

The effects of wheat pill poisoning (aluminum phosphide) dosage on arterial blood gases and their clinical outcome

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Abstract

Objective: To analyse the effects of aluminum phosphide poisoning dosage on arterial blood gases and the clinical outcome.

Method: The cross-sectional study was conducted at the intensive care unit of Mardan Medical Complex, Mardan, Pakistan, from January 2021 to May 2022, and comprised patients of either gender who had attempted suicide using aluminum phosphide. Data was collected using a predesigned questionnaire. Data was analysed using SPSS 26.

Results: Of the 116 patients, 42(36.2%) were males and 74(63.8%) were females. There were 75(64.65) survivors; 31(41.33) males and 44(58.66) females with overall mean age 26.30±9.45 years. There were 41(35.35%) non-survivors; 11(26.82%) males and 30(73.18) females with overall mean age 28.21±11.16 years. During hospitalisation, the non-survivors showed drastically decreased levels of all arterial blood gas parameters with severe clinical outcomes ($p<0.05$). As the number of aluminum phosphide pills increased, the chance of survival decreased ($p<0.05$). The non-survivors spent an average of 32.51±16.02 hours in hospital (range: 6-59 hours).

Conclusion: Patients who ingested more aluminum phosphide pills had more abnormal arterial blood gas parameter with severe clinical outcomes. Also, they had lower chance of survival and unfavourable response to treatment.

Keywords: Aluminum phosphide, Poisoning, Emergency management, Critical care. (JPMA 73: 2189; 2023)

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Introduction

Aluminum phosphide (AIP), commonly known as the 'wheat pill', is a fumigant used in agriculture and household settings for pest control. AIP, a common and inexpensive insecticide, is highly poisonous and a significant cause of severe poisoning in developing countries. In Asia, where it is widely available, people use it as a method of suicide, making it a significant public health concern. Unfortunately, there is no known treatment or antidote for individuals who have been thus poisoned.^{1,2}

Its ingestion, inhalation, or contact with the body can lead to serious health hazards. When exposed to moisture, AIP releases a highly toxic gas called phosphine, which interferes with mitochondrial protein synthesis and enzyme function in the heart and the lungs. This can result in heart failure, circulatory collapse, pulmonary oedema and hepatic necrosis. The toxicity of AIP depends on the quantity and quality of the tablets, with fresher tablets having a more significant impact.³

Each wheat pill tablet contains 56.4% AIP and 44.6% ammonium carbonate and weighs 3g. The lethal dose for a person weighing 70kg is between 150mg and 500mg.^{2,4} Upon contact with moisture in the stomach, each tablet can release 1g phosphine gas with the help of hydrochloric acid.² The phosphine released in the stomach is absorbed extensively, causing unknown mechanisms of organ damage, and unaltered phosphorus is expelled through the lungs. Phosphine blocks electron transport in cytochrome oxidase non-competitively, leading to cellular hypoxia.⁵

While inhalation was previously the primary cause of AIP poisoning, cases of ingestion have increased in recent years, usually as attempted suicide. AIP poisoning poses a severe challenge to doctors in Pakistan and other Asian countries, where the toxicity of the wheat pill is increasingly known. The current study was planned to analyse the effects of AIP poisoning dosage on arterial blood gas (ABG) and clinical outcomes.

Materials and Methods

The cross-sectional study was conducted at the intensive care unit (ICU) of Mardan Medical Complex (MMC), Mardan, Pakistan, from January 2021 to May 2022. After approval from the institutional ethics review boards of MMC and Bacha Khan Medical College, Pakistan, the sample was raised using convenience sampling technique. Those

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included were patients of either gender who had attempted suicide by ingesting AIP and tested positive for silver nitrate. Those who tested negative for silver nitrate those with missing arterial blood parameters were excluded.

Data was collected after taking informed consent from the participants who were free to opt out of the study at any point.

Arterial blood samples from the patients were collected, and their diagnoses were based on available history at the time of admission to the emergency department, including investigating the caretaker to determine the type of poisoning or the container in which the AIP tablets were found. The number of pills ingested by each patient was estimated by confirming with the patients at the time of admission, with each tablet containing 3g of dosage, including 56.4% AIP and 44.6% ammonium carbonate.⁴ Patients were grouped according to the number of pills ingested: group 1=1 tablet (3g), group 2=2 tablets (6g), group 3=3 tablets (9g), group 4=4 tablets (12g), group 5=5 tablets (15g), and group 6=8 tablets (24g).

