Case Report

Pediatric ECMO for toxin exposure: A Case Report

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ABSTRACT

Introduction - Treatment of shock and refractory hypoxemia in acute paediatric poisonings can be really challenging. Aluminium Phosphide (ALP) poisoning is a common in Northern India and is associated with very high mortality rate owing to development of cardiac dysfunction, resistant shock, refractory hypoxemia and severe metabolic acidosis. It is proposed that extracorporeal membrane oxygenation (ECMO) can improve survival in patients with toxic exposures by providing cardiorespiratory support and giving time to the heart and lungs to recover by itself. Case Report - In this case series two cases of adolescent girls with ALP poisoning suffering from refractory cardiogenic shock, fatal arrhythmias and severe metabolic acidosis were treated with veno-arterial ECMO. Extracorporeal cardiopulmonary resuscitation (ECPR) was done in both the patients, and hemodynamics improved after the commencement of ECMO. Ischemic changes in the cannulated limb were seen in both the patients. In one patient myocardium recovered and patient was weaned off the ECMO on the fourth day, while in the second case, myocardium did not show any recovery after 56 hours on ECMO and parents decided to discharge the child against medical advice because of the ischemia of the cannulated limb and girl died after the discontinuation of ECMO.

Conclusion - With this report, we would suggest that ECMO might be considered as a bridge to recovery to tide over the acute critical phase in ALP or any paediatric poisoning associated with intractable cardiorespiratory failure not responding to maximal intensive care therapy, keeping in mind the risk-benefit ratio.

Key Words - Aluminium Phosphide, Extracorporeal Membrane Oxygenation, Poisoning, Refractory shock, Refractory hypoxemia, Metabolic acidosis

Introduction:

Acute poisoning in children is a major public health problem and is associated with significant morbidity and mortality.1 Drugs account for the commonest poisonous agents ingested by the children, while pesticides accounts for 3-10% of the poisonings.2,3 Among pesticides, Aluminium Phosphide (ALP) is a cheap, solid fumigant and a highly toxic pesticide used mainly for grain preservation. ALP poisoning has been the commonest mode of suicide in Northern India.4 It is associated with a very high mortality rate, up to 70-100% in cases where myocardial depression sets in.5,6 After ingestion it releases phosphine gas which results in cellular hypoxia, cardiotoxicity, refractory hypotension, Acute respiratory distress syndrome, fatal arrhythmias and severe metabolic acidosis, which are the commonest causes of mortality among patients with ALP poisoning.7,8,9

The mainstay of therapy in any poisoned child is symptomatic supportive care, but circulatory shock and refractory hypoxemia still remains a huge challenge. ECMO improves survival in patients with toxicological exposures as it can support cardiopulmonary system, while xenobiotic is being eliminated or metabolised, when given in conjunction with other supportive therapies.10 Venovenous ECMO (VV-ECMO) is used in children with refractory hypoxemia; however, venoarterial ECMO (VA-ECMO) is used in patients with cardiopulmonary failure.11,12 It has been proposed that ECMO improves short term survival in patients with severe ALP poisoning by supporting the hemodynamics and oxygenation, while giving time to the cardiovascular system and lungs to recover by itself.10

We present two cases of adolescent girls with severe ALP poisoning treated via VA-ECMO. Both of these patients required Extracorporeal CPR (ECPR) because of refractory bradycardia while inserting Veno arterial Cannula. We aim to suggest ECMO for ALP as well as any other toxin ingestion among children, causing refractory hypoxemia and cardiopulmonary failure. We also want to highlight the problems faced by
our institution, such as hypo perfusion and ischemic changes in the limbs of the patient on VA-ECMO.

