

# Comparative Study of Management of Aluminium Phosphide Poisoning - Our Experience

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## ABSTRACT

### BACKGROUND

We wanted to do a retrospective study of the distribution pattern, outcome with possible predictors affecting the mortality in patients who had consumed aluminium phosphide and were admitted in our ICU and compare difference in mortality among the two different regimens used during two different time frames.

### METHODS

63 patients who were admitted to the ICU between Jan 2011 to Dec 2017 after consumption of aluminium phosphide were studied. Baseline clinical assessment and routine investigations including complete blood counts, renal function tests, electrolytes, ECG, ABG and 2D Echo were done. For the first 4 years from 2011 - 2014, a standard regimen based mainly on supportive care was followed. For the remaining 3 years from 2015 - 2017, an aggressive regimen involving coconut oil, ascorbic acid, magnesium, NaHCO<sub>3</sub> and supportive measures were followed.

### RESULTS

Out of the 63 patients admitted during the study period, 16 patients died, and the remaining 47 patients survived. Serum lactate, MAP (Mean Arterial Pressure) at admission, MAP after 24 hours, and presence of arrhythmias were found to be significantly associated with both need for ventilatory support and mortality. The time elapsed since consumption of compound was not found to be associated with either mortality or the need for ventilatory support. On subgroup analysis of two different regimens followed, one with only supportive measures and the other with coconut oil, ascorbic acid, magnesium and sodium bicarbonate, it was found that there was no significant difference with either of the regimens with respect to mortality or need for ventilatory support. ( $p > 0.05$ )

### CONCLUSIONS

The overall treatment in these cases is highly favourable as the mortality is 25.39% compared to the 40 - 80% mortality reported in literature. Serum lactate, Mean Arterial Pressure (MAP) at admission, MAP after 24 hours and presence of arrhythmias on admission were found to be significantly associated with mortality though none of them were found to predict mortality independently. Coconut oil-based regimens are very popular in the management of aluminium phosphide poisoning. However, in our study it didn't show any added advantage in terms of either ventilatory requirement or mortality difference over conventional supportive measures.

### KEYWORDS

Aluminium Phosphide Toxicity, Poisoning, Phosgene, Coconut Oil

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**BACKGROUND**

Aluminum phosphide (ALP) is a cheap, effective and commonly used pesticide. However, unfortunately it is also one of the most commonly used compounds as a cause of suicide among agricultural workers and labourers.<sup>1</sup> It liberates a lethal gas, phosphine (PH<sub>3</sub>) when it comes into contact either with atmospheric moisture or with hydrochloric acid in the stomach. The mechanism of toxicity of phosphine is by inhibition of cytochrome c oxidase and other enzymes leading to the generation superoxide radicals and cellular peroxides. Cellular injury subsequently occurs through lipid peroxidation and other oxidant mechanisms.<sup>2</sup> The toxicity of ALP particularly affects the cardiac and vascular tissues, manifesting as profound and refractory hypotension and shock. Severe arrhythmias and renal failure is common. Death is usually due to profound shock, associated acidosis or severe arrhythmias.<sup>3</sup>

**METHODS**

63 patients who were admitted to the ICU between Jan 2011 to Dec 2017 after consumption of Aluminium Phosphide were studied. Baseline clinical assessment and investigations including complete blood counts, random blood sugar, renal function tests, ECG, ABG and 2D Echo were done. For the first 4 years from 2011-2014, a standard regimen based mainly on supportive care was followed. For the remaining 3 years from 2015-2017, an aggressive regimen involving coconut oil, ascorbic acid, magnesium, sodium bicarbonate (NaHCO<sub>3</sub>) and supportive measures were followed.

