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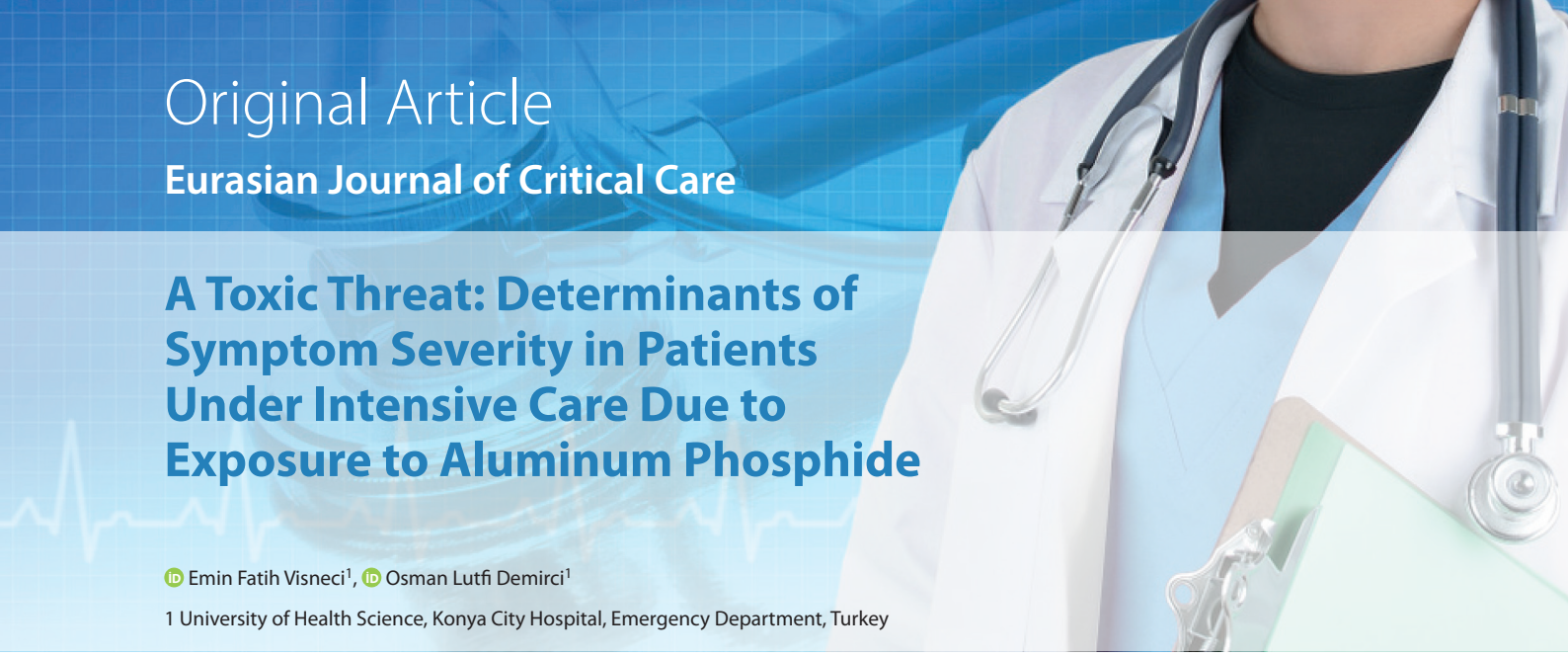

A Toxic Threat: Determinants of Symptom Severity in Patients Under Intensive Care Due to Exposure to Aluminum Phosphide

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Abstract

Objective: This study aims to identify the factors determining the severity of poisoning resulting from respiratory exposure to Aluminum Phosphide (AlP), commonly used as a rodenticide against pests in households in low socio-economic regions.

Materials and Methods: This is a single-center, retrospective observational study that reviewed the data of patients admitted to the emergency department due to AlP exposure and subsequently accepted into the toxicology intensive care unit between 2023 and 2024. The study utilized patients' demographic characteristics, mode and duration of exposure, clinical findings, and outcomes. Student's t-test was used for binary group comparisons, and one-way Analysis of Variance (ANOVA) was employed for comparisons among more than two groups. Continuous data not conforming to normal distribution were presented as median (interquartile range) and analyzed using the Mann-Whitney U test for two-group comparisons and the Kruskal-Wallis test for multiple-group comparisons. A p-value of <0.05 was considered statistically significant in all analyses.

