhale breath samples.[17]

Subjects with a history of diabetes mellitus, cardiovascular, respiratory, renal, hepatic failure, or co-ingestions were excluded from data analysis as were those who received medical management for AlP poisoning prior to admission.

In all cases, gastric decontamination was performed with sodium bicarbonate (44 mEq, orally), permanganate potassium (1:10 000 orally), and activated charcoal (1 g/kg, orally) in the first 6 hours. The patients were also treated with magnesium sulfate (4–6 g/IV infusion for 24 hours), calcium gluconate (4–6 g/IV infusion for 24 hours), fluid therapy, vitamin E (400 mg/q12 hours for 24 hours, IM), and N-acetylcysteine (100 mg/kg/q8 hours for 24 hours, IV infusion). Blood lactate levels were analyzed every two hours for 24 hours using a portable lactometer (StatStrip® Lactate Xpress™ Meter, Nova Biomedical, USA).

Data collection

Data collected on each subject included demographic information, the amount of AlP ingested, time between exposure and admission to the hospital, GCS, vital signs, laboratory data on admission, and clinical outcome. Individual data of the patients were kept confidential in all stages of the study. This study was approved by the ethical committee of Shahid Beheshti University of Medical Sciences (Grant No. 5980).

Statistical analysis

All data were analyzed by social package for statistical analysis (SPSS) software version 16. The data were expressed as mean±SD for continuous or discrete variables and as a frequency and percentage for categorical variables. Chi-square test was used for statistical analysis of qualitative variables. The normal distribution of quantitative variables was tested by Kolmogorov-Smirnov test. The statistical comparison was done with Mann-Whitney U-test for nonparametric variables and independent student t-test for parametric variables. Optimal threshold for lactate levels were determined by receiver operating characteristics (ROC) analysis. P values of 0.05 or less were considered to be statistically significant.

RESULTS

A total of 39 patients (27 male, 12 female) were included in the study. In all of the cases, the reason for admission was suicide. The mortality rate was 38.5% (15/39). Table 1 shows the comparison between survivors and non-survivors groups based on demographic, clinical, and laboratory data.

Plots of the distribution of blood lactate levels according to survival status and time after onset of poisoning are presented in Figures 1 and 2. Blood lactate levels were significantly higher in the non-survivors group between 8 and 16 hours post ingestion (Table 2). Figure 3 indicates

### Table 1. Comparison of survived and non-survived AlP intoxicated cases based on demographic data, clinical, and paraclinical parameters on admission time

<table>
<thead>
<tr>
<th>Parameters</th>
<th>All patients (n=39) (%)</th>
<th>Survivors group (n=24) (%)</th>
<th>Non-survivors group (n=15) (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>27 (61.5)</td>
<td>16 (66.7)</td>
<td>11 (73.3)</td>
<td>0.66</td>
</tr>
<tr>
<td>Female</td>
<td>12 (38.5)</td>
<td>8 (33.3)</td>
<td>4 (26.7)</td>
<td>0.66</td>
</tr>
<tr>
<td>Age (year)</td>
<td>31.0±11.3 (17–65)</td>
<td>30.5±11.7 (17–65)</td>
<td>31.8±11.1 (23–61)</td>
<td>0.83</td>
</tr>
<tr>
<td>Number of AlP tablets</td>
<td>1.2±0.3 (0.25–6)</td>
<td>1.2±0.3 (0.5–6)</td>
<td>1.1±0.3 (0.25–6)</td>
<td>0.35</td>
</tr>
<tr>
<td>The use of AP tablets with water</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>5 (12.8)</td>
<td>5 (20.8)</td>
<td>0</td>
<td>0.06</td>
</tr>
<tr>
<td>Negative</td>
<td>34 (87.2)</td>
<td>19 (79.2)</td>
<td>15 (100)</td>
<td>0.06</td>
</tr>
<tr>
<td>TBOPAH (hour)</td>
<td>3.0±1.5 (0.5–6)</td>
<td>3.5±1.6 (0.5–6)</td>
<td>2.2±0.9 (0.5–4)</td>
<td>0.006</td>
</tr>
<tr>
<td>Glasgow Coma Scale</td>
<td>12.5±2.8 (3–15)</td>
<td>13.2±2.4 (7–15)</td>
<td>11.6±3.3 (3–15)</td>
<td>0.08</td>
</tr>
<tr>
<td>Systolic blood pressure (≤120 mmHg)</td>
<td>96.4±23.3 (50–152)</td>
<td>104.7±21.9 (60–152)</td>
<td>83.1±19.3 (50–120)</td>
<td>0.006</td>
</tr>
<tr>
<td>Diastolic blood pressure (≤80 mmHg)</td>
<td>59.9±16.1 (30–106)</td>
<td>64.6±17.0 (30–106)</td>
<td>52.3±14.4 (30–70)</td>
<td>0.008</td>
</tr>
<tr>
<td>Pulse rate (60–100 beats/minute)</td>
<td>96.1±22.8 (49–144)</td>
<td>104.5±20.9 (61–144)</td>
<td>82.7±19.4 (49–117)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

SD=Standard deviation; ‘’ : time between onset of poisoning and admission on hospital.