**Regimen 1- Standard Regimen - Mainly Supportive**

- IV fluid boluses.
- Injection Pantoprazole 40 mg IV OD
- Injection Ondansetron 4 mg IV TID
- Injection Noradrenaline as when required when MAP <65 mmHg
- Injection Sodium Bicarbonate as and when required when base excess is less than 3 or blood Ph<7.15
- Injection Magnesium Sulphate 2 gm IV BD if serum magnesium is less than 2 mmol/l

**Regimen 2- Aggressive Regimen with Coconut Oil, Ascorbic Acid, Magnesium and Sodium Bicarbonate**

- IV fluid boluses
- Coconut oil 30 mL TID for 24 hours.
- Injection Magnesium Sulphate 5 gm IV BD
- Injection Vitamin C 100 mg IV TID
- Injection Sodium Bicarbonate infusion 5 mL per Hour
- Injection Pantoprazole 40 mg IV OD
- Injection Ondansetron 4 mg IV TID
- Injection Noradrenaline as when required

**Statistical Analysis**

Software R version 3.1.2 was used for statistical analysis. Parameters significant on univariate analysis (P<0.05) were identified as potential predictors of mortality and were further evaluated using multivariate logistic regression analysis, with the clinical outcome as the dependent variable. Cross tab analysis was done to compare the two regimens with both mortality or need for ventilatory support as dependent variables.

**RESULTS**

Age Group (Years)	Frequency	%
Less than or = 20	11	17.46
21-30	34	53.97
31-40	13	20.63
41-50	4	6.35
51-60	1	1.59
>65	0	0
Total	63	100

**Table 1. Age Wise Distribution of Patients**

Distribution	Number	Percentage
Total no. of Patients	63	--
Male	31	49.20
Female	32	51.80

**Table 2. Distribution of Patients According to Sex**

As can be seen from the tables above, the incidence of deliberate self-harm due to aluminium phosphide consumption is more prevalent in the Socio-economically most productive age group of 20-30 yrs. and there were no gender specific variations.

Variable	Alive	Dead	t-Value	p- Value
Presence of Arrhythmia	2	15	X <sub>2</sub> Value = 40.18	0.0001**
MAP at the time of Admission	88.41	49.29	t- value = 4.9149	0.0001**
MAP after 2 hrs.	83.39	29.76	t- value = 5.3083	0.0001**
S – lactate	2.73	9.45	t- value=4.58	0.0001**
Time elapsed since consumption	4.75	5.27	t- value = 0.5208	0.6058

**Table 3. Univariate Analysis for Mortality**

Out of the 63 patients admitted during the study period 16 patients died and remaining the 47 patients survived. Serum lactate, Mean Arterial Pressure (MAP) at admission, MAP after 24 hours and the presence of arrhythmias were found to be significantly associated with mortality. (p<0.05) The time elapsed since consumption of the compound was not found to be associated with mortality.

Variable	Odds Ratio	95% CI	p- Value
MAP on admission	1.040	0.842 -1.285	0.717
MAP after 24 hours	0.907	0.676-1.216	0.515
S-Lactate	3.041	0.111-80.662	0.511
Presence of Arrhythmia	0.001		0.998

**Table 4. Multiple Logistic Regression Analysis**

However, when these four variables namely the serum lactate level, MAP at admission, MAP after 24 hours and the presence of arrhythmia were analysed further using the multiple logistic regression analysis, none of them were found to predict mortality independently.

	Regimen 1		Regimen 2		X <sub>2</sub> - Value	p- Value
	Yes	No	Yes	No		
Ventilator	12	23	6	19	0.1343	0.714
Mortality	10	28	6	19	0	1

**Table 5. Cross Tab Analysis**

On subgroup analysis of the two different regimens followed- regimen 1 only with supportive measures and regimen 2 with coconut oil, ascorbic acid, magnesium and sodium bicarbonate along with supportive measures, it was found that there was no significant difference in either the need for ventilatory support or mortality with either of the regimens ( $p > 0.05$ ).

