Effect of Aluminium Phosphide Poisoning on Blood Cortisol Level

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ABSTRACT

Background: Acute intoxication with ALP is extremely lethal. The present study was conducted to determine the range of serum cortisol levels in ALP poisoning and its correlation with patient outcome.

Methods: This study was carried out on patients who were intoxicated with ALP. Their demographic data and pertinent findings in their history and physical examination were recorded at the time of arrival and also when shock and severe metabolic acidosis emerged. 5cc blood was taken from the patients to measure blood cortisol level, when shock and severe metabolic acidosis developed. Blood cortisol level analysis was performed using ELISA method. Data analysis was done using SPSS software version 16.0.

Results: The average ingested dose was 1.98+1.79 tablets each containing 3 grams of ALP. Overall, 77% of the patients presented tachycardia and hypotension. Blood cortisol level less than 15 µg/dl, 15-33 µg/dl, and more than 34 µg/dl were regarded as adrenal insufficiency, critical illness-related corticosteroid insufficiency, and adequate adrenal response, respectively. Eventually, 3 patients fell within the first category, 24 patients matched with the second category, and 3 patients corresponded to the last category.

Conclusion: Blood cortisol concentration is satisfactory only in 10% of the patients. In majority of the patients although it is not apparently low, it has not shown the expected rise comparable to the shock and stress state of such patients. It defines a role for corticosteroids therapy in management of ALP poisoning, particularly if it does not respond to conventional treatments.

Keywords: Adrenal Insufficiency, Aluminum Phosphide, Cortisol, Poisoning, Shock.

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INTRODUCTION

Aluminum phosphide (ALP) is widely used all over the world as a fumigant to protect stored grain from pests and rodents (1). Acute intoxication with ALP is extremely lethal. It is usually suicidal and rarely accidental. Unfortunately, lack of specific antidote complicates the toxicity (2).

ALP is a highly effective and inexpensive insecticide. As a rodenticide, it is formulated in solid form as tablets or pellets placed in porous bags or blister packs. ALP may be synthesized as dark gray or dark yellow crystals. Zinc phosphide, on the other hand, is a steel gray crystalline powder which is synthesized by direct combination of zinc and phosphorus. It is a slow acting rodenticide as compared to ALP (3).

Once ingested, ALP is decomposed into highly toxic phosphine gas by the

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dilute hydrochloric acid content of the stomach (3). Two main known mechanisms of action of phosphine are induction of oxidative stress and inhibition of cellular respiration through disruption of mitochondrial electron transport chain (4). Phosphine gas is rapidly absorbed from the stomach and inhibits the mitochondrial respiratory chain and, thus, leads to cell necrosis and death. Mitochondrial cytochrome C oxidase inhibition may also lead to pulmonary and cardiac toxicity (3). Phosphine-induced impairment of myocardial contractility and fluid loss lead to circulatory failure. Other features include metabolic acidosis, pulmonary edema, disseminated intravascular coagulation, hepatic necrosis, and renal failure.

Appraisal of the related literature reveals a wide range of clinical features associated with ALP poisoning, an ill-defined pathophysiology, and lack of consensus on treatment. Clinically, cases of ALP poisoning present with nausea, vomiting, severe hypotension, shock, acute respiratory distress, altered sensorium, and coma. Various neurobehavioral changes like ataxia, stupor, tremors, and convulsions have been observed following ALP poisoning. Acute hypoxic encephalopathy on ALP exposure has been reported, which may lead to death as a result of complete depression of the central nervous system and paralysis of the respiratory centers of the brain (5). Uncommon complications of ALP poisoning include hemolysis, gastroduodenitis, hepatitis, acute tubular necrosis, and delayed esophageal stricture (6).