Results: The median age of the 11 patients included in the study was 60 years (range 22–85). Of these, 64% were male (7 males, 4 females), and 36% were female. The relationship between Glasgow Coma Scale (GCS) and symptom severity was analyzed using the Kruskal-Wallis test and found to be significant ($p = 0.027$). Similarly, the relationship between lactate levels and symptom severity was significant ($p = 0.009$). Patients with lower GCS values exhibited higher lactate levels; for instance, all patients with GCS ≤ 8 had lactate levels >4 mmol/L. A strong negative correlation was observed between GCS and lactate levels (Spearman's $\rho \approx -0.82$, $p < 0.01$). The relationship between gender and lactate levels was analyzed using the Mann-Whitney U test, revealing significantly higher lactate levels in females ($p = 0.015$).

Conclusion: Advanced age, low GCS, high lactate levels, and female gender appear to necessitate more intensive monitoring and treatment in AlP poisonings. These findings may facilitate risk stratification.

Keywords: Aluminum Phosphide, Respiratory Exposure, Gender, Lactate, Intensive Care

Introduction

Aluminum Phosphide (AlP) is a fumigant commonly used for pest control in grain storage. In agricultural settings, grain warehouses, and occasionally in homes, it is utilized as a rodenticide. AlP tablets are available in the market as formulated products. When it reacts with moisture, water, or stomach acid, it releases phosphine (PH_3) gas, which is primarily responsible for its toxicity (1). AlP is rapidly absorbed through the skin, gastrointestinal tract, and respiratory tract, depending on the mode of exposure. There are few case reports associated with AlP poisoning. The majority of cases involve poisonings resulting from oral ingestion with gastrointestinal absorption, while respiratory AlP poisonings are rare (2). In the literature, poisonings through oral ingestion are often reported as suicide attempts. When ingested orally, aluminum phosphide reacts with hydrochloric acid in the stomach, releasing PH_3 gas, which is a potential source of poisoning (3,4). Respiratory exposure typically arises from the use of AlP for pest control within homes or agricultural areas. It is more readily available and widely used in underdeveloped countries. Although the exact mechanism of action is still not fully understood, various animal studies have indicated that its most significant effect is the inhibition of mitochondrial cytochrome c oxidase enzyme. This leads to impaired cellular oxygen utilization, accelerated formation of free oxygen radicals, lipid peroxidation in cell membranes,

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and protein denaturation. The net effect is multiple organ failure resulting from disrupted mitochondrial oxidative phosphorylation (5). The most commonly affected organs are the lungs, heart, kidneys, gastrointestinal system, and liver. Due to the absence of a known antidote, mortality rates remain high, especially in cases presenting late to the hospital, despite intensive care monitoring. In the literature, mortality rates following aluminum phosphide poisoning have been reported to range between 40% and 80%. In patients developing resistant myocardial dysfunction, this rate can rise up to 77% (37–100%) (6-8).

In contrast to the frequent suicide attempts through oral AlP ingestion reported in the literature, our study examined the management in the emergency department, intensive care monitoring, demographic characteristics, laboratory findings, and mortality rates of PH_3 gas poisonings resulting from respiratory exposure to AlP following fumigation intended to kill rodents and insects.

Materials and Methods

Study Design

This single-center, retrospective observational study analyzed data from patients who presented to the emergency department due to AlP exposure and were subsequently admitted to the toxicology intensive care unit between 2023 and 2024.

Patient Population

A total of 11 patients who experienced respiratory AlP exposure during the specified period were included in the study. Cases involving intentional (deliberate) oral ingestion of aluminum phosphide and those with dermal contact exposure were excluded. Thus, only accidental poisoning cases resulting from inhalation exposure were evaluated.

