

Venoarterial Extracorporeal Membrane Oxygenation is Effective in Severe Aluminum Phosphide Overdose Despite Delayed Presentation

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ABSTRACT

Aluminum phosphide (ALP) is a potentially lethal poison. The mortality rate in ALP overdose is close to 100%. ALP has no specific antidote, and only supportive therapy is possible, with timely extracorporeal support mentioned as a modality. We present a case of severe ALP overdose in a young female with delayed presentation (>24 hours) and multiorgan failure (MOF)/shock successfully managed with veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Unique features of this case include consumption of lethal quantity of ALP (5 g), severe toxicity with MOF, and shock secondary to a delayed presentation, all of which incrementally added to a high mortality. This was managed with the help of VA-ECMO as a last option with a successful outcome. This highlights the fact that late ECMO deployment, despite absorption of a large quantity and MOF/shock/acidosis, can still be salvageable with appropriate management.

Keywords: Aluminum phosphide, ECMO, Multi-organ dysfunction.

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INTRODUCTION

Aluminum phosphide (ALP) overdose is the most common agricultural pesticide overdose in India.¹ Human exposure can be accidental or suicidal.² ALP is an extremely lethal poison which releases phosphine upon contact with moisture, particularly in acidic environment. Phosphine acts as cellular toxin and inhibits cytochrome oxidase in mitochondria, and the resultant inability to utilize oxygen leads to lactic acidosis and eventually cell death and multi-organ dysfunction. ALP has no specific antidote, and only supportive therapy is possible, with timely extracorporeal support mentioned as a modality. We present a case of severe ALP overdose in a young female with delayed presentation (>24 hours) and multi-organ failure (MOF)/shock successfully managed with veno-arterial extracorporeal membrane oxygenation (VA-ECMO).

CASE DESCRIPTION

A 29-year-old female presented after consuming 10 tablets (5 g) of ALP. She was initiated on vasopressors for hypotension, dialyzed for worsening metabolic acidosis, and referred to our center for hemodynamic worsening with persistent metabolic acidosis.

On presentation, she had hypotension requiring three vasopressors. She was conscious and irritable. There was severe lactic acidosis with serum lactate (9 mmol/dL). Initial echocardiography showed severe left ventricular dysfunction (LVEF = 30–35%). In view of refractory shock, persistent metabolic acidosis, and imminent collapse, VA-ECMO was proposed. She was intubated and ventilated, and ECMO was initiated within 5 hours of hospital admission. The left femoral artery was cannulated with a 15Fr proximal cannula and an 8Fr distal cannula for distal limb perfusion. The right femoral vein was cannulated with 24Fr venous

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cannula with tip positioned at the right atrium. After heparinization, VA-ECMO was initiated, and initial ECMO pump flows were set at 3.5 L per minute.

Serial echocardiography showed improvement in LV function, and she was weaned off vasopressor support with resolving lactic acidosis. With clinical improvement, ECMO flows were slowly tapered and ECMO discontinued successfully after 48 hours (Table 1). Her stay in ICU was complicated with acute kidney injury (AKI) (serum creatinine—2.2, EGFR—40 mL/minute), but she did not require renal replacement therapy (RRT). She had thrombocytopenia (nadir-75,000/μL) probably related to heparin exposure requiring platelet transfusion, with no bleeding. She was successfully weaned off the ventilator on the third day, transferred to ward on the fifth day and discharged subsequently.

Table 1: Trend of various parameters till the patient got discharged

Parameter	Post-ECMO/before			
	At admission	12-hours after ECMO initiation	extubation	At discharge
pH	7.16	7.30	7.40	7.41
Bicarbonate	13.5 mmol/L	16.7 mmol/L	22.8 mmol/L	23 mmol/L
Lactate	9.0 mmol/L	10.0 mmol/L	1.2 mmol/L	0.8 mmol/L
Vasopressor support	Noradrenaline—5 µg/kg/minute Adrenaline—2 µg/kg/minute Vasopressin—0.04 units/hour	Noradrenaline—2 µg/kg/minute Adrenaline—1 µg/kg/minute	Nil	Nil
Serum creatinine	1.18 mg/dL	2.2 mg/dL	1.32 mg/dL	0.8 mg/dL
Ejection fraction	30–35%	40%	50%	55%
Sensorium	Conscious, irritable	Conscious	Conscious	Conscious

DISCUSSION

ALP is a potentially lethal poison. The lethal dose described in the literature is 10 mg per kg, and a dose of 0.5–1.0 g can be fatal.^{2–4} The amount ingested by our patient was significantly above the fatal dose (5 g).

