

“PGI Score”: A Simplified Three-point Prognostic Score for Acute Aluminum Phosphide Poisoning

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ABSTRACT

Introduction: Aluminum phosphide (AIP) ingestion for self-harm is associated with a high case-fatality rate (CFR) in low- and middle-income countries. A reliable and accurate prognostic scoring tool is required for appropriate triaging, to guide clinical decision-making, and to evaluate the efficacy of therapeutic interventions for the patients with AIP toxicity.

Materials and methods: We performed a prospective cohort study in a tertiary care hospital in north India in patients aged 15 years and over with acute AIP poisoning, investigating the parameters associated with CFR, and developing a reliable and simple prediction score.

Results: The CFR was 51% in this cohort of 105 patients. Three parameters—pH <7.25, score on Glasgow coma scale (GCS) <13, and systolic blood pressure (SBP) <87 mm Hg were most robust predictors of CFR (odds ratio; 12.614, 18.621, and 17.600, respectively; area under the receiver operating characteristic curve—0.808, 0.796, and 0.776, respectively). Based on these parameters (with 1 point to each), a prognostic score was developed, ranging from 0 to 3 points. A total score of 3 had a 98.2% specificity and a positive predictive value of 96.4%, whereas a score ≤1 had a 100% sensitivity and 100% negative predictive value.

Conclusion: A scoring system based on low pH (P), low GCS score (G), and impaired or low SBP (I) (“PGI” score) may provide a simplified predictive model for mortality in AIP poisoning.

Keywords: Aluminum phosphide, Case-fatality rate, Grain fumigants, Mortality, Pesticide poisoning, Prognostic tool, Scoring system, Severity. *Indian Journal of Critical Care Medicine* (2020); 10.5005/jp-journals-10071-23555

INTRODUCTION

Pesticides are preferred agents of self-harm in low- and middle-income countries (LMIC) because of the ease of availability and low cost.^{1,2} Organophosphate poisoning is the most prevalent cause, but the availability of antidotes and adequate supportive treatment have reduced the case-fatality rate (CFR). Aluminum phosphide (AIP) is one of the most extensively used metal phosphides to protect stored products and crops but is severely toxic to both humans and animals. The rapidity of mitochondrial dysfunction following exposure to phosphine and non-availability of an effective antidote is responsible for very high CFR.^{1–12} Cardiac myocytes are earliest to be affected by cellular hypoxia. Thus, refractory hypotension and cardiac arrhythmias are responsible for the majority of early deaths.^{4,7,13}

Prognostic scoring tools for acute AIP poisoning are required for appropriate triaging of the patients, guide clinical decision-making, and evaluate therapeutic interventions’ efficacy. In the absence of a universally acceptable severity tool, it is challenging to compare most studies, including intervention trials. Most of the studies have used the other established scoring systems, e.g., Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score, the Sequential Organ Failure Assessment (SOFA) score, and the Simplified Acute Physiology Score (SAPS) to grade or evaluate the severity of this poisoning.^{14–16} Because these scoring systems have been developed to address the issue of multiorgan dysfunction in critically ill patients and have not been explicitly developed for poisoned patients, their use in assessing severity could be questioned.

Various studies have looked at numerous demographic, physiological, and biochemical parameters to access the severity of AIP poisoning; however, none of these factors, either alone or in combination, have been validated.^{10,11,14–20} A simplified prognostic or severity scoring system, preferably clinical, is the need of the

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hour. In this study, we have looked at various predictors of CFR and sought to develop a precise and simple outcome prediction score for acute AIP poisoning.

MATERIALS AND METHODS

Study Design and Setting

This prospective cohort study was conducted in the medical emergency of the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, during a study period of 18 months. Approval of the study by the Institutional Ethics Committee was obtained. Written informed consent was taken in all the study cases.

Participants

The patients aged above 15 years admitted with a history of consumption of AIP, presence of features of the toxidrome, such as metabolic acidosis and hypotension, and a confirmed silver nitrate breath test. The patients, who had the poisoning with

an unknown compound, or more than one compounds were excluded. Hemodynamic parameters, i.e., systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), and central venous pressure, score on the Glasgow coma scale (GCS), and basic routine investigations (including blood sugar, electrocardiogram, blood gas analysis, renal function tests, and serum bilirubin), were recorded at admission and 6-hourly intervals till death or discharge from the hospital. We defined hypotension as SBP of <90 mm Hg and tachycardia as HR of >100 beats/minute. Scores on the GCS range from 3 (worst) to 15 (best), with 13 or higher indicating only mild cerebral dysfunction. On blood gas analysis, a pH <7.35 with low bicarbonate value (normal range; 22–28 mEq/L) was used to define metabolic acidosis.