**Case 1:** A 14 year old adolescent girl was referred to our hospital one and a half hour after the ingestion of 3 gm tablet of Aluminium Phosphide. The girl experienced severe nausea at home, On examination in the emergency department, patient was drowsy but arousable, had a Heart rate (HR) of 100 beats/min, Respiratory rate(RR) of 30 breaths/ min, Blood pressure (BP) of 76/50 mm of Hg, along with signs of poor perfusion and shock. Nasogastric tube was inserted and gastric lavage was performed. Other laboratory parameters like renal function tests and blood counts were within normal limits. First arterial blood gas revealed pH7.453; Pco2 19 mm Hg bicarbonate 13.5 mmol/L and Lactate 5.2 mmol/L. Echocardiography done revealed mild global hypokinesia, mild left ventricular systolic dysfunction (Ejection Fraction [EF] 50%). She was resuscitated with restricted fluid boluses in view of shock along with the treatment of AIP poisoning performed with vasoactive agents (epinephrine, norepinephrine and dopamine), intravenous magnesium sulphate, intravenous calcium gluconate and other supportive care. She was electively intubated and a jugular central venous line was inserted. One hour later, she developed severe hypotension (systolic BP 50 mm of Hg), and her left ventricular ejection fraction dipped to 10%. The subsequent ABG after intubation showed severe metabolic acidosis (pH 7.10; Bicarbonate 9 mmol/L, Lactate 13.6 mmol/L). She was considered to be a candidate for V-A ECMO due to presence of refractory hypotension and severe metabolic acidosis. She was immediately shifted to Operation Theatre where she developed bradycardia and cardiopulmonary resuscitation (CPR) was initiated and cannulas were inserted in right femoral artery (17Fr) and vein (24x 29 Fr) while performing ECPR. ECMO was started within two and half hours of presentation to the emergency department. Subsequently, her hemodynamics stabilized after the initiation of ECMO. The ECMO pump flows were maintained at 3.2-3.8 L/ min. She was started on heparin infusion to maintain Activated Clotting time (ACT) between 180-250 sec. 6 hours later, Sustained Low Efficiency Haemodialysis (SLED) was initiated on account of worsening blood lactates and metabolic acidosis (ABG pH 6.96 Lactate 18 mmol/L, Bicarbonate 8.3 mmol/L) and decreased urine output. 12 hours after the commencement of ECMO, her blood pressures dropped and subsequently developed ventricular tachycardia, which responded to Direct current (DC) cardioversion and intravenous magnesium sulphate. Vasoactive drugs were stepped up and fluid boluses were given so as to maintain a fair systolic blood pressure. Multiple blood transfusions were given to maintain haemoglobin of 10 gm/dl. On the 3rd day her blood pressures and heart rates stabilised, while rhythm became sinus. Also left ventricular ejection fraction improved to 35%, lactates decreased; therefore, vasoactive drugs were tapered and ECMO weaning trial began. On the fourth day, ischemic changes were noted in the right lower limb, owing to the arterial cannulation. Thereafter, patient was weaned off from ECMO and arterial and venous cannulas were removed. Fasciotomy of the right leg was done and heparin was continued and regular monitoring of limb perfusion was done. 2 days later she was extubated and discharged after 10 days of hospital stay. At discharge, there was a significant improvement in her left ventricular ejection fraction (EF 45%). Regular dressings of the right lower limb were prescribed. She visited out patient department 3 days after discharge when she was advised surgery for the debridement of the ischemic muscles, and after that the patient didn’t follow up.

**Case 2:** A 16 year old female presented to the emergency department approximately 4 hours after the ingestion of 2 tablets of AIP. After she ingested the tablets, she experienced recurrent vomiting and abdominal pain. She was taken to a local hospital where a gastric lavage was done, following which she was referred to our hospital. On arrival, she had Glasgow coma scale of 8, HR of 78/min, Saturation of 50% in room air, Blood pressure was not recordable, had signs of poor perfusion with poor respiratory efforts. She was immediately intubated in the emergency department and was placed on mechanical ventilator. Arterial Blood gas drawn after intubation revealed hyperlactatemia and severe metabolic acidosis. (pH 7.10, Bicarbonate 12 mmol/L, Lactate 10 mmol/L). Other laboratory parameters were within normal limits. Echocardiography done revealed mild global hypokinesia, mild mitral regurgitation with severe left ventricular systolic dysfunction (EF 25%). She was treated with restricted fluid resuscitation, vasoactive drugs (dopamine and adrenaline), intravenous calcium gluconate, magnesium sulphate along with other supportive measures. Because of worsening hemodynamics, bradycardia (HR 30/min) and severe metabolic acidosis, the patient was put on VA-ECMO.
with a cardiac output of 2 litres/min via right femoral and arterial cannulation (venous cannula 24x29 Fr, arterial cannula 17 Fr, Distal perfusion catheter 7 Fr). ECPR was performed during the entire procedure as she had persistent bradycardia with slow ventricular rhythm. ECMO was successfully initialised and Initial ECMO flows were targeted to 3-3.5 litres/min. Unfractionated heparin was started and was adjusted to maintain ACT between 180-250 seconds. Half an hour after the initiation of ECMO she developed multiple episodes of ventricular fibrillation for which she received multiple DC cardioversions along with lignocaine boluses, amiodarone infusion and intravenous magnesium sulphate, after which rhythm got converted into a slow ventricular rhythm (Figure 1) with HR of 60-80/min, and her Left ventricular Ejection dropped to 5-10%. Her Lactates and metabolic acidosis also worsened (pH 7.090; Bicarbonate 6.8 mmol/L; Lactate 18 mmol/L); therefore child was placed on SLED. Vasoactive drugs along with fluid boluses were required to maintain a mean systemic blood pressure of 50-55 mm of Hg. She was also given blood transfusions to maintain her haemoglobin. One day later, she developed ischemic changes in the right lower limb, which progressed rapidly. Although after 48 hours of ECMO, her lactates normalized, acidosis got corrected, but no significant improvement in the myocardial function was noted. She continued to have slow ventricular rhythm, and EF remained low (5-10%), and she started developing ischemic changes in the other limbs also, despite maintaining good ECMO flows. Patient, however, remained neurologically intact. On the 3rd day the parents were counselled about the ischemic changes in the right lower limb and need for amputation later, after which they decided to take the patient home against medical advice. ECMO was discontinued after 56 hours of hospital stay, and the patient expired.