Data Collection

Demographic characteristics, mode and duration of exposure, clinical findings, and outcomes of all patients were retrospectively obtained by reviewing hospital records. Data were compiled using a standard form and recorded digitally.

Statistical Analysis

The conformity of continuous variables to normal distribution was evaluated using the Kolmogorov-Smirnov test. Normally distributed data were expressed as mean ± standard deviation and analyzed using Student's t-test for two-group comparisons and one-way Analysis of Variance (ANOVA) for comparisons among more than two groups. Continuous data not conforming to normal distribution were presented as median (interquartile range) and analyzed using the Mann-Whitney U test for two-group comparisons and the Kruskal-Wallis test for multiple-group comparisons. A p-value of <0.05 was considered statistically significant in all analyses.

Results

The median age of the 11 patients included in the study was 60 years (range 22–85). Of these, 64% were male (7 males, 4 females), and 36% were female. Regarding symptom severity, 3 patients (27%) were classified as mild, 5 patients (45%) as moderate, and 3 patients (27%) as severe. The median Glasgow Coma Scale (GCS) score at presentation was 11 (range 6–15). The initial mean lactate level was 3.1 ± 1.2 mmol/L, with a median value of 3.0 mmol/L (range 1.2–5.0). The demographic data of the patients are presented in Table 1. The relationship between age and symptom severity was evaluated using the ANOVA test, with values presented as mean ± standard deviation (SD). A significant relationship was found between age and symptom severity ($p = 0.041$) (Table 2). The relationship between GCS and symptom severity was analyzed using the Kruskal-Wallis test, with values presented as mean ± SD. A significant relationship was found between GCS and symptom severity ($p = 0.027$) (Table 3). The relationship between lactate level and

Table 1. Symptoms and Severity by Duration of Exposure

	Symptoms					Duration of Exposure
	Skin Lesions (itch)	Mild neurological symptoms (dizziness, headache)	Gastrointestinal Symptoms (Nausea vomiting)	Shortness of breath, chest pain	Severe neurologistic alteration (Change of consciousness)	
Cases with mild symptoms (n:3)	+	-	-	-	-	4 hours
Cases with moderate symptoms (n:5)	-	+	+	+	+	15 hours
Cases with severe symptoms (n:5)	-	-	+	+	+	48 hours

Table 2. Demographic and Clinical Characteristics of Patients

Characteristic	Value
Age (years)	60 (median), Range (22-85)
Gender (Female/Male)	4/7 (4 females,7 males)
Symptom Severity	3 Mild (%27), 5 Moderate (%45), 3 Severe (%27)
Glasgow Coma Scale (GCS)	11 (median) Range (6-15)
Lactate (mmol/L)	3.0 (median), Range (1.2-5.0)

Note: The data is presented as median values and ranges; gender and symptom severity are indicated categorically by the number of patients (percentage, %).

Table 3. Symptom Severity Scores by Age Group

Age Group (years)	n	Symptom Severity Score (mean ± SD
≤30	3	5.7 ±1.3
31-60	4	6.0 ±1.4
≥60	4	6.5 ±1.5

Note: Relationship between Age and Symptom Severity (ANOVA Test Results). Distribution of symptom severity scores by age groups (age: categorical; symptom severity score: continuous). Values are presented as mean ± standard deviation (SD). ANOVA test result p = 0.041.

Table 4. Lactate Levels by Symptom Severity Level

Symptom Severity Level	n	Lactate (median [IQR],(mmol/L)
Mild	3	1.2 ± [0.8-1.8]
Moderate	5	2.5 ± [1.9-3.5]
Severe	3	4.0 ± [3.2-5.6]

Note: Relationship between Lactate Level and Symptom Severity (Kruskal-Wallis Test Results). Distribution of lactate levels by symptom severity categories (symptom severity: categorical; lactate level: continuous). Values are presented as median [interquartile range [IQR]. Kruskal-Wallis test result p = 0.009.