All the patients received gastric lavage at admission with potassium permanganate, intravenous vasopressor support for circulatory failure, sodium bicarbonate for metabolic acidosis, and intravenous magnesium sulfate as per standard protocol followed in the institute. The patients were admitted to an emergency observation unit or a high-dependency unit and were followed till discharge from hospital or death. The outcome was expressed as in-hospital CFR.

Statistical Analysis

Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) was used for data analysis. Categorical variables (e.g., CFR) were described as frequency (percentage) and continuous variables (e.g., SBP, DBP, and HR) as mean \pm standard deviation (SD). The student's *t*-test was used to compare continuous variables between the groups, and the Chi-square test analyzed categorical data. The associations of demographic, physiological, and biochemical parameters with the CFR were analyzed by univariate analysis. The variables with a two-sided *p* value of <0.05 (i.e., statistically significant) on univariate analysis were included in the multivariable logistic regression model to determine the independent predictors with the calculation of adjusted odds ratio (OR). The area under the receiver operator characteristic (AUROC) curve was calculated for the variables with the most robust relationship to CFR, subsequently used to develop an objectively weighted multivariate prognostic scoring tool. The scoring tool performance was evaluated by comparing sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy.

RESULTS

Study Patients and Baseline Characteristics

A total of 115 patients were enrolled during the study period, of which 10 were excluded as complete data were not available. Out of the 105 patients available for final analysis, 62% were males, and 90.6% were in the age group of 15–45 years. About three-fourth patients (74.2%) reached the hospital within 6 hours of ingestion, and the mean interval between ingestion and reporting to the hospital was 3.6 hours. The mean dose of AIP consumed was 3.6 g. 78.4% of the cases took the tablet form (3 g) of poison, 12.1% consumed powder or sachet form (10 g), and the nature of poisoning remained unknown in 9.5%.

The most common symptom was vomiting (99.1%), followed by pain in the upper abdomen (61%), and shortness of breath (35%). Tachycardia (74.1%) and hypotension (69.0%) were the most typical signs. An abnormal level of consciousness with a GCS score of 10 or less was seen in 22.4% of patients. Metabolic acidosis was detected in 90.5% of cases with severe acidosis (pH <7.0) in 14.6% cases.

Predictive Factors for Mortality

The CFR was 51% in our study. Baseline clinical and laboratory data on admission were analyzed to determine which variables were associated with mortality. Low SBP, increased HR, low GCS score, elevated values of blood sugar, creatinine, and total leukocyte count, and reduced blood pH and bicarbonate levels showed statistical significance on univariate analysis (Table 1). Subsequently, after multivariate analysis, the most robust predictors of CFR were blood pH <7.25, GCS score <13, and SBP <87 mm Hg (Table 2).

Each of the three predictors was given a score value of 1. Among study patients with a total score of 3, 96.4% died, compared with 39% in score 2, 15% in score 1, and 0% in score 0. A total score of 3 had a 98.2% specificity and a PPV of 96.4%, whereas a score \leq 1 had a 100% sensitivity and 100% NPV (Table 3). A score of 2 had a 93.2% sensitivity, 76.8% specificity, and 84.8% diagnostic accuracy for the prediction of mortality.

DISCUSSION

Prognostic stratification of patients with acute AIP poisoning is needed to gauge the performance of emergency and intensive care units and improve the delineation of subsets for clinical trials. In the present study, we observed that the essential parameters correlated with CFR were metabolic acidosis, shock, and a low score on GCS.

Singh et al., in 1996, demonstrated that the dose ingested, the number of vomits, the severity of hypotension, and the metabolic acidosis were associated with worse outcome in AIP poisoning.¹⁷ However, in an acute ingestion setup, dose ingested and the number of vomiting may not be reliably reported. The accurate and reproducible predictors of severity and outcomes are clinical and biochemical parameters of impaired circulation (low blood pressure, altered mental status, and decreased urine output) and metabolic acidosis (blood pH and serum bicarbonate level). Louriz et al. reported that the CFR correlated with shock (SBP <90 mm Hg) and altered mental status (GCS <14).¹⁰ One hundred percent CFR with blood pH <7.0 and 100% survival with pH >7.35 was observed by Shadnia et al.¹¹ Navabi et al. also demonstrated blood pressure, pH as well as the time interval between ingestion and treatment as significant predictors.²⁰ Low SBP, metabolic acidosis, and electrocardiographic abnormality were associated with poor outcome in a retrospective study from Egypt.¹⁹ In another Egyptian study from a university hospital, Sheta et al. studied the role of echocardiography for predicting the mortality which can detect low ejection fraction resulted from cardiac ischemia and decreased myocardial contractility in AIP poisoning.¹⁶ However, echocardiography is not readily available in the majority of emergency rooms in LMIC.