Each patient provided arterial blood samples at the time of admission and during hospitalisation for ABG analysis (OPTI CCA-TS2 Blood Gas and Electrolyte Analyser). The clinical outcome data was collected using a questionnaire that included demographic characteristics, such as age, gender, weight, marital status and education status, as well as clinical characteristics, such as Glasgow coma scale (GCS), hyperthermia, systolic blood pressure (SBP), diastolic blood pressure (DBP), respiratory rate, pulse rate, glycaemia levels, shortness of breath, vomiting, arrhythmias, diarrhoea and chest pain as well as treatment data.

Data was analysed using SPSS 26. Data was presented as frequencies and percentages or mean and standard deviation as appropriate. Categorical variables were compared using chi-square test or Fisher exact test, while continuous variables were compared using one-way analysis of variance (ANOVA) to compare the means of multiple variables. $P < 0.05$ was considered statistically significant.

Results

Of the 121 patients assessed, 116(%) were included; 42(36.2%) males and 74(63.8%) females. There were 75(64.65) survivors;

31(41.33) males and 44(58.66) females with overall mean age 26.30 ± 9.45 years. There were 41(35.35%) non-survivors; 11(26.82%) males and 30(73.18) females with overall mean age 28.21 ± 11.16 years. The mean weight of survivor patients was 59.12 ± 10.77 kg and it was 56.75 ± 7.97 kg in non-survivor patients. Of all the patients, 57(49.1%) were single, 48(41.3%) were educated, 48(41.3%) were unemployed and 73(62.9%) had satisfactory socioeconomic status (SES) (Table 1).

AIP dosage and ABG parameters were inversely proportional, and as the dosage increased, the ABG parameters decreased (Table 2).

Table-1: Demographic characteristics of survivors and non-survivors.

Characteristics	Survivor	Non-Survivor	p-value
Patients	75(64.65)	41(35.35)	0.04
Sociodemographic Characteristics			
Mean Age (years)	26.30±9.45	28.21±11.16	0.01
Gender			
Male	31(41.33)	11(26.82)	0.12
Female	44(58.66)	30(73.18)	0.19
Mean Weight (kg)	59.12±10.77	56.75±7.97	0.08
Marital Status			
Single	35(46.66)	22(52.65)	0.39
Married	40(53.33)	19(46.34)	0.47
Education Status			
Educated	36(48.00)	12(29.26)	0.03
Uneducated	39(52.00)	29(70.73)	0.04
Job			
Teenage	06(08.00)	02(04.87)	0.52
On Job	12(16.00)	04(9.78)	0.35
Jobless	26(34.66)	22(53.65)	0.03
Housewife	31(41.33)	13(31.70)	0.29
Economic			
Poor	22(29.33)	15(36.58)	0.59
Satisfactory	47(62.66)	26(63.41)	0.93
Good	06(08.00)	00(00.00)	0.06

Data is presented as frequency and percentage or as mean and standard deviation; p -value < 0.05 is statistically significant.

Table-2: Wheat pill poisoning dosage among survivors and their arterial blood gas (ABG) parameters.

Wheat pill poisoning dosage	1. tablets/3gm	2. tablets/6gm	3. tablets/9gm	> 3 tablets/ > 9gm	p-value
Patients	36(48.00)	27(36.00)	12(16.00)	Nil	0.04
Arterial Blood Gas Parameters During Admission					
PO ₂	73.79±7.08	67.00±6.02	68±5.89	Nil	0.01
PCO ₂	33.00±1.54	30.35±2.8	24.50±0.28	Nil	0.00
HCO ₃	20.68±13.52	18.61±3.00	13.0±5.00	Nil	0.00
O ₂	88.74±2.26	85.12±5.7	83.00±5.88	Nil	0.00
PH	7.36±0.1	7.33±0.03	7.22±0.00	Nil	0.03
Arterial Blood Gas Parameters During Hospitalization					
PO ₂	93.87±4.21	69.75±6.38	75.5±11.83	Nil	0.00
PCO ₂	36.93±1.15	35.71±2.36	35.32±3.11	Nil	0.00
HCO ₃	23.19±0.91	24.87±2.61	23.50±0.86	Nil	0.00
O ₂	94.2±3.01	93.64±1.95	93.47±2.01	Nil	0.00
PH	7.42±0.00	7.39±0.09	7.44±0.03	Nil	0.00

Data is presented as frequency and percentage or as mean and standard deviation; PO₂: Partial pressure of oxygen, PCO₂: Partial pressure of carbon dioxide, HCO₃ Bicarbonate, O₂: Oxygen content, Ph: Power of hydrogen; p -value < 0.05 is statistically significant.