**Discussion:** Acute poisonings is one of the commonest causes of paediatric emergency admissions. Certain Poisonings are extremely fatal and continues to be a great challenge for the paediatricians. Majority of them are accidental, while others are intentional for suicidal or homicidal purpose. Suicidal poisonings are mostly observed among adolescent females. Both our cases were young adolescent girls, and they intentionally consumed tablets of Aluminium phosphide.

ALP is an extremely lethal poison used as a pesticide in grain storage facilities, and its ingestion is usually suicidal in nature. The severity of ALP poisoning depends upon the amount of toxin ingested, route of entry, and duration between exposure to poison and admission to the hospital. Each tablet of aluminium phosphide weighs 3 grams. The lethal dose (LD50) is 10mg/kg, and the fatal dose is 0.5-1gram. The mortality is higher among those who consume more than 2 tablets and 100% mortality is seen among those who consume 3 tablets or more. 95% of deaths due to ALP poisoning occur in the first 24 hours. Average time interval between consumption and death being 3 hours (range 1-48 hours). One of our patient consumed one tablet and the 2 second one consumed 2 tablets and mean duration of presentation to the hospital was 3 hours.

The high mortality is due to the release of phosphine gas on ingestion, which inhibits mitochondrial cytochrome C oxidase and cellular oxygen utilisation. It also results in generation of superoxide and peroxide radicals that cause cellular damage by lipid peroxidation. When ingested it can cause refractory hypotension, ARDS, fatal arrhythmias and severe metabolic acidosis. Furthermore, neurological complications, nephrotoxicity and hepatotoxicity can also occur. Phosphine induced myocardial damage and cardiovascular collapse is most common complication of AIP poisoning. The hallmark of cardiac insult is the global hypokinesia of left ventricle. Both of our cases presented with refractory hypotension, low left ventricular ejection fraction, global hypokinesia and severe metabolic acidosis. Both experienced bradycardia and fatal arrhythmias (VT/VF/Slow ventricular rhythm). It has been suggested that cardiac function starts improving by the fifth day and the half-life of phosphine gas is 5-24 hours. Aggressive cardiovascular support in the form of fluids resuscitation and vasoactive drugs can be given to prevent end-organ damage due to poor perfusion and to tide over the critical period. There is no specific antidote and other treatment modalities suggested are intravenous magnesium sulphate, N-acetyl cysteine and decontamination with vegetable oils, with variable outcomes. But most of the patients who develop refractory shock and severe metabolic acidosis die despite maximal intensive care therapy.

Extracorporeal Membrane Oxygenation (ECMO) is now a well-documented modality in improving survival among children with severe respiratory failure, cardiogenic shock or refractory hypotension. Institution of ECMO has been proposed to support...
the oxygenation and hemodynamics and improve the survival among paediatric and adult patients with various pharmacological and non-pharmacological toxic exposures as well as in patients that require CPR.\textsuperscript{10} V-AECMO has also shown promising benefits in various case reports and observational studies on adult patients with severe ALP poisoning, in terms of significant mortality reduction \textsuperscript{13,21} V-A ECMO is a circulatory assist device that oxygenates the blood and removes carbon dioxide, and pumps blood to support the circulatory system. We used V-A ECMO in both our paediatric cases who presented with refractory shock and severe metabolic acidosis. ECPR was done in both the cases and hemodynamics stabilised after the initiation of ECMO. Since ALP causes reversible myocardial damage and severe ARDS, V-A ECMO acts as a bridge to recovery, prohibits end organ damage due to poor perfusion and buys time for heart and lungs to recover from acute toxicity. One important consideration is that ECMO should be started before multiorgan failure sets in. In our first case ECMO was weaned off after the recovery of the myocardium. In our second patient, the hemodynamics stabilised on ECMO but the myocardium did not show any recovery by the third day and patient continued to have slow ventricular rhythm and episodes of bradycardia with low left ventricular ejection fraction.

Although ECMO supports cardiopulmonary system it is associated with severe complications such as significant bleeding limb ischemia/ amputation, stroke, infection compartment syndrome, acute kidney injury and other neurological complications.\textsuperscript{22} Limb ischemia in the cannulated limb occurred in both of our patient. In the first patient we did not use a distal perfusion catheter, which is a catheter arising from the arterial cannula to maintain the arterial flow in the cannulated limb. In the next case we used smaller arterial cannula with a distal perfusion catheter but still we encountered limb ischemia. This is probably due to the emergent nature of the procedure and because our centre is still in the learning curve. In the second case ischemic changes were noted in the rest of the limbs also despite maintain a good flow of ECMO, probably because her myocardium showed no recovery and her hemodynamics were maintained with the non-pulsatile flow of the ECMO.

**Conclusion:** We suggest that ECMO should be studied further as a promising agent as a bridge to recovery to tide over the acute critical phase in ALP or any paediatric poisoning associated with refractory hypoxemia, refractory shock or refractory arrhythmias which does not respond to maximal intensive care therapy. However ECMO is associated with significant complications and acceptable risk benefit ratio should be kept in mind before the commencement of ECMO.

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**References:**


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![Figure 1: Ventricular fibrillation converted to slow ventricular rhythm case2](image-url)