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The Role of Levosimendan in Acute Aluminum Phosphide Induced Myocardial Toxicity

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Abstract

Acute aluminum phosphide poisoning (AAlPP) or celphos is one of the most commonly used poisons for suicidal purpose. Number of cases reported to the hospital represents only the tip of an iceberg. Most of the patients succumb to this poison due to inadequate or lack of treatment. In our case, we added levosimendan to the already established treatment guidelines for AAlPP poisoning and we got surprising result as we could discharge the patient from our Intensive Care Unit in just 2 days with all vitals stable.

Keywords: Aluminum Phosphide, Celphos, Levosimendan, Toxicology

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1. Introduction

Aluminum phosphide (AIP) is the most commonly used pesticide or rodenticide for the preservation of grains in rural India. Easy availability, cheap rate, higher mortality rate, and unavailability of specific antidote makeit an ideal poison mostly for suicidal purpose (94%),sometimes for accidental (5%), and rarely for homicidal purpose (1%).[1]The mortality rates from AAlPP published in literature vary from 40% to 80%.[1]A recent study for 2 years period published by Mathai and Bhanu in which mortality rate from Acute aluminum phosphide poisoning (AAlPP) is 59.3%. [2]Levosimendan is a calcium sensitizer – it increases the sensitivity of the heart to calcium, thus increasing cardiac contractility without a rise in intracellular calcium. Levosimendan offers a new effective option for the treatment of acutely decompensated heart failure. [3,4]Literature search did not reveal any information regarding the role of levosimendan in AAIPP. We found drastic role of this combination in AAlPP

2. Case Report

A 20-year-old, 70 kg male presented to casualty department with a history of suicidal ingestion of one tablet (10 g) of aluminum phosphide (AlP), 2 h ago, which was not exposed to air. He had a heart rate of 104 beats/min with blood pressure of 114/60 mm of Hg, respiratory rate of 30/min, and oxygen saturation (SpO_2) of 98%. He was conscious and oriented. Arterial blood gas(ABG) analysis pH 7.48, PCO_2 28.8 mm of Hg, PO 123.2 mm. Levosimendan offers a new effective option for the treatment of acutely decompensated heart of Hg, HCO_3 21.1 mmol/L, and base excess 21.0 mmol/L.

The patient was shifted to Intensive Care Unit, where all the monitors attached (which includes electrocardiogram [ECG], SPO_2, and noninvasive blood pressure). Random blood sugar level was within normal limit. Gastric lavage was done with sodium bicarbonate and 50 ml coconut oil; the samecycle was repeated 6 times over next 1 h. He was treated with intravenous crystalloids (1/L sterofundin over 30/min) to keep mean arterial pressure (MAP) above 70 mm of Hg and started oxygen supplementation by mask at a rate of 6 L/min. Meanwhile, central venous catheterization, invasive arterial line insertion, and Foley's catheterization were done with all aseptic precautions. ECG showed normal sinus rhythm. Myocardial contractility and cardiac index were found normal on bedside echocardiography (Echo). After 2 h, ABG revealed pH 7.51, PCO2 22.4 mm of Hg, PO_2 110.0 mm of Hg, HCO_3 17.6 mmol/L, and base excess 3.1 mol/L (metabolic acidosis with overcompensated respiratory alkalosis). As the patient was in respiratory distress with the rate of 40/min, endotracheal intubation was done by rapid sequence induction technique and put on controlled

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mechanical ventilation to keep minute ventilation of 7–8 l/min.

We started infusion of N-acetyl cysteine (NAC) 600 mg over 24 h, magnesium sulfate ($MgSO_4$) with loading dose of 1 g over 20 min followed by 1 g/h for 3 h, then 1 g every 6 hourly for 24 h, and combination of midazolam at a rate of 4 mg/h and fentanyl at a rate of 75 g/h. One 26 hour after treatment, ABG revealed metabolic acidosis, so 27 sodium bicarbonate infusion started at a rate of 50/mmol/h.Gradually, the patient become hemodynamically unstable and despite of adequate fluid resuscitation, he required norepinephrine infusion to maintain MAP above 70 mm of Hg. Six hours after AIP ingestion, ECG showed arrhythmia and bedside Echo was performed which showed decreased myocardial contractility and cardiac index (1.5/L/min/m2). Hence, levosimendan infusion was started (loading dose - 6 g/kg followed by 0.6 g/kg/h) and for arrhythmia, injection amiodarone 150 mg was given over 10 min followed by 1 mg/min for 6 h then 0.5 mg/min for next 18 h.