The mean survival ratio for patients who ingested <3 pills was 75(66.6%). Patients who took >3 tablets, or <9g of wheat pills showed substantial differences in all clinical characteristics, and the interventions during hospitalisation were also significantly different between the groups, while clinical and chemical outcomes improved for all survivors who were discharged after receiving intensive care for 7-10 days and appeared to be doing well on follow-up examination a week later (Table 3).

The group ingesting 8 AIP tablets, or 24g, had the lowest ABG parameters, with all non-survivors showing drastically decreased ABG levels at admission and during hospitalisation, while survivors responded favourably to the treatment (Table 4).

Higher AIP dosage meant worse clinical outcomes, while specific indications were also associated with poor outcomes among non-survivor patients (Table 5).

The non-survivors had a mean hospitalisation stay of

Table-3: Wheat pill poisoning dosage among survivors and their clinical outcomes.

Wheat pill poisoning dosage	1. tablets/3gm	2. tablets/6gm	3. tablets/9gm	> 3 tablets/ > 9gm	p-value
Patients	36(48.00)	27(36.00)	12(16.00)	Nil	0.04
Intervention during hospitalization					
Clinical characteristics					
GSC	12.18±2.16	12.15±1.0	9.00±1.15	Nil	0.00
Hyperthermia	36(100)	27(100)	12(100)	Nil	**
Systolic pressure	110.21±11.02	108.13±9.19	102.00±10.61	Nil	0.00
Diastolic pressure	76.44±10.40	72.13±4.00	63.00±5.77	Nil	0.00
R/R	20.11±0.92	20.47±1.34	19.21±0.51	Nil	0.00
P Rate	93.55±17.25	83.12±23.20	74.00±11.54	Nil	0.00
Glycemia	151±19.10	164±10.33	191±26.19	Nil	0.00
Shortness of breath					
None	Nil	Nil	Nil	Nil	**
Mild	11(30.55)	02(7.40)	Nil	Nil	0.00
Moderate	19(52.77)	09(33.33)	04(33.33)	Nil	0.00
Severe	06(16.66)	16(59.25)	08(66.67)	Nil	0.00
Vomiting					
Grade 1	06(16.66)	00(0.00)	2(16.66)	Nil	0.00
Grade 2	29(80.55)	23(85.18)	00(0.00)	Nil	0.00
Grade 3	01(2.77)	04(14.81)	10(83.33)	Nil	0.00
Grade 4	Nil	Nil	Nil	Nil	**
Grade 5	Nil	Nil	Nil	Nil	**
Arrhythmias					
SVT	02(5.55)	11(40.74)	12(100)	Nil	0.04
VT	12(33.33)	14(51.85)	09(75.00)	Nil	0.07
Diarrhoea					
Grade 1	30(83.33)	12(44.44)	00(0.00)	Nil	0.00
Grade 2	04(11.11)	08(29.62)	00(0.00)	Nil	0.00
Grade 3	02(5.55)	07(17.07)	12(100)	Nil	0.00
Grade 4	Nil	Nil	Nil	Nil	**
Grade 5	Nil	Nil	Nil	Nil	**
Chest pain					
Cardiac	06(16.66)	10(37.03)	8(66.66)	Nil	0.03
Possible Cardiac	22(61.11)	11(40.74)	4(33.33)	Nil	0.05
Non Cardiac	08(22.22)	06(22.22)	Nil	Nil	0.09
Treatment Characteristics					
Vasoactive Drugs	12(33.33)	15(55.55)	12(100)	Nil	0.00
Mechanical Ventilation	18(50.00)	22(81.48)	12(100)	Nil	0.00
Gastric Lavage	10(27.77)	24(88.88)	12(100)	Nil	0.00
Glucocorticoids	24(66.66)	26(96.29)	12(100)	Nil	0.00
GI Decontamination	30(83.33)	27(100)	12(100)	Nil	0.02
Herbal Remedies	18(50.00)	27(100)	12(100)	Nil	0.04
Saline	36(100)	27(100)	12(100)	Nil	**