symptom severity was analyzed using the Kruskal-Wallis test, with values presented as median [interquartile range (IQR)]. A significant relationship was found between lactate level and symptom severity (p = 0.009) (Table 4). Patients with severe symptoms had notably higher lactate levels compared to those with mild symptoms (mean ≈4.6 mmol/L vs ≈1.7 mmol/L). Similarly, patients with lower GCS scores exhibited higher lactate levels; for instance, all patients with GCS ≤ 8 had lactate levels >4 mmol/L. A strong negative correlation was observed between GCS and lactate levels (Spearman's ρ ≈ –0.82, p < 0.01), indicating that increased lactate levels are associated with decreased levels of consciousness. (Table 5). The relationship between gender and age was evaluated using the t-test, with values presented as mean ± SD. The independent samples t-test result (p = 0.055) indicated no significant relationship between gender and age (Table 6). The relationship between gender and lactate levels was analyzed using the Mann-Whitney U test, with values presented as median [IQR]. Lactate levels were found to be significantly higher in females (p = 0.015) (Table 7).

Table 5. Glasgow Coma Scale Scores by Symptom Severity Level

Symptom Severity Level	n	Glasgow Coma Scale (GCS) (mean ± SD)
Mild	3	14.0 ±1.2
Moderate	5	12.8 ± 2.1
Severe	3	11.0 ± 3.0

Note: Relationship between GCS and Symptom Severity (Kruskal-Wallis Test Results). The distribution of Glasgow Coma Score (GCS) values according to symptom severity levels (symptom severity level: categorical; GCS: continuous). Values are presented as mean ± standard deviation. Kruskal-Wallis test result p = 0.027.

Discussion

The data obtained in this study highlight the prognostic importance of parameters such as age, level of consciousness, and lactate in clinical toxicology. Firstly, it was observed that older patients had significantly increased symptom severity. This finding is consistent with previous studies in the literature; for example, large patient series have reported that advanced age is associated with more severe clinical presentations and a higher risk of mortality in poisoning cases (9,10). The effect of age may be explained by reduced physiological reserves and comorbidities in elderly patients, which can exacerbate the outcomes of toxic effects. However, it should also be noted that in certain specific types of poisoning, age has not always been found to be a significant prognostic indicator; variations in population characteristics and the speed of intervention may lead to these differing results. Inhalation poisonings resulting from rodent use in small, enclosed spaces like homes have generally been reported in limited numbers and in limited cases. The symptoms of inhalation exposure in our

Table 6. Age Distribution by Gender

Gender	n	Age (mean ±SD,years)
Male	7	54.3 ± 17.5
Female	4	47.8 ± 18.9

Note: Relationship Between Gender and Age (T-Test Results). Comparison of mean age of male and female patients (gender: categorical; age: continuous). Values are presented as mean ± standard deviation. Independent sample T-test result p = 0.055.

Table 7. Lactate Levels by Gender

Gender	n	Lactate (median [IQR], (mmol/L)
Male	7	1.7 [1.0-2.6]
Female	4	2.5 [1.8-3.6]

Note: Relationship Between Gender and Lactate Level (Mann-Whitney U Test Results). Comparison of lactate levels of male and female patients (gender: categorical; lactate level: continuous). Values are presented as median [IQR]. Mann-Whitney U test result p = 0.015.

study are consistent with the symptoms presented in the cases, ranging from simple gastrointestinal symptoms to shock. (11). In our study, the inverse relationship between GCS and symptom severity is also an important finding. As GCS values decreased, symptom severity worsened, indicating a deterioration in the patient's neurological status. This supports the use of GCS as a prognostic indicator in acute poisonings, aligning with the literature. Indeed, a study on organophosphate poisoning reported that the mean GCS at admission was as low as 4 in patients who did not survive, while it was approximately 12 in survivors (12). The same study found a strong correlation between low GCS and mortality, emphasizing the prognostic value of GCS. Similarly, Eddleston et al. recommended that patients presenting with critical GCS levels (≤13) in pesticide poisonings should receive intensive care monitoring and aggressive treatment, as a significant portion of these patients experienced deterioration and death (13). Therefore, a low GCS score can be considered an early indicator of severity not only in trauma but also in toxicology patients. On the other hand, some studies have noted that GCS alone may not be a reliable prognostic indicator in all types of poisoning. In a study involving cases of mixed drug ingestion, no statistical relationship was found between initial Glasgow Coma Scale (GCS) scores and hospital course (e.g., length of stay), suggesting that GCS may have limited predictive power in heterogeneous overdose groups (14). These conflicting results indicate that the prognostic value of GCS may depend on the type of poisoning and accompanying factors. However, our findings generally confirm that patients with particularly low GCS scores may be in critical condition and require close monitoring.

