Journal of Toxicological Studies 2025, 3(1), 3031.
https://doi.org/10.59400/jts3031

Case Report

Case report: Levosimendan as a possible inotropic drug for acute aluminum phosphide toxicity

Meray Medhat Shokry Zaghary[1,*], Salah Eldeen Tag Elsir Ali[2], John Medhat Shokry Zaghary[3], Bishoy Reyad GabAllah Issa[3], Nourseen Effat Abd El_Gaber Ajamy[3]

[1] Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Sohag University, Sohag 82524, Egypt
[2] Faculty of Pharmacy, Stellenbosch University, Stellenbosch 7602, South Africa
[3] Faculty of Medicine, Sohag University, Sohag 82524, Egypt
*** Corresponding author:** Meray Medhat Shokry Zaghary, meraymedhat@med.sohag.edu.eg, drevanho2013@gmail.com

CITATION

Zaghary MMS, Ali SETE, Zaghary JMS, et al. Case report: Levosimendan as a possible inotropic drug for acute aluminum phosphide toxicity. Journal of Toxicological Studies. 2025; 3(1): 3031. https://doi.org/10.59400/jts3031

ARTICLE INFO

Received: 31 March 2025
Accepted: 15 May 2025
Available online: 13 June 2025

Abstract: Background: Aluminum phosphide is a severe poisoning that can lead to death. Easy availability with no specific antidote is the leading cause of the higher mortality with it. **Case report:** The study represents a case report of a 5-year-old male who came after oral ingestion of aluminum phosphide and presented with vomiting, sleep, low blood pressure of 80/20, and a regular and rapid pulse of about 140 per minute. Gastric lavage was done rapidly with 3 bottles of paraffin oil, then 1 bottle was given every 1 h for 4 cycles. Complete laboratory investigations were performed for the patient, such as arterial blood gas, liver enzymes, electrolytes, full blood count, and renal function, which showed normal function except for metabolic acidosis with overcompensated respiratory alkalosis. The patient was transferred to the pediatric intensive care unit, where we gave a dose of 1 mEq sodium bicarbonate per kg with N-acetylcysteine 150 mg/kg in 100 mL of 5% glucose for 2 h under coverage of hydrocortisone and Avil. Antiemetics and proton pump inhibitors were given regularly every 12 h. After discussion with the pediatric specialist, the ejection fraction of the child by echocardiography was low, about 40%, and levosimendan was recommended to be given to the patient. The patient was given a bolus dose of 6 µg/kg over 10 min, followed by an infusion of 0.1 µg/kg/min with excellent response for 48 h. After admission for one week, the patient recovered completely, the ejection fraction became 55%, and the patient was discharged safely to home. **Conclusion:** Acute accidental exposure to AlP, either accidentally or suicidally or rarely homicidally, presents a significant threat to human life with many toxic effects, especially on the heart. Levosimendan is a drug that is used in decompensated heart failure and can be used as an inotropic agent in acute AlP toxicity.

Keywords: aluminum phosphide; levosimendan; inotropic; acute toxicity

1. Introduction

In underdeveloped countries, the most often utilized pesticide or rodenticide for grain preservation is aluminum phosphide (AlP). It is an excellent poison for suicidal purposes, occasionally for accidental purposes, and infrequently for homicidal purposes due to its easy availability, low cost, high fatality rate, and lack of a specific antidote [1,2].

Suicidal intake of wheat-preserving medicines is becoming more common in Egypt each year [3].

The most deadly of these metal phosphides is AlP, which belongs to the same family as magnesium, calcium, and zinc phosphide [4].

When AlP is taken orally, it quickly releases the highly poisonous phosphine (PH_3)

gas, which disrupts cellular respiration [5]. Phosphine gas, when inhaled, is involved in multi-organ failure with various mechanisms [6].

By inhibiting cytochrome oxidase activity and adenosine triphosphate (ATP) synthesis, PH_3 disrupts mitochondrial function. Furthermore, by boosting the generation of reactive oxygen species (ROS) and blocking enzymatic antioxidants such as catalase (CAT), glutathione reductase (GR), and superoxide dismutase (SOD), phosphine induces oxidative stress. Lipid peroxidation, which results from an unbalanced redox state, damages numerous cellular components and accelerates cellular death [5].

The toxic effects of AlP poisoning frequently manifest as dysfunction in multiple organs, with the liver, the kidneys, and the heart being particularly susceptible to its harmful impact [7].

AlP causes serious poisoning in which severe cardiac suppression is a significant lethal consequence [8].

Clinically, acute AlP poisoning manifests with severe metabolic acidosis and refractory cardiogenic shock [9].

Due to the absence of an antidote, the treatment for phosphide poisoning is limited to providing supportive measures. Regrettably, acute AlP poisoning is linked to a significant fatality rate [3].

As a calcium sensitizer, levosimendan increases the heart's sensitivity to calcium, enhancing cardiac contractility without elevating intracellular calcium levels. A novel and efficient therapy for abruptly decompensated heart failure is levosimendan [10,11].