Data is presented as frequency and percentage or as mean and standard deviation; GSC: Glasgow Coma Scale, SVT: Supraventricular tachycardia, VT: Ventricular tachycardia, GI: Gastrointestinal; p-value <0.05 is statistically significant while p value with ** Represent the variables' effect is either present in 100% of the population or in 0% of the population, no difference was calculated between groups.

Table-4: Wheat pill poisoning dosage among non-survivors and their arterial blood gas (ABG) parameters.

Wheat pill poisoning dosage	1. tablets/3gm	2. tablets/6gm	3. tablets/9m	4. tablets/12gm	5. tablets/15gm	8 tablets/24gm	p-value
Patients	7(17.07)	10(24.39)	7(17.07)	9(21.95)	6(14.63)	2(4.87)	0.03
Arterial Blood Gas Parameters During Admission							
PO ₂	55.0±20.20	59.50±24.66	63.50±3.75	63.33±7.62	25.00±0.12	32.00±5.11	0.00
PCO ₂	29.50±0.86	15.47±3.04	22.50±4.28	20.26±2.63	24.32±2.19	22.01±2.41	0.00
HCO ₃	20.95±2.30	11.88±2.7	13.00±0.57	5.80±1.41	7.00±0.23	5.60±1.22	0.00
O ₂	71.00±1.73	72.50±8.1	79.00±2.88	67.66±4.61	61.00±2.00	61.00±0.19	0.00
PH	7.27±0.10	7.23±0.51	7.22±0.21	6.21±0.11	6.12±0.18	6.44±0.09	0.00
Arterial Blood Gas Parameters During Hospitalization							
PO ₂	69.0±2.80	79±5.42	66.51±3.83	61.66±5.33	55.19±2.33	45.21±2.11	0.00
PCO ₂	29.66±4.19	25.37±3.4	28.00±4.31	31.66±3.33	25.41±1.09	24.33±2.00	0.01
HCO ₃	13.33±3.44	14.00±3.67	15.50±0.86	8.22±0.89	8.23±1.22	9.54±1.95	0.00
O ₂	66.19±2.89	74.29±5.91	85.31±2.88	65.66±3.91	62.45±4.33	56.00±1.21	0.00
PH	7.39±0.05	6.22±0.08	6.44±0.00	6.28±0.28	6.00±0.12	6.10±0.11	0.00

Data is presented as frequency and percentage or as mean and standard deviation; (PO₂: Partial pressure of oxygen, PCO₂:Partial pressure of carbon dioxide, HCO₃: Bicarbonate, O₂: Oxygen content: Ph: Power of hydrogen; p-value <0.05 is statistically significant.