Another significant result of our study is the close association between lactate levels and the clinical picture. As patients' blood lactate levels increased, symptom severity and clinical deterioration were observed to escalate. Lactate is considered a biomarker of tissue hypoxia and perfusion disorders; therefore, high lactate values in acute poisoning cases may indicate severe systemic involvement. Indeed, the literature has repeatedly demonstrated the prognostic value of lactate levels in various toxicology scenarios. For instance, a study on patients with carbon monoxide poisoning found a positive correlation between initial lactate levels and clinical severity, with higher lactate associated with worse outcomes. Abd El Razik et al. emphasized that lactate could be a prognostic indicator in acute CO poisoning, reporting significantly elevated initial lactate levels in severe cases (15). Similarly, recent studies have identified serum lactate as a strong predictor of mortality in pesticide intoxications such as paraquat. For example, Huang et al.'s (2014) study on paraquat poisoning showed that patients with high initial lactate levels had a significantly increased risk of death (OR ~7) (16). Additionally, a carbon monoxide poisoning study conducted in our country revealed that lactate concentration at emergency admission predicted whether patients would develop neurological and cardiac complications. When these data are considered alongside our findings, it suggests that lactate measurement could serve as a simple yet effective risk indicator in acute poisonings (17). In patients with elevated lactate, early initiation of more aggressive oxygenation, fluid therapy, and, if necessary, advanced supportive treatments may help improve prognosis. Conversely, normal lactate levels may indicate relatively better tissue perfusion, guiding the identification of mild poisoning cases.

Another noteworthy finding in our study is the biochemical difference between genders: female patients had significantly higher average lactate levels compared to male patients. Interestingly, although some toxicology series in the literature report that male gender is associated with more severe outcomes (18), our data suggest that female patients may be under greater metabolic stress. Several mechanisms could explain this phenomenon. Firstly, physiological differences: female patients may generally have lower average body mass and baseline hemoglobin levels. At the same exposure level, receiving a higher toxin dose per kilogram or having relatively lower oxygen-carrying capacity could lead to tissue hypoxia and, consequently, more rapid lactate accumulation in women. Secondly, hormonal and metabolic differences may also play a role. Estrogen and other sex hormones affect cardiovascular and metabolic responses; during stress responses, catecholamine release, microcirculation distribution, and lactate clearance may differ between women and men. Indeed, gender differences have been observed in critical illnesses: some large-scale studies have reported higher mortality in female patients with severe sepsis and shock, suggesting that women may be at a disadvantage under severe physiological stress (19). On the other hand, animal models and some human studies have proposed that women have immunological advantages against infectious stress; the impact of gender differences on outcomes can be inconsistent in the literature (20-22). Therefore, our finding of higher lactate levels in women may be specific to our patient group's characteristics or reflect an underlying pathophysiological difference. Other factors,

such as delayed hospital admission, gender-related differences in the amount of toxin ingested, or variations in distribution/metabolism within the body, may also contribute to this disparity. The lack of a significant relationship between gender and age (p=0.055) suggests that age is not a confounding factor and that the higher lactate levels in women may be directly related to gender. Future studies examining whether similar findings are replicated could provide a better understanding of physiological response differences between male and female patients.

Limitations

The limited number of cases in our study stems from the rarity of aluminum phosphide rodenticide use in small, enclosed areas. Although some variables reached statistical significance, the small sample size limits the generalizability and strength of the results. The aluminum phosphide level was not measured.

Conclusion

Advanced age, low GCS scores, elevated lactate levels, and female gender are associated with greater severity in AlP poisoning. These factors may guide risk stratification and management, though larger studies are needed to confirm these findings and clarify gender-related differences.

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