Continuous Renal Replacement Therapy as a Novel Therapy for Management of Aluminum Phosphide Poisoning

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Purpose of the study (AIM)

Aluminum phosphide (AP) poisoning is very common in India and carries a high mortality with no established modality of treatment or antidote. We present a retrospective analysis of Aluminum phosphide poisoning in last 1 year at a tertiary care hospital in North India to demonstrate the usefulness of early initiation of CRRT in such cases.

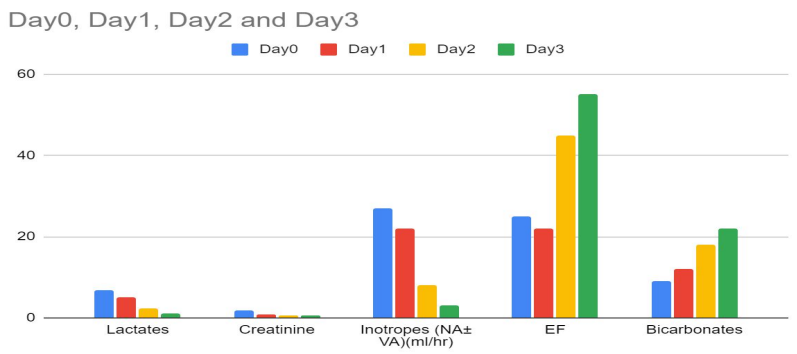
Introduction

Aluminum phosphide (AP) (Na3P) is an insecticide and rodenticide which when consumed in an evaporable tablet form, comes in contact with gastric HCl and releases Phosphine gas which rapidly get absorbed and inhibits mitochondrial cytochrome peroxidase and oxygen utilisation, leading to increased production of reactive oxygen species. Exposure to Phosphine at the dose of 1400 mg/m3 in 30 min can be fatal (WHO, 1988). Its poisoning is very common in India and carries a high mortality with no established modality of treatment or antidote. Its usual presentation would be hypotension resistant to medical treatment, lactic acidosis and multiorgan failure (MOF), most prominent being rapid reduction in Left Ventricular Ejection Fraction. Ongoing metabolic (including Lactic) acidosis along with mitochondrial inhibition of cardiomyocytes with phosphine leads to myocardial depression and MOF. Several reports on successful utilization of hemofiltration in hypotension with metabolic and lactic acidosis, especially in cases of Salicylate and Metformin overdose exist. There also have been case reports of AP poisoning being treated successfully with CRRT[1,2,3].
We present a retrospective analysis of Aluminum phosphide poisoning in last 1 year at a tertiary care hospital in North India and demonstrate the usefulness of early initiation of CRRT in such cases.

Methods and Materials

We retrospectively analyzed 140 poisoning cases out of which 35 AP poisoning cases were identified for analysis. AP cases that received CRRT were compared with those managed conservatively for survival, inotropic requirement, AKI, lactic acidosis, ECHO findings, time of presentation to ER and to CRRT initiation. Since most of the patients could not define the quantity consumed, this criteria was excluded from the analysis. CRRT (CVVHDF) was done with a Fresenius multiFilterate machine using Primasol® (Baxter). The average delivered dose was 30 ml/Kg/hr. Replacement flow rates were kept at an average of 1600 ml/hour. CRRT was discontinued once serum lactate normalized, inotrope requirements improved and hemodynamic stability was achieved.

Observation (Trend in survivors- CRRT Arm)



Observation (N=35)

	Conservative Arm (N=26)		CRRT Arm (N=9)	
	Survived (n=7, 26.9%)	Deceased (n=19, 73.1%)	Survived (N=4, 44.4%)	Deceased (N=5, 56.6%)
Time to presentation to ER/ CRRT	45 min	270 min	50 min (CRRT in 5.5 hr)	150 min (CRRT in 11 hrs)
Rising serial lactates (n)	3 (42.8%)	19 (100%)	4 (100%)	5 (100%)
Need for Inotropes (n)	3 (42.8%)	19 (100%)	4 (100%)	5 (100%)
Depressed EF (n)	3 (42.8%)	19(100%)	4 (100%)	5 (100%)
AKI (n)	1(14.2%)	17 (89.4%)	1 (25%)	4 (75%)

Results

Incidence of AP poisoning was 25.7%. Patients having lactates of more than 1.0mmol/L, depressed ejection fraction(EF), requirements of inotropes and AKI were offered CRRT and 9 out of 35 cases opted for it. In the CRRT arm, 4 out of 9 survived (44.4%) vs 7 out of 26 (26.9%) in conservative arm. In the conservative arm, average time to ER after AP poisoning was 45 minutes in all survivors vs 4.5 hours in 12 out of 19 deceased. Amongst survivors 4 out of 7 were hemodynamically stable with normal lactates, no inotropes, normal EF and 1 out of 7 (14%) had AKI . All the deceased (19) had progressively worsening lactates, required inotropes, had low EF and 17 out of 19 deceased (89.4%) had AKI. In the CRRT arm, all 9 cases had inotrope requirements, depressed EF and progressively rising lactates. All 4 survivors presented from ingestion of AP to ER in an average 50 minutes and CRRT initiated in 5.5 hours compared to the deceased where average time to ER was 2.5 hours and CRRT initiated in 11 hours. AKI was observed in 4 out of 5 deceased (80%) and 1 out of 4 survivors(25%).

Discussion

Cardiogenic shock in AP Poisoning is due to direct myocardial toxicity of phosphine gas and severe metabolic/ lactic acidosis which further suppresses myocardial contractility thus perpetuating the vicious circle of refractory shock and death.The management of AP poisoning is supportive as no antidote is available. Correction of metabolic acidosis has shown to improve outcomes in patients with profound shock[4]. There have been multiple case reports of successful use of ECMO in such patients. However, it is costly and is not readily available at most of the places. In our patients, we initiated CRRT with bicarbonate based solutions and continued till lactates/ bicarbonates were corrected or AKI improved. Improvement in hemodynamic status was noted with it. CRRT, which uses hemodiafiltration with convection scores over intermittent hemodialysis due to hemodynamically instability and helps to maintain metabolic milieu and resolution of shock state till AP gets excreted.

Conclusions

Mortality benefits could be achieved with early use of CRRT in patients of Aluminum Phosphide poisoning.
Factors favouring the outcome were:

- Early presentation to ER
- Early CRRT initiation
- Absence of AKI, Lactic acidosis and Myocardial depression requiring inotropic support.

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