PROFILE OF ALUMINIUM PHOSPHIDE POISONING PATIENTS ATTENDING A TERTIARY CARE CENTER IN KUMAON REGION OF UTTARAKHAND WITH SPECIAL REFERENCE TO THE ROLE OF N-ACETYL CYSTEINE IN OUTCOME OF PATIENTS

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Abstract:

Background: Aluminium Phosphide is used as a pesticide in developed nations and found in tablet form, often known as rice tablets. The present study was conducted to study the profile of aluminium phosphide poisoning patients.

Methods: A total of 70 patients presenting with aluminium phosphide poisoned admitted to the hospital were enrolled.

Results: The mean amount of Aluminium Phosphide consumed by the study population (N=70) is 5.7 grams, with a standard deviation of 2.6 grams. Hypotension was prevalent (65.7%), while ECG abnormalities such as ST depression (4%), QRS widening (3%) and ST elevation (6%) were observed. Biochemical markers like elevated CPK and CK-MB indicated toxicity and the potential role of antioxidant like NAC in preventing ALP induced cardiotoxicity and its effect on biochemical, clinical and hemodynamic parameters were assessed.

Conclusion: These findings emphasize the critical need for early intervention and supportive care in Aluminium Phosphide poisoning cases.

Keywords: Aluminium Phosphide, ECG abnormalities, N-acetyl cysteine

Introduction:

Aluminium Phosphide poisoning presents a formidable challenge to healthcare providers worldwide due to its high mortality rate and limited treatment options. Aluminium Phosphide is extensively utilized as a pesticide in developed nations. Instances of suicide involving Aluminium Phosphide are increasing, notably in developing countries such as India, Sri Lanka, and Iran.[1,2,3]Aluminium Phosphide is commonly found in tablet form, often known as rice tablets, containing 56%Aluminium Phosphide. Upon contact with water or stomach acids, it emits hydrogen phosphine gas (PH3).[4,5]Diagnosis typically relies on clinical suspicion or history, but a straightforward silver nitrate test on gastric content or breath can confirm Aluminium Phosphide exposure.There is no specific antidote for Aluminium Phosphide poisoning, and treatment primarily involves supportive measures.In recent years, N-acetyl cysteine, a potent antioxidant and precursor of glutathione, has emerged as a promising adjunctive therapy in the management of Aluminum Phosphide poisoning. Thus, the present study was conducted to study the profile of aluminium phosphide poisoning patients attending a tertiary care centre in kumaon region of Uttarakhand with special reference to the role of n-acetyl cysteine in outcome of patients.

Materials and Methods:

The present study was an observational, prospective, institution based, single centre study conducted in Government medical college and associated Dr.Susheela Tiwari Hospital,Haldwani. A total of 70 patients presenting with aluminium phosphide poisoned admitted to the hospital were enrolled. An informed consent was obtained from alert patients or their first-degree families or relatives before commencement of the study.

INCLUSION CRITERIA:

1. All Aluminum phosphide poisoning patients.
2. Age > 16 yrs

EXCLUSION CRITERIA:

1. Patients not willing to participate
2. Age < 16yrs

A detailed history and a detailed clinical examination of patients was done.The treatment group (case group) received intravenous NAC plus a conventional treatment.The data collected included Demographic details, Aluminium phosphide form and quantity, Episodes of hypotension and use of vasopressors, Electrocardiogram change, SGOT/SGPT levels and CPK and CK MB levels. Statistical analysis was performed using SPSS version 25.

Results:

In the present study, the highest number of cases was observed in the 31-40 age group (21 cases), followed by the 21-30 age group (20 cases), 16-20 age group (11) and >60 age group (2 cases).Male (65.7%) predominance was seen in the study as compared to females (34.3%). Consumption of Aluminium Phosphide showed that thecommon consumption amount was 6.00 gm in 21.4%, followed by 7.50gm, consumed by 12 17.1%, and 3.00gm, consumed 14.3%. Other amounts consumed included 5.00gm (10.0%), 1.50gm and 10.00gm (each consumed by 8.6%), 4.50gm and 9.00gm (each consumed by 7.1%), and 2.50gm (4.3%). Only 1 participant (1.4%) consumed 12.00gm. The mean amount of Aluminium Phosphide consumed by the study population (N=70) is 5.7 grams, with a standard deviation of 2.6 grams. The mean time lag to Intensive Care Unit (ICU) admission for the study population (N=70) following Aluminium Phosphide poisoning is 3.6 hours, with a standard deviation of 1.9 hours.