The mortality rate in ALP overdose is close to 100% in some studies.^{5–7} The high mortality is due to lack of specific antidote and also due to the lethal action of phosphine which acts as a cellular toxin causing cellular hypoxia.^{8,9} The average time interval between consumption and death reported was 3 hours (range: 1–48 hours) with 95% mortality within 24 hours. Cardiovascular involvement is the major issue,⁹ with severe reduction of LV systolic function.^{13,14} Acute deterioration followed by cardiovascular collapse is the commonest clinical presentation, also seen in our case. Various autopsy studies have reported microscopic findings in the form of myocardial congestion with necrosis, vacuolar changes, and infiltration of myocytes by neutrophils and eosinophils.^{9–12} Studies have reported that the cardiac dysfunction starts to improve by the fifth day onward (range 10–14 days).^{15,16} Aggressive cardiovascular support during the acute phase is recommended to prevent end-organ damage due to poor perfusion and halts progression to MOF and death.

Severe ALP toxicity in our patient was evident with several parameters.^{17–19} These included cardiogenic shock, metabolic acidosis (pH <7.2), bicarbonate <15 mmol per L, Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores, need for mechanical ventilation, and elevated leucocyte count. Mathai et al. reported mortality rates of 73% in cases with APACHE-II scores of >8, and 69.2% in cases with SAPS-II score in excess of 30. APACHE-II score was a better predictor of mortality than SAPS-II scores in their study.¹⁷ The APACHE-II score was 14, and sequential organ failure assessment score was 7 in our case. The case for VA-ECMO as a last resort was clear with such severe ALP toxicity. The timing of ECMO initiation was however an issue, as success is limited after delayed deployment as discussed below.

In a study by Mohan et al., the average duration from exposure to ECMO initiation in survivors was 8.9 ± 3.3 hours.²¹ In our case, there was a significant delay in presentation (29 hours). In another study by Mohan et al., the average duration from admission to ECMO initiation was 3.5 ± 3.2 hours.²² In our case, admission to ECMO initiation was 5 hours. The mortality rate described in their study was 40 and 33%, respectively.^{21,22} Our patient survived despite two adverse factors—consumption of large doses of ALP and presenting with significant delay (>24 hours).

The major complication observed in patients on ECMO is bleeding.^{20,23} In our patient, bleeding was not an issue despite a drop in platelet count (nadir-75,000/µL) secondary to heparinization. A meta-analysis by Cheng et al. showed that the incidence of bleeding in patients with shock on ECMO was 41%.²³ The incidence of AKI was 56% in patients with shock requiring ECMO, and in patients requiring RRT, it was 46%.²³ Our patient also had AKI (non-oliguric) and did not require RRT. In terms of technical issues, the incidence of arterial ischemic complications related to arterial cannulation is high.²³ However, ischemic complications can be reduced significantly with the distal perfusion cannula, which was placed in our patient with no ischemic complications.²⁴

Unique features of this case include consumption of higher quantity of ALP (5 g), severe toxicity with MOF, and shock secondary to a delayed presentation, all of which incrementally added to a high mortality. This was managed with the help of VA-ECMO as a last option with a successful outcome. This highlights the fact that late ECMO deployment despite absorption of a large quantity and MOF/shock/acidosis can still be salvageable with appropriate management.

CONCLUSION

Aluminum phosphide (ALP) is a highly toxic substance, and its consumption is associated with high mortality. There is no antidote, and various treatment options over the years had little impact on mortality. Our report shows that VA-ECMO can reduce mortality even in patients who consume large doses and with late presentation (>24 hours). Early referral to an ECMO center is important, and VA-ECMO should be considered as salvage therapy in severe ALP overdose despite delayed presentation.

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