Levosimendan may reduce cardiovascular toxicity caused by AlP poisoning in the rat model, according to experimental research. Administration of levosimendan improved the lowering of heart rate, blood pressure, cardiac output, ejection fraction, and stroke volume. Additionally, after acute AlP poisoning, levosimendan markedly enhanced complex mitochondrial IV activity, the ADP/ATP ratio, apoptosis, malondialdehyde, lactate, and troponin I levels. According to Armandeh et al. [8], they concluded that levosimendan may improve heart function and reduce AlP-induced cardiotoxicity by modifying mitochondrial activity, so further research is necessary to determine levosimendan's possible clinical application in acute AlP toxicity.

In our case report, we utilized levosimendan to enhance the heart's contractility and improve the patient's medical condition, in addition to standard treatment.

2. Case report presentation

On the 1st of March 2025, at 6 pm, a 22-year-old female, accompanied by her 6-year-old daughter, 8-year-old son, and 5-year-old son, presented to the Emergency Hospital in New Sohag, Sohag, Egypt, with a 4-h delay after oral AlP ingestion, and they presented with acute AlP toxicity signs. The history was that after the three children came from school, the mother gave them a glass of water after dissolving an aluminum phosphide tablet, and they all drank from the glass of water. The mother came with the clinical manifestations of severe cardiogenic shock, non-palpable pulse, dilated fixed pupil, bradypnea (10 respiratory rates per minute), oxygen saturation of 70%, unconsciousness, poisoning severity score (PSS) of 4, and hypothermia of 34 °C. Cardiopulmonary resuscitation was started immediately for the mother, but

unfortunately, she passed away within 1 h in the emergency room. The 6-year-old female child also came with severe shock, an unpalpable pulse, and monitors attached, which showed premature ventricular contraction with a slow pulse of 60/min, SPO_2 < 80%, high random blood sugar, and hypothermia. The female child was intubated and admitted to the pediatric intensive care unit to be put on mechanical ventilation and norepinephrine, but she passed away within 6 h after resuscitation.

The 8-year-old male child was vitally stable, S_{PO2} > 97%, HCO_3- is 23 mEq/L, and PCO_2 = 37 mmHg. He was fully conscious and came only with a history of vomiting once before arrival at the hospital. Washing with paraffin oil was performed rapidly on the child using 3 bottles of paraffin oil, followed by 1 bottle administered every hour for 4 cycles. The child was admitted inpatient for two days on fluids, antiemetics, proton pump inhibitors, hydrocortisone, and parenteral N-acetylcysteine as an antioxidant. The child's general condition was excellent, and his arterial blood gas (ABG), electrocardiogram (ECG), echocardiography, and renal and liver function tests were normal, and he was discharged after two days.

Finally, the last child, 5 years came with vomiting, sleep, low blood pressure (80/20), and a regular and rapid pulse of about 140 per minute. Gastric lavage was performed rapidly with 3 bottles of paraffin oil, followed by 1 bottle administered every hour for 4 cycles.

Complete laboratory investigations were performed on the patient, including arterial blood gas analysis, liver enzyme levels, electrolyte measurements, a complete blood count, and renal function tests, which revealed normal function except for metabolic acidosis with overcompensated respiratory alkalosis. His ABG was pH = 7.46, PCO_2 = 30 mmHg, PO_2 = 110 mmHg, and HCO_3 = 16 mEq/L. Serum pseudocholinesterase levels were measured and found to be normal.

The patient was transferred to the pediatric intensive care unit, where a dose of 1 mEq of sodium bicarbonate per kg was given with 150 mg/kg of N-acetylcysteine on 100 mL of 5% glucose for 2 h under coverage of hydrocortisone and Avil. Then, 100 mg of N-acetylcysteine per kg was administered over 500 mL of 5% glucose for 16 h to avoid the load of intravenous fluids that would occur with 1000 mL. Antiemetics and proton pump inhibitors were given regularly every 12 h. After discussion with the pediatric specialist, the child's ejection fraction, as measured by echocardiography, was found to be low, approximately 40%, and levosimendan was recommended for the patient.

The patient was given a bolus dose of 6 µg/kg over 10 min, followed by an infusion of 0.1 µg/kg/min with excellent response for 48 h.

After admission for one week, the patient recovered completely, the ejection fraction became 55%, and the patient was discharged safely to home.

3. Discussion

One of the leading causes of acute aluminum phosphide toxicity is phosphine gas, which results from the catalytic interaction of AlP with gastrointestinal acid (HCl). The stomach mucosa quickly absorbs the phosphine gas, which enters the bloodstream and travels to different tissues. It impacts the heart, lungs, kidneys, and liver, exhibiting severe cardiac arrhythmias and cardiogenic shock that is untreatable in many cases

and leads to death [11].

Acute AlP toxicity cases have a high mortality rate even in intensive care units due to early hemodynamic failure and multi-organ failure [12].

Many prognostic factors in acute AlP toxicity indicate poor outcomes, like suicidal purposes, the delayed time till presentation, increasing the ingested dose of AlP, metabolic acidosis, abnormal ECG, and hypotension at the time of admission [13].