Hypotension is a common manifestation in ALP poisoning. It has been attributed to severe cardiovascular collapse after volume depletion, myocardial depression, and adrenal insufficiency (7). It leads to decreased perfusion of vital organs and can cause altered sensorium, renal and hepatic failure, and shock. Damage to adrenal glands may contribute to clinical features of ALP poisoning especially hypotension. Adrenal gland damage can increase or decrease blood cortisol levels. Changes in adrenal cortex could be due to shock or the cellular toxic effect of phosphine. The histopathological changes after ALP poisoning in various viscera have shown congestion, edema and cellular infiltration, hemorrhage, and necrosis (8). As for the microscopic examinations in various organs of the body, they may show complete lipid depletion, hemorrhage, and necrosis in the adrenal cortex (1).

On the other hand, in clinical situations, such as stress, hypotension, and shock, or in critically ill patients, there is evidence of altered cortisol metabolism based on changes in secretion, responsiveness, protein binding, and activity of glucocorticoids. These changes have been described by the terms "Relative Adrenal Insufficiency" (RAI). More recently "critical illness-related corticosteroid insufficiency" (CIRCI) has been used to designate those patients in whom cortisol production did not sufficiently increase in response to stress situations (9, 10, 11).

There is no published study on serum cortisol concentration in ALP poisoning. The present study was conducted to determine the range of serum cortisol levels in ALP poisoning and its correlation with patient's outcome.

MATERIALS AND METHODS

This study was carried out on patients who were intoxicated with ALP based on history taking and appearance of signs and symptoms compatible with the poisoning, such as hypotension, shock, and/or metabolic acidosis. They were selected from patients admitted at Loghman-Hakim Hospital, Tehran, Iran, a university referral center for management of poisonings, from March 2010 to March 2011. Asymptomatic or normotensive patients, patients with history of co-ingestions, and history of use of steroid

drugs were excluded from the study. Their demographic data, pertinent findings in their history and physical examination were recorded. Systolic and diastolic blood pressure, pulse rate, blood PH, and bicarbonate concentration were recorded at the time of arrival and also when shock and severe metabolic acidosis emerged. From each patient, 5cc whole blood was taken to measure blood cortisol level when shock and severe metabolic acidosis developed. Blood cortisol level analysis was performed by Loghman-Hakim Laboratory using ELISA method. Blood cortisol level less than 15 µg/dl, 15-33 µg/dl, and more than 34 µg/dl were considered as adrenal insufficiency, potential critical illness-related corticosteroid insufficiency, and adequate adrenal response respectively, according to Kronenberg (12). Data were analyzed using SPSS software version 16.0.

RESULTS

Thirty patients with ALP intoxication were evaluated and 14 (47%) of them were male and 16 (53%) were female. The mean age was 26± 12.78 years, ranging from 16 to 77 years. Most of the patients (64%) were between 20 and 29 years old. All of the patients had been poisoned after suicidal attempts. The average ingested dose was 1.98±1.79 tablets each contained 3 grams of ALP, ranging from 0.5 to 10 tablets. Overall, 27% of the patients had consumed one tablet only. A wide range of symptoms and signs was seen upon admission, but the most common findings were cardiovascular manifestations, 77% of the patients showed tachycardia and hypotension. Electrocardiographic changes in the patients are presented in Table 1.

Mean systolic/diastolic blood pressure was 90±1.65/60±1.37 upon arrival at the hospital. At this time, their pulse rate was 94±1.5, mean arterial blood PH was 7.35±0.13, and mean bicarbonate concentration was 14.75±5 mEq/L. Mean systolic/diastolic blood pressure was 76.5±1.47/44±9.8 at the time of appearance of the most severe signs. At this time, the pulse rate was 108+1.5, mean arterial blood PH was 7.19±0.16, and mean bicarbonate concentration was 11.5±3.5 mEq/L.

Mean blood cortisol level of the patients was 24± 0.16 µg/dl. The blood cortisol level had an inverse relationship with bicarbonate concentration, though the correlation was statistically insignificant (P>0.05). No association was found between the numbers of ingested tablets, dose of vasopressors infused to the patients, and severity of shock with blood cortisol level.