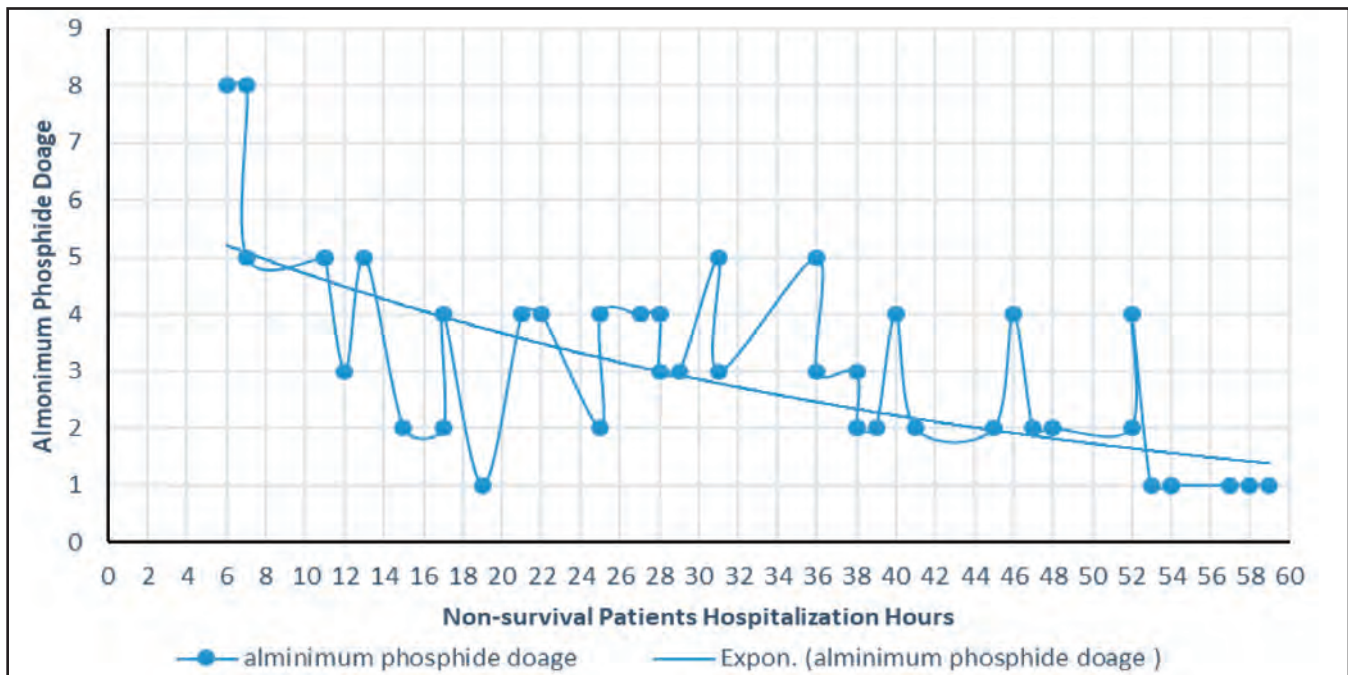


Figure-1: Hospital stay among non-survivors.

32.51±16.02 hours (range: 6-59 hours (Figure 1).

Increasing doses of AIP resulted in changes in ABG parameters, while the clinical outcomes could refer to the overall impact of AIP toxicity on the patient, such as mortality or the need for intensive care (Figure 2).

Discussion

To the best of our knowledge, the current study is the first study to examine how different doses of AIP, a poisonous substance commonly used as a wheat preservative, affect ABG levels and clinical outcomes. In the existing literature, there is a lack of data on the effects of AIP poisoning on ABGs and clinical outcomes. Rehab et al. concluded that

power of hydrogen (pH) <7.27 and bicarbonate (HCO₃) <13.3 were the best cut-off points for predicting mortality in poisoned patients.⁶ Shadnia et al. discovered a statistically significant difference in blood pH and HCO₃ between people who died from acute AIP poisoning and those who survived.⁷ The current results were comparable. Chugh SN et al. reported cases of acute respiratory distress syndrome (ARDS) in patients who had ingested doses ranging from 2 tablets (6g) to 3 tablets (9g) of AIP.⁸ Non-survivors of AIP poisoning had more severe clinical and chemical manifestations of respiratory distress, such as higher respiratory rates, shortness of breath, and lower ABG parameters, as per the current findings. A dose-dependent

Table-5:Wheat pill poisoning dosage among non-survivors and their clinical outcomes.