Table 1:Distribution of laboratory parameters of study subjects.

		Frequency	Percentage
Serum Creat (mg/dl)	≤1.4	61	87%
	>1.4	9	13%
Serum Urea (mg/dl)	≤40	63	90%
	>40	7	10%
SGOT (U/L)	≤40	52	75%
	>40	18	25%
SGPT (U/L)	≤35	55	79%
	>35	15	21%
CPK (U/L)	≤170	11	16%
	>170	59	84%

CK-MB (U/L)	≤20	28	40%
	>20	42	60%

Table 1 presents the distribution of various laboratory parameters among study subjects, indicating the frequency and percentage of those falling below or above specified thresholds for each parameter.

Blood gas analysis showed that a significant majority (70%) of the cases show a pH level of less than 7.35, indicating a state of acidosis.Only 30% of the cases have a pH level of 7.35 or higher.An overwhelming majority (88%) have bicarbonate levels below 24 mEq/L, indicating a significant metabolic acidosis. Only 12% have bicarbonate levels of 24 mEq/L or higher.Majority of cases(58%)have lactate levels of 1 mmol/L or higher, which could indicate lactic acidosis, often associated with tissue hypoperfusion and hypoxia. In terms of lactate levels, 42% of cases have lactate levels below 1 mmol/L, suggesting some patients may have normal lactate metabolism or less tissue hypoxia.

Table 2: ECG changes of study subjects

	Frequency	Percentage
Sinus Tachycardia	9	12%
Sinus Bradycardia	3	4%
Ventricular tachycardia	0	0%
Atrial Fibrillation	0	0%
Atrial Flutter	0	0%
ST segment elevation	4	6%
ST segment Depression	3	4%
T wave inversion	7	10%
Broad QRS	2	3%

Table 2 showed distribution of ECG changes among study subjects, indicating the frequency and percentage of those falling below or above specified thresholds for each parameter.

Among the participants, 36 individuals (51.4%) died, 4 individuals (5.7%) left against medical advice (LAMA), and 30 individuals (42.9%) survived. This indicated that just over half of the

participants did not survive, while a significant portion did survive, and a small number left the hospital against medical advice.A majority of participants, 46 individuals (65.7%), experienced episodes of hypotension, while 24 participants (34.3%) did not. This highlights the prevalence of hypotension episodes within the study cohort, showing that more than half of the participants experienced hypotension. Apart from this,maximum participants, 44 individuals (62.9%), required inotropic support, while 26 participants (37.1%) did not. The outcomes among the study participants showed that 36 individuals (51.4%) died, 4 individuals (5.7%) left against medical advice (LAMA), and 30 individuals (42.9%) survived.

Table 3: Association of laboratory parameters with mortality

	Death	Percentage
Deranged kidney profile	9	25%
Deranged liver profile	16	44%
Deranged cardiac markers	36	100%
Metabolic acidosis	36	100%

Table 3 showed the frequency of mortality among the participants with different laboratory parameters.

Table 4: Association of ECG changes with mortality

	Frequency	Death	Percentage
Sinus Tachycardia	9	4	44%
Sinus Bradycardia	3	0	0%
Ventricular tachycardia	0	0	0%
Atrial Fibrillation	0	0	0%
Atrial Flutter	0	0	0%

ST segment elevation	4	2	50%
ST segment Depression	3	3	100%
T wave inversion	7	6	86%
Broad QRS	2	2	100%

Table 4 showed the mortality among participants due to ECG changes.

Discussion:

Aluminium Phosphide poisoning presents a formidable challenge to healthcare providers worldwide due to its high mortality rate and limited treatment options. The incidence of its poisoning is rising in the developing countries. Hence, the present study was planned and conducted on 70 patients of Aluminium Phosphide poisoning presenting in the Department of General Medicine of Government Medical College and Hospital Haldwani,with an aim to study the clinical profile with special reference to the role of n acetyl cysteine in the outcome of patients.