We monitored the patient up to 24 h with serial ABG, bedside Echo, and all vital parameters including urine output, which showed an improving trend. Then, all infusions gradually tapered off, and the patient was extubated after 36 h. As the patient was hemodynamically stable up to 36 h after extubation, we transferred the patient to ward and from there he was discharged successfully.

3. Discussion

Major culprit of AAlPP is phosphine gas (PH_3), which is liberated after catalytic reaction of AlP with hydrochloric acid (HCl) in gut. PH_3 is rapidly absorbed from gastric mucosa and reaches blood stream then to various tissues and affects organs such as heart, lung, kidney, and liver with manifestation of serious cardiac arrhythmias, intractable shock, acidosis, and pulmonary edema.[4]The specified fatal dose of AlP is 0.15–0.5 g. [5]Ninety-five percentage of the patients die within 24 h and the most common cause of death in this group is cardiac dysrhythmia. Death after 24 h is usually due to shock, acidosis, acute respiratory distress syndrome, and cardiac dysrhythmia.[6]

As the major culprit of AAlPP is PH_3, effective oxygenation, ventilation, and circulation are needed for excretion of this gas. Continuous invasive hemodynamic monitoring and early resuscitation with fluid and vasoactive agents are After 2 h, ABG revealed pH 7.51, PCO_2 22.4 mm of Hg, PO_2 110.0 mm of Hg, HCO_3 17.6 mmol/L, and base excess required. Specific management toward AAlPP includes reducing absorption of PH_3, increasing excretion through 23 3.1 mmol/L (metabolic acidosis with over compensated respiratory alkalosis). As the patient was in respiratory distress with the rate of 40/min, endotracheal intubation was done by rapid sequence induction technique and put on controlled mechanical ventilation to keep minute ventilation of 7–8 l/min. We started infusion of N-acetyl cysteine (NAC) 600 mg over 24 h, magnesium sulfate ($MgSO_4$) with loading dose of 1 g over 20 min followed by 1 g/h for 3 h, then 1 g every 6 hourly for 24 h, and combination of midazolam kidney and lungs, and reducing cellular toxicity. For gastric lavage, we used coconut oil with sodium bicarbonate. Coconut oil reduces the toxicity of AlP by forming aprotective layer around the gastric mucosa, thereby preventing the absorption of PH_3. It also helps in diluting the HCl and inhibits the breakdown of phosphide from the pellet. Sodium bicarbonate inhibits the release of PH_3 by neutralizing the HCl.[7] Adequate hydration and renal perfusion with intravenous fluid enhance the excretion through urine. We kept minute ventilation on higher side to excrete PH_3 from lung. [4]For reducing cellular3 toxicity of PH_3, we used $MgSO_4$ and NAC. $MgSO_4$ acts as a free radical scavenger and antioxidant through glutathione recovery and also helps in stabilizing the cardiac cell membrane.[8]NAC acts primarily by reducing oxidative stress over the cells by its antioxidant property and scavenging the free radicals. NAC after absorption gets converted to cysteine, which helps in counteracting oxidative stress and inflammation, is a precursor for the synthesis of intracellular glutathione.[9]

As bedside Echo showed decreased cardiac contractility and cardiac index, levosimendan infusion was started. Cardiac markers (troponin-I, B-type natriuretic peptide, and creatine kinase-MB) were sent. Report revealed positive which indicates the presence of myocardial necrosis. AAlPP causes cardiac arrhythmias because of focal myocardial necrosis and changes in membrane action potential by PH^3 due to altered permeability to sodium, magnesium, and calcium channels.[10]Levosimendan is an inotropic agent used in the treatment of heart failure. It is a myocardial calcium sensitizer, binding to cardiac troponin-C, and a vascular K^+ adenosine triphosphate-channel agonist producing peripheral vasodilatation.[11]Levosimendan, through its unique troponin-C interaction, may preserve diastolic function.[12]Combined positive inotropic effect and vasodilation causes an increase in cardiac contractility, decreased preload and afterload.[3,13] We preferred

levosimendan because of less increase in myocardial oxygen demand and preserve diastolic function as compared to dobutamine.[12]

Limitation of this case report is that we had not assessed the superior vena cava SpO_2 and lactate level. We had also Toxicology International ??? / ??? / ???2not assessed whether combined use of NAC, $MgSO_4$, and levosimendan have any favorable outcome in AAlPP or not so this is further area for research. So far, there is no proven study of levosimendan in AAlPP, hence regarding the use of levosimendan in AAlPP and comparing it with dobutamine, there is a need of prospective randomized study. To conclude, levosimendan can be used in AlP-induced myocardial toxicity as an inotropic agent, but to prove this as a large sample sized, prospective randomized study to be needed.

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Nil.

3.2 Conflicts of Interest

There are no conflicts of interest.

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