Wheat pill poisoning dosage	1. tablets/3gm	2. tablets/6gm	3. tablets/9m	4. tablets/12gm	5. tablets/15gm	8 tablets/24gm	p-value
Patients	7(17.07)	10(24.39)	7(17.07)	9(21.95)	6(14.63)	2(4.87)	0.03
Intervention during hospitalization							
GSC	12.25±1.03	9.0±3.46	8.41±1.26	7.33±2.88	7.03±0.19	6.00±0.23	0.00
Hyperthermia	07(100)	10(100)	07(100)	09(100)	6(100)	2(100)	**
Systolic pressure	105.49±5.21	104.63±4.97	94.25±3.54	90.36±6.21	89.29±5.97	89.74±1.11	0.03
Diastolic pressure	65.31±5.02	60.27±4.91	58.09±3.96	51.22±4.59	51.36±3.96	51.69±1.29	0.00
R/R	19.67±6.16	20.19±5.95	19.34±4.51	24.69±5.31	28.72±5.61	24.56±0.96	0.00
P Rate	98.34±8.94	98.21±5.56	103±8.32	105±8.91	104±9.38	106±2.01	0.00
Glycemia	144±15.33	171±10.69	162±9.3	190±29.61	190±20.33	192±3.61	0.00
SOB							
None	Nil	Nil	Nil	Nil	Nil	Nil	**
Mild	01(14.28)	Nil	Nil	Nil	Nil	Nil	0.41
Moderate	01(14.28)	03(30.00)	01(14.28)	02(22.22)	Nil	Nil	0.21
Severe	05(71.42)	07(70.00)	06(85.71)	07(77.78)	06(100)	02(100)	0.00
Vomiting							
Grade 1	Nil	Nil	Nil	Nil	Nil	Nil	**
Grade 2	Nil	Nil	Nil	Nil	Nil	Nil	**
Grade 3	01(14.28)	Nil	Nil	Nil	Nil	Nil	0.32
Grade 4	05(71.42)	07(70.00)	01(14.28)	Nil	01(16.66)	Nil	0.00
Grade 5	01(14.28)	03(30.00)	06(85.71)	9(100)	05(83.33)	2(100)	0.00
Arrhythmias							
SVT	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
VT	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
Diarrhoea							
Grade 1	Nil	Nil	Nil	Nil	Nil	Nil	**
Grade 2	Nil	Nil	Nil	Nil	Nil	Nil	**
Grade 3	Nil	Nil	Nil	Nil	Nil	Nil	**
Grade 4	03(42.85)	4(40.00)	Nil	Nil	Nil	Nil	0.04
Grade 5	04(57.14)	6(60.00)	7(100)	09(75.00)	6(100)	2(100)	0.02
Chest pain							
Cardiac	6(85.71)	8(80.00)	7(100)	07(77.78)	6(100)	2(100)	0.02
Possible Cardiac	1(14.28)	02(20.00)	Nil	02(22.22)	Nil	Nil	0.87
Non Cardiac	Nil	Nil	Nil	Nil	Nil	Nil	**
Treatment characteristics							
Vasoactive Drugs	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
Mechanical Ventilation	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
Gastric Lavage	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
Glucocorticoids	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
GI Decontamination	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
Herbal Remedies	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**
Saline	07(100)	10(100)	07(100)	09(100)	06(100)	02(100)	**

Data is presented as frequency and percentage or as mean and standard deviation; GSC: Glasgow Coma Scale, SVT: Supraventricular tachycardia, VT: Ventricular tachycardia, SOB: Shortness of breath, GI: Gastrointestinal; p-value <0.05 is statistically significant while p value with ** Represent the variables' effect is either present in 100% of the population or in 0% of the population, no difference was calculated between groups.

decrease in ABG parameters was also observed with increasing doses of AIP poisoning, ranging from 1 to 8 tablets, or 3 to 24g.

A study reported high mortality rate of 55-90%,⁹ while another study reported it to be 33%.¹⁰ In the current study, the mortality rate was 35.3%.

Several factors were discovered during detailed clinical examination which were prognostic factors for AIP poisoning, including lower GCS score, abnormal

electrocardiogram, high-grade diarrhoea, shortness of breath, severe vomiting, chest pain, and the use of treatments, such as vasoactive drugs, mechanical ventilation, glucocorticoids, gastric lavage, gastrointestinal (GI) decontamination, and herbal remedies, such as coconut oil etc. A previous study only reported low GCS score, shock, electrocardiogram abnormalities, vasoactive drugs, and mechanical ventilation in this regard.¹¹ Eizadi-Mood N et al. discovered that patients with low GCS were more likely to develop complications, such as aspiration