In the present study of 70 participants, there was a male preponderance with 65.7% males and 34.3% females. Most studies showed female predominance with 57.6% females and 42.4% males among 125 participants, resulting in a female to male ratio of 1.4 (**Muhammad Arshad Qureshi(2018) and Dereje Endeshaw Bogale(2021)**)[6,7]. A study by **Tarun Sharma(2018)**[8]the gender distribution among 117 patients had 52.1% males and 47.9% females. These variations in gender distribution across different studies highlight the potential influence of demographic and regional factors on the prevalence of conditions under investigation. The present study's older mean age might indicate regional or temporal variations in exposure risks or healthcare-seeking behaviours. This could be due to factors such as occupational exposure, intentional ingestion, or accidental contact, emphasizing the need for targeted prevention and education efforts in younger populations.

In this study, the amount of Aluminium Phosphide consumed by the 70 participants varied widely, with the most common amount being 6.00 grams, followed by 7.50 grams and 3.00 grams. **Dereje Endeshaw Bogale's study (2021)**[7]reported that the amount of Aluminium

Phosphide tablets taken ranged from one-fourth of a tablet to six tablets, with nearly half of the cases (51.2%) taking one full tablet, averaging to 1.2 tablets or approximately 3.6 grams. Similarly, **Mathai et al[9]**(2010) found an average consumption of 1.53 grams of Aluminium Phosphide among their study participants.The higher amounts reported in the present study could reflect different regional usage patterns, access to the substance, or possibly differences in the form or packaging of the poison. In the present study, the mean time lag to Intensive Care Unit (ICU) admission following Aluminium Phosphide poisoning was 3.6 hours. **A study by Mathai et al.[9](2010)** reported a mean delay of 2.1 ± 1.55 hours before presenting to the hospital which was in contrast to our study.

The study showed, majority of participants, 44 individuals (62.9%), required inotropic support, while 26 participants (37.1%) did not. This finding is consistent with the study by **Dereje Endeshaw Bogale (2021)[7]** out of 63 hypotensive patients, 9 expired upon arrival or shortly after admission before receiving treatments such as MgSO4, calcium gluconate, hydrocortisone, and dopamine infusion in the ICU. The remaining 54 hypotensive patients were treated with this regimen, yet the mortality rate in this treated group remained high at 55.6% (30/54). The need for inotropic support in a majority of patients in both studies highlights the importance of rapid and robust medical intervention to stabilize patients and improve survival outcomes.

In the present study, 46 individuals (65.7%), experienced episodes of hypotension, while 24 participants (34.3%) did not. A review by **Chugh et al [10] (2019)** highlighted that the presence of hypotension significantly worsens the prognosis of AlP poisoning, often leading to multi-organ failure and death. Another study by **Singh et al. (2020)[11]**demonstrated that early and aggressive management of hypotension, including the use of vasopressors and fluid resuscitation, could improve survival rates in these patients.

In the present study, prevalence of electrocardiographic abnormalities were observed. A study by **Siwach et al. (2018)[12]**reported that ST segment changes, including depression, were common in AlP poisoning cases and were associated with a poorer prognosis. Furthermore, a review by **Ranga Rao et al.[13] (2020)** highlighted the critical nature of cardiac complications in AlP poisoning. The review found that ECG abnormalities, including ST depression, were frequently observed and were correlated with higher mortality rates. A

study by **Bhalla et al. (2019)**[14]examined the incidence of various ECG abnormalities with ST elevation could be a marker of severe myocardial damage in the context of AlP toxicity. Another review by**Singh et al. (2020)**[11]highlighted that while ST elevation is not as prevalent as other ECG abnormalities. Present study indicated that only 7 individuals (10%) exhibited T wave changes similar to study by **Mehrpour et al.**[15]**(2018) and Chugh et al. (2020)**[10]reported that while T wave changes were less prevalent compared to other ECG abnormalities. In the present study 2 individuals (3%) exhibited QRS widening similarly study by **Soltaninejad et al (2019)**[16] highlighted that QRS widening is a predictor of severe cardiac involvement and increased mortality in AlP poisoning. 9 individuals (12%) in our study experienced sinus tachycardia and 3 individuals (4%) experienced sinus bradycardia, similar to a study by **Chugh et al.**[10] **(2018) andMehrpour et al. (2019)**[17]emphasized that their occurrence is a red flag for severe cardiac involvement.This study found that among the participants, 2 individuals (3%) experienced QRS widening. A study by **Chugh et al (2019)**[10]**Soltaninejad et al (2019)**[16] **Mehrpour et al.(2021)**[17]reported that conduction disturbances are common in AlP poisoning and are associated with increased morbidity and mortality.