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blood lactate levels in survivors and non-survivors groups during the first 24 hours post ingestion.

Table 3 shows the results of ROC analysis and relative risk for death with regard to blood lactate levels at 4 to 24 hours post ingestion. An area under the ROC

Table 2. Blood lactate level in survivors and non-survivors groups in different times post ingestion (mmol/L)

<table>
<thead>
<tr>
<th>Time (hours)</th>
<th>Survivors group (n=24) Mean±SD</th>
<th>Non-survivors group (n=15) Mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>9.9±2.6</td>
<td>8.8±4.3</td>
<td>0.54</td>
</tr>
<tr>
<td>4</td>
<td>6.9±3.7</td>
<td>9.5±4.7</td>
<td>0.08</td>
</tr>
<tr>
<td>6</td>
<td>6.0±3.7</td>
<td>8.4±3.6</td>
<td>0.09</td>
</tr>
<tr>
<td>8</td>
<td>6.2±3.4</td>
<td>10.2±4.1</td>
<td>0.007</td>
</tr>
<tr>
<td>10</td>
<td>5.5±3.1</td>
<td>10.1±5.4</td>
<td>0.004</td>
</tr>
<tr>
<td>12</td>
<td>5.4±3.0</td>
<td>10.0±6.1</td>
<td>0.008</td>
</tr>
<tr>
<td>14</td>
<td>4.6±2.4</td>
<td>10.1±5.6</td>
<td>0.001</td>
</tr>
<tr>
<td>16</td>
<td>4.3±2.6</td>
<td>8.6±5.6</td>
<td>0.008</td>
</tr>
<tr>
<td>18</td>
<td>4.1±2.6</td>
<td>5.3±4.1</td>
<td>0.39</td>
</tr>
<tr>
<td>20</td>
<td>3.7±2.8</td>
<td>4.8±4.7</td>
<td>0.92</td>
</tr>
<tr>
<td>22</td>
<td>2.7±1.8</td>
<td>4.8±4.2</td>
<td>0.43</td>
</tr>
<tr>
<td>24</td>
<td>2.7±1.7</td>
<td>5.1±3.8</td>
<td>0.40</td>
</tr>
</tbody>
</table>

SD: standard deviation.
DISCUSSION

AIP is a fumigant with a high mortality rate in acute poisoning. The most common clinical manifestations are due to cardiovascular and respiratory toxicity which are the most common causes of mortality.

There is no specific antidote for the treatment of acute AIP poisoning. Early diagnosis and reliable predictors of mortality may guide care and appropriate resource utilization for these patients.

Previously studied prognostic variables including age, lack of vomiting, dose ingested, GCS, blood pressure, severe acidosis, hyperglycemia, and electrocardiographic abnormality have yielded inconsistent results.

Our study demonstrated that blood pressure, pulse rate, blood pH, and serum bicarbonate level were significantly different between survivors and non-survivors groups, which is in concordance with the results of our previous studies.

Hyperlactatemia is defined as the serum lactate level of ≥2 mmol/L. In general, the mechanisms of hyperlactatemia including hypoperfusion lead to cellular hypoxia, increased activity of Na⁺/K⁺-ATPase in normoxia, increased pyruvate and lactate due to increased anaerobic glycolysis, decreased lactate clearance, muscle hyperactivity due to seizures, and impaired electron transfer and oxidative phosphorylation.

Evaluation of the blood lactate level is generally used in diagnosis and management of the patients with signs and symptoms of sepsis or shock and is a sign of tissue hypoperfusion. Blood lactate level has been reported to be a poor prognostic factor predicting death in hospital and ICU-admitted patients. The role of blood lactate level has been studied as a prognostic factor in drug and chemical poisoning too.

Hyperlactatemia in AIP toxicity is a result of both energy insufficiency and oxidative stress, with a possible interaction with mitochondrial electron transport chain and the inhibition of cytochrome c, which may lead to metabolic acidosis and increased lactate production.

Within our study population, AIP poisoned patients generally have higher levels of blood lactate within the first hours post ingestion. Blood lactate level could be successfully used as a prognostic factor in acute AIP poisoning within the 8 to 16 hours post ingestion. Also our results show significant correlation between blood lactate levels and pH at 6 to 22 hours post ingestion.

The limitation of this study is the small number of cases, so it is suggested that the same study be done as a multicenter with a large number of cases.

CONCLUSION

Evaluation of blood lactate level could be used as an index of severity of poisoning and for decision making about treatment provided in acute AIP poisoning.

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