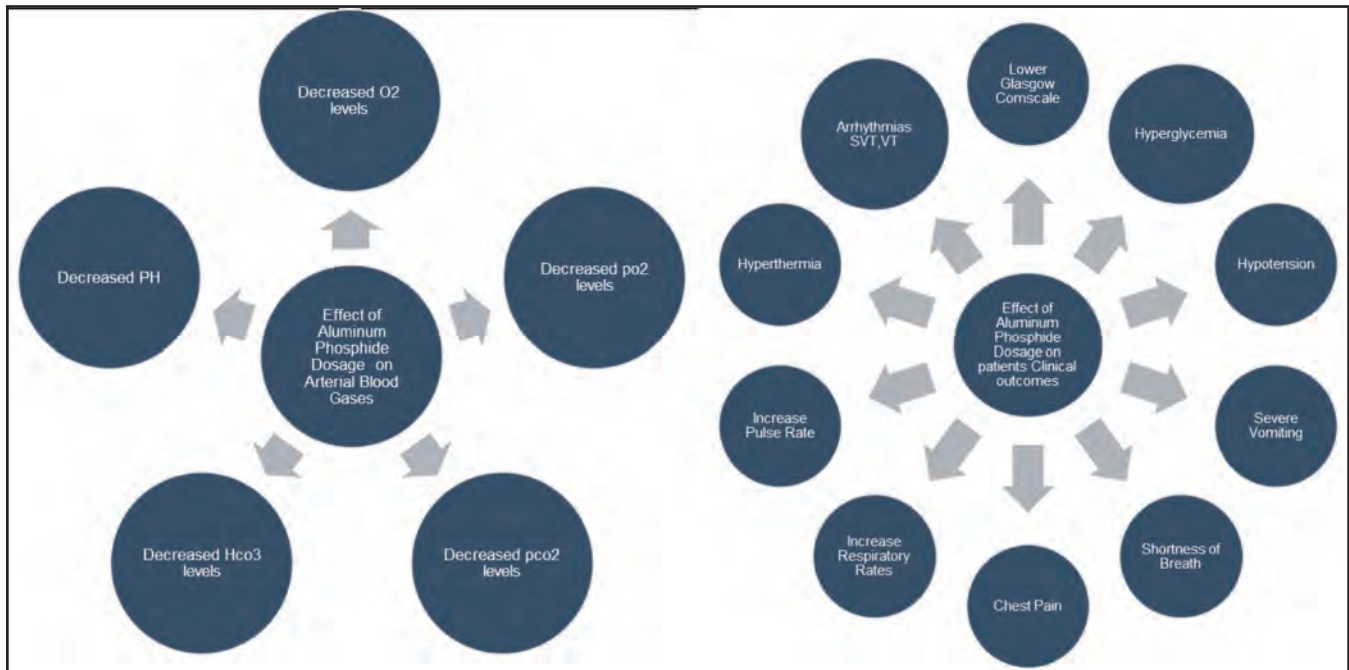


Figure-2: Summary diagram (left) showing the relationship between aluminum phosphide dosage and arterial blood gas (ABG) parameters, and the relationship (right) between aluminum phosphide dosage and clinical outcomes.

pneumonia, due to a lack of airway reflexes.¹² Because the GCS is a scoring system that has been shown to assess brain functions and predict the outcomes of nervous system integrity,¹³ physicians should consider the levels of consciousness of poisoned patients and carefully document their medical history.

Mehrpour et al. discovered that patients poisoned with AIP had significantly higher mean blood glucose levels than those with lower levels.³ This suggests that measuring blood glucose levels could aid in risk assessment and treating AIP poisoning. Management of hyperglycaemia may be beneficial by increasing glucose entry into cells and decreasing oxygen consumption. The current study found that hypoxaemia and hyperglycaemia levels were significantly higher in non-survivor patients than in survivors and related to the AIP dosage.

Multiple studies have reported that hypotension occurs in 76% to 100% of cases of AIP poisoning.⁸ Certain factors, such as blood pressure and heart rate, were significantly different between people who died from AIP poisoning and those who survived after ingestion of AIP tablets in a study¹⁴ and the current findings were consistent with literature.

The time of death in the current study was associated with the AIP dosage, with most deaths occurring between 8 and 59 hours after hospitalisation which was consistent with a previous study.¹⁴

The current study has some limitations, as it was carried out at a single centre, and the time between AIP ingestion and hospitalisation was not measured.

Conclusion

The effect of AIP dosage was found to be inversely proportional to ABG parameters. Because there is no specific antidote or treatment for AIP poisoning, supportive care is essential for slowing the progression of the illness to improve the patient's chances of survival. For hospitalised patients with AIP poisoning, monitoring of ABG parameters and their clinical outcomes is critical, particularly for those who ingest >3 AIP pills.

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Conflict of Interest: None.

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