In the present study, the mean SGOT/ SGPT level was 50.3 U/L and 53.4 U/L respectively.In comparison, **Dereje Endeshaw Bogale(2021)**[7] measured SGOT / SGPT levels in 20 patients and reported a mean value of 67.1 U/ and 51.6 U/L respectively.In this study of 70 patients , the mean ph was 7.2 with standard deviation of 0.2 and out of total patients 65 % of cases experienced metabolic acidosis and were treated with traditional treatment plus N acetyl cysteine and it was noted that out of 65% cases of poisoning patient who experienced metabolic acidosis 11.3% patient survived similarly study done **in 2019** by **Adil mahmood khanet al**[18] total 46 cases were taken into consideration of aluminium phosphide poisoning and out of which 34.7% cases experienced metabolic acidosis and out of which survival rate was 37.5% cases after management. Metabolic acidosis may be present probably due to the accumulation of lactic acid caused by blockage of oxidative phosphorylation and poor tissue perfusion.

In this study we observed, out of total 70 participants, 36 individuals (51.4%) died, 4 individuals (5.7%) left against medical advice (LAMA), and 30 individuals (42.9%) survived. When comparing these findings with other studies, **Tarun Sharma's2018**[8]study reported a higher mortality rate of 58.1%, with only 41.9% of patients showing improvement. Similarly,

Muhammad Arshad Qureshi's[19]2018 research indicated that 56.36% of patients did not survive despite resuscitative efforts, while 43.64% survived and were discharged. On the other hand, **Dereje Endeshaw Bogale's[7]2021** study found a mortality rate of 31.2%, with a significant portion of patients (62.4%) improving and a smaller fraction (6.4%) leaving against medical advice. These variations in outcomes highlight differences in patient populations, treatment protocols, and possibly the severity of the conditions being studied.

In this study out of total 70 participants mortality rate was 51.4%, cardiogenic shock and cardiotoxicity are the most important cause of mortality, as out of total 65.7% patients who experienced hypotension mortality was 87% , various types of cardiac dysrhythmia such as ST depression(4%),ST elevation (6%),Twaves inversion(10%),QRS widening (3%),sinus tachycardia(12%),sinus bradycardia (4%) were observed and the mortality was seen 50% in ST segment elevation, 100% in ST segment depression, 86% in Twave changes, and 100% in broad QRS complexes, 44% in sinus tachycardia patients and no mortality was seen in sinus bradycardia patients. The study done by **Omid Mehrpour et al[20] in 2016 in Iran** conducted out of 23 patients who were treated with conventional treatment the mortality rate was 43.47% and 23 patients who were treated with n acetyl cysteine the mortality was 30% , and there were no significant ecg changes seen in both the groups. Similarly a study conducted by **Heba Othman Shaker et al[21] in 2023 Egypt** in 177 patients under randomized controlled trial and distributed in 2 groups in which 91 patient received N acetyl cysteine and 86 patients received conventional treatment   and the mortality rate in both groups was 43.95% and 66.27% respectively, the study also concluded the rate of mechanical ventilation in which 35.8% patients gets ventilated in case group and 48.3% gets ventilated in non – N acetyl cysteine group. A Indian study conducted by **Ashish Bhalla et al** in **2017[22],** total 50 patients were randomized in NAC group and Placebo group and concluded the mortality in NAC group was 87.5% and in Placebo group it was 88.5%.

Conclusion:

Acute Aluminium Phosphide poisoning remains a major type of fatal poisoning worldwide and this study on 70 patients concluded a predominantly male population (65.7%), with a mean age of 33.7 years. Most cases (80%) were intentional, with poisonings occurring mainly in summer (57.1%). The average amount of ALP consumed was 5.7g, and ICU

admission occurred within an average of 3.6 hours. Hypotension was prevalent (65.7%), while ECG abnormalities such as ST depression (4%), QRS widening (3%) and ST elevation (6%) were observed. Biochemical markers like elevated CPK and CK-MB indicated toxicity and the potential role of antioxidant like NAC in preventing ALP induced cardiotoxicity and its effect on biochemical, clinical and hemodynamic parameters were assessed. The overall mortality rate was 51.4%, with 42.9% surviving and 5.7% leaving against medical advice. These findings emphasize the critical need for early intervention and supportive care in Aluminium Phosphide poisoning cases.

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