If blood cortisol level less than 15 µg/dl and 15-33 µg/dl and more than 34 µg/dl were regarded as adrenal insufficiency, critical illness-related corticosteroid insufficiency, and adequate adrenal response; 3 (10%) patients were in the first category, 24 (80%) patients matched with the second category, and 3 (10%) patients corresponded to the last category.

Table 1. Electrocardiographic changes in the studied ALP poisoning patients

ECG changes	No. of the patients	% of the patients
Sinus tachycardia	23	77%
Ischemic changes	11	37%
AF rhythm	6	20%
VT rhythm	5	17%
VF rhythm	1	3%
Brugada pattern	1	3%

Calcium gluconate and magnesium sulfate were administrated to 23 (77%) patients. Norepinephrine and/or dopamine were used for 24 (80%) patients.

The overall case fatality rate was 63% (19 patients). There were no statistically significant differences between blood cortisol level among the fatal and non-fatal cases.

DISCUSSION

The present study was conducted to assess blood cortisol concentrations in patients with ALP poisoning. The results indicated that blood cortisol concentration did not rise to the expected levels corresponding to the shock and stress status of the patients.

There are few reports with inconsistent results about blood cortisol concentrations in ALP poisoning and the optimal range of serum cortisol in ALP poisoning has not yet been clearly defined.

Unlike poisonings, cortisol level and adrenal gland involvement in other forms of shock, typically septic shock, have been studied frequently. Venkatesh *et al*. showed that plasma cortisol to cortisone ratio was significantly elevated in sepsis and multiple trauma and remained elevated for a long time (10).

Chugh and his colleagues have reported the effect of aluminum phosphide (ALP) on the adrenal cortex in 30 patients with ALP poisoning (13). A significant increase in the plasma cortisol level (greater than 1048 nmol/l) was observed in 20 patients and the mortality rate was 50%. Histopathologic study after autopsy showed mild to moderate changes in the adrenal glands in 10 patients. In the rest 10 patients, adrenal cortex had been seriously involved and blood cortisol level had failed to rise beyond normal levels (less than 690 nmol/l). Histopathologic study revealed severe changes (complete lipid depletion, hemorrhage, necrosis etc.); all the patients had died.

Schein and his coworkers found that plasma cortisol concentrations increased in patients with septic shock, whereas the degree of increase was variable (14). They concluded that plasma cortisol concentrations increased in patients with septic shock, but the degree of increase was variable (14).

If cortisol levels remain low or even at normal level in the critically ill patients, it may imply severe adreno-cortical compromise. Changes in the adrenal cortex could be due to shock or cellular toxic effect of phosphine. Histopathological changes in various viscera showed congestion, edema, and cellular infiltration in ALP poisoning. In the heart, there were patchy areas of necrosis, while the liver showed fatty changes and the lungs showed areas of gray/red hepatization, in addition. There was no adrenal apoplexy or extensive hemorrhage that could explain shock in these patients. Cardiogenic shock could not be confirmed due to lack of facilities for hemodynamic monitoring, but there was histopathological evidence in support of cardiovascular shock (13).

The present study demonstrated that blood cortisol concentration is satisfactory only in 10% of the patients. In the majority of the patients, although it is not apparently low, it has not shown the expected rise comparable to the shock and stress state of such patients. This has been named incomplete adrenal response, partial or suboptimal adrenal response, or relative or functional adrenal insufficiency in the literature (12). However, if more accurate diagnosis is needed, confirmatory analyses, such as ACTH stimulation test, should be performed (12); which seems inappropriate and time-consuming with regard to the urgent critical condition of such patients.

CONCLUSION

This study defined a role for corticosteroids therapy in management of ALP poisoning, particularly if it does not respond to conventional treatments. Nevertheless, conducting further studies is recommended to elucidate the effect of corticosteroids therapy on patients.

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