We formulated a prognostic scoring system based on the three most important prognostic factors identified in our study — pH, GCS, and SBP, which were also confirmed in prior studies. Given the small sample size, it was challenging to determine the exact mathematical score for different variables; therefore, each parameter was given similar importance and was assigned a point value of 1, which would result in a maximum score of 3 and a minimum of 0. This three-point prognostic scoring system showed a very high NPV with low scores (\leq 1) and a very high PPV for a score of 3. The prognostic system comprises two easily identifiable and readily reproducible clinical parameters (SBP and GCS) and one lab parameter (pH) readily available in the majority of the tertiary care centers at a reasonable cost. Thus, this simple and precise model would provide great prognostic information to emergency

Table 1: Univariate analysis for predictive factors of mortality in acute aluminum phosphide poisoning ($n = 105$)

Parameters	Survived (mean \pm SD)	Died (mean \pm SD)	<i>p</i> value
Age (years)	28.0 \pm 8.9	29.6 \pm 11.3	0.283
Interval between ingestion and hospitalization (hours)	6.1 \pm 7.4	8.6 \pm 22.0	0.952
Systolic blood pressure (mm Hg)	106.0 \pm 28.9	77.0 \pm 20.4	<0.001
Heart rate (beats/min)	101.0 \pm 15.1	109.0 \pm 12.1	<0.001
Central venous pressure (cmH ₂ O)	14.5 \pm 4.2	19.3 \pm 6.2	0.393
Score on Glasgow coma scale	12.9 \pm 0.13	2.3 \pm 0.75	<0.001
Blood sugar (mg/dL)	119.9 \pm 35.7	159.7 \pm 92.5	<0.001
Serum sodium (mg/dL)	142.5 \pm 7.0	144.6 \pm 7.4	0.058
Serum potassium (mg/dL)	4.0 \pm 0.7	4.1 \pm 1.1	0.216
Serum creatinine (mg/dL)	0.8 \pm 1.0	1.4 \pm 1.2	0.003
Total leukocyte count (per μ L)	8592 \pm 3464	12223 \pm 5101	0.005
Blood pH	7.29 \pm 0.73	7.10 \pm 1.3	<0.001
Serum bicarbonate (mEq/L)	16.3 \pm 4.8	11.3 \pm 5.6	<0.001

Note: bold values are statistically significant

Table 2: The independent predictors with the strongest relationship to mortality with their odds ratio (OR) and area under receiver operating characteristic (AUROC) curve, sensitivity, and specificity

Parameters	OR	AUROC	Sensitivity (%)	Specificity (%)
Blood pH <7.25	12.614	0.808	71	91
Score on Glasgow coma scale <13	18.621	0.796	94	64
Systolic blood pressure (mm Hg) <87	17.600	0.776	81	84

Table 3: Measures of the accuracy of "PGI" score for predicting mortality in aluminum phosphide poisoning

Total score	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Diagnostic accuracy (%)
≤ 1	100	46.4	62.0	100	71.4
2	93.9	76.8	78.0	93.5	84.8
3	55.1	98.2	96.4	71.4	78.1

physicians and intensivists for triaging and clinical decision-making in real time. The score can also be useful for immediately commencing the emerging novel interventions with improved survival (e.g., glucose–insulin–potassium infusion, extracorporeal membrane oxygenation) in high-risk patients from resource-limited countries.^{12,21}

Recently, Farzaneh et al. proposed a risk prediction nomogram approach based on a group of similar clinical and biochemical variables, i.e., SBP, GCS score, bicarbonate level, and urine output.²² However, the relatively larger sample size in our study allows for greater accuracy in determining the relative importance of mortality parameters.

We propose the name "PGI score" for this prognostic scoring system where "P" stands for pH, "G" for GCS score, and "I" for impaired or low SBP ("PGI" also represents the short form of the name of our institute PGIMER, Chandigarh, India).

STRENGTHS AND LIMITATIONS

A prospective study, reasonable sample size, analysis of different demographic, physiological, and biochemical parameters, and specific cut-off values for individual prognostic parameters are the strengths of our study. "PGI score" has the advantage of variables that are readily and immediately available on admission and potentially an excellent predictive ability.

A single-center observation limits the generalizability of our results. The proposed prognostic system also needs to be validated in a large multicenter study and to be compared with other established scoring systems. A prospective study to validate this scoring tool and comparing it to SAPS and SOFA score is currently underway at our center.

CONCLUSION

Our study results show that pH <7.25, GCS score <13, and SBP <87 mm Hg are essential predictors of CFR in acute AIP poisoning. Based on these parameters, a three-point scoring system ("PGI" score) could be a simple and clinically sensible prognostic model in these patients, most relevant to the emergency setting.

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