## DISCUSSION

Traditionally the management of aluminium phosphide poisoning has been largely considered unsatisfactory since it doesn't have any specific antidote and the care remains primarily supportive.<sup>4</sup> The mortality due to such cases ranges from 45-80% as described in the literature.<sup>2</sup> The major determinant of success remains the treatment of shock. Aggressive intravenous fluid boluses, vasopressors and acidosis correction is invariably required. Multiple modalities like dialysis, CRRT and intra-aortic balloon pump (IABP) have been tried with mixed benefits.<sup>4,5,6</sup> Coconut oil-based regimens have gained popularity recently. The proposed mechanism by which coconut oil reduces the toxicity of phosphides is by the formation of a protective layer around the gastric mucosa, thereby preventing the absorption of phosphine gas. Secondly, it helps in diluting the hydrochloric acid (HCl) and inhibits the breakdown of phosphide from the pellet. Coconut oil should be given as early as possible after ALP ingestion.<sup>4</sup> Sodium-bicarbonate mainly neutralizes the hydrochloric acid (HCl) and thus diminishes the catalytic reaction of phosphide with (HCl), thereby inhibiting the release of phosphine. Sodium bicarbonate has also been hypothesized to correct the acidosis and thereby minimize the shock and also decrease the vasopressors or inotrope requirements.<sup>7</sup>

Magnesium ions help in scavenging free radicals through glutathione (GSH) recovery hence is effective as parenteral antioxidant in this poisoning. Magnesium is anti-hypoxic and is a membrane stabilizer which can reverse arrhythmias and hence is an anti-arrhythmic agent as well. Hence due to all its beneficial effects, it is considered effective in reducing the mortality in aluminium phosphide poisoning and has been consistently used in many earlier studies. Further magnesium levels are found to be consistently decreased in ALP poisoning, thus supporting the hypothesis that improving magnesium level can be regarded as a step towards treatment of ALP poisoning.<sup>8</sup> Consistent with this hypothesis, it was suggested that hypomagnesaemia might be the major cause of high mortality in ALP-intoxicated patients and its rectification is lifesaving.<sup>8</sup>

Vitamin C is said to benefit by restoring the oxidative phosphorylation system and also mitigate the cellular

hypoxia which might have been caused by phosphine gas. Therapeutic interventions for these patients are based on the recovery of oxidative phosphorylation system. Further occasionally aluminium phosphide poisoning is also associated with instances of methemoglobinemia and haemolysis which responds best to methylene blue and ascorbic acid (Vitamin C). Therefore, the administration of vitamin C (Vit. C) may have beneficial effects and decrease the fatality rate of ALP intoxication and has been tried by many investigators before.<sup>5,9</sup>

A study comparing the benefits of all these drugs with standard measures alone have not been attempted so far although there have been innumerable anecdotal case reports or case series claiming benefit with each of these modalities.<sup>2,4,10</sup> This study has been a retrospective study comparing the effects of an aggressive regimen based on coconut oil, ascorbic acid, magnesium, sodium bicarbonate and standard supportive measures alone. In our study we couldn't find any beneficial effect of the regimen over standard supportive measures in contrast to some of the earlier case series or anecdotal reports.<sup>4,11</sup>

Serum lactate has consistently been found to be associated with poor outcome and increased mortality in many earlier studies and the same has been noted in our study as well.<sup>12,13,14</sup> Similarly mean arterial pressure or systolic pressure on admission was associated with mortality in many earlier studies similar to our findings. However presence of arrhythmia has seen the most consistent correlation with mortality in the majority of the earlier published studies.<sup>15,16,17</sup> Presence of arrhythmias was significantly associated with mortality in our study as well. However on multiple logistic regression analysis none of these variables were found to predict mortality independently. Interestingly the time elapsed since consumption of the compound was also not found to be associated with mortality in our study. Some other variables which were analysed by earlier investigators like serum Creatinine, organ failure scoring systems like APACHE II or SOFA scores were not considered in our study.<sup>2,13</sup>

## CONCLUSIONS

The overall treatment in these cases is highly favorable as the mortality is 25.39% compared to the 40 - 80% mortality reported in literature<sup>2</sup>. Though the time elapsed since consumption of the compound is said to be an important determinant of mortality, it was not found to be significantly associated with mortality in our study. Serum lactate, MAP at admission, MAP after 24 hours and presence of arrhythmias on admission were found to be significantly associated with mortality; however, on logistic regression analysis none of them were found to predict mortality independently. Coconut oil based regimens are very popular in the management of aluminum phosphide poisoning. However, in our study, it didn't show any added advantage in terms of either ventilatory requirement or mortality difference over conventional supportive measures. Further

studies with large sample size may be required for a definitive conclusion.

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