The mother and the 6-year-old daughter presented with poor prognostic factors such as low blood pressure, metabolic acidosis, and severe arrhythmia that resulted in death within less than 24 h.

Shadnia et al. [14] explained that within 24 h, 95% of patients pass away, and cardiac dysrhythmia is the leading cause of death in this group. After 24 h, shock, acidosis, acute respiratory distress syndrome, and cardiac dysrhythmia are typically the causes of death.

Gastric lavage was done to each of the 8-year-old and 5-year-old sons rapidly using 3 bottles of paraffin oil, followed by 1 bottle administered every hour for 4 cycles.

Previous studies proved that paraffin oil was found to lower the emission of phosphine gas due to limiting AlP's reactivity with water and stomach acid and by lowering phosphine absorption from the gastric mucosa; furthermore, paraffin oil improves GIT motility, which increases phosphide excretion [3].

The 5-year-old child was found to be sleepy with low blood pressure, 80/20, and a regular rapid pulse of about 140 per minute. He was admitted to the pediatric intensive care unit, where echocardiography was approximately 40%, and levosimendan was recommended for the patient. The patient was given a bolus dose of 6 μg/kg over 10 min, followed by an infusion of 0.1 μg/kg/min with an excellent response after 48 h.

Levosimendan is an inotropic drug that is used to treat heart failure. It binds to cardiac troponin-C and a vascular K+ adenosine, making it a myocardial calcium sensitizer. Levosimendan may maintain diastolic function due to its distinct troponin-C interaction. Vasodilation and the positive inotropic effect reduce preload and afterload and promote cardiac contractility. Levosimendan was favored over dobutamine because it preserved diastolic function and increased myocardial oxygen demand [1].

The potential benefits of levosimendan are highlighted by its capacity to make contractile proteins more sensitive to calcium, which has a positive inotropic effect. Levosimendan immediately affects the shocked myocardial tissue's contractility and enhances its functionality [15,16]. Levosimendan causes coronary and systemic vasodilation by activating potassium channels susceptible to adenosine triphosphatase [17]. Using levosimendan in advanced heart failure was approved to be safe and associated with clinical improvement despite no effect on mortality rate [18].

Searching for new treatments that increase the ejection fraction became an important topic; levosimendan was the best drug for improving ventricular contractility [19].

In a clinical trial on patients with severe, low-output heart failure conducted by Follath et al. [20], levosimendan improved hemodynamic performance more effectively than dobutamine. This benefit was accompanied by lower mortality in the levosimendan group than in the dobutamine group for up to 180 days.

Levosimendan is a promising, safe drug in cases associated with low ejection fraction and should be applied in a large clinical study to see its effectiveness [1].

4. Conclusion

This case report in the current study suggests that levosimendan can be used as an inotropic agent in acute aluminum phosphide toxicity in cases with hypotension and low ejection fraction with promising effects.

5. Recommendations

Randomized clinical trials are recommended to use levosimendan as a possible antidote for acute AlP toxicity cases with cardiovascular manifestations in comparison to the standard treatment, like dobutamine.

Informed consent statement: The relative had signed informed consent before admission. Participation in the study was optional, and confidentiality and privacy were guaranteed.

Conflict of interest: The authors declare no conflict of interest.

References

1. Gupta BK, Yadav G, Barik AK, et al. The Role of Levosimendan in Acute Aluminum Phosphide Induced Myocardial Toxicity. Toxicology International (Formerly Indian Journal of Toxicology). 2015; 22(2): 116. doi: 10.22506/ti/2015/v22/i2/137675
2. Zaghary MMS, Ali HAA, Ahmed AMK. The performance of ejection fraction as a predictor of mortality and morbidity in acute aluminium phosphide poisoning. Toxicology Research. 2024; 14(1). doi: 10.1093/toxres/tfae232
3. Abdelkader M, Elsayed R, Shokry M. Pattern and Outcome of Acute Aluminium Phosphide Intoxicated Cases at Sohag University Hospitals: Special Consideration to Paraffin Oil as a Supportive Treatment. Zagazig Journal of Forensic Medicine. 2023; 21(1): 133-156. doi: 10.21608/zjfm.2023.180421.1133
4. Sobh ZK, Kholief M, Sobh EK, et al. Exploring research gaps and trends in the management of acute phosphide poisoning: a systematic review. Critical Reviews in Toxicology. 2023; 53(3): 181-206. doi: 10.1080/10408444.2023.2225539
5. Naddafi M, Eghbal MA, Ghazi Khansari M, et al. Sensing of oxidative stress biomarkers: The cardioprotective effect of taurine & grape seed extract against the poisoning induced by an agricultural pesticide aluminum phosphide. Chemosphere. 2022; 287: 132245. doi: 10.1016/j.chemosphere.2021.132245
6. Baeeri M, Rahimifard M, Armandeh M, et al. The Effect of Levosimendan on Phosphine-Induced Nephrotoxicity: Biochemical and Histopathological Assessment. Drug Research. 2021; 72(02): 109-118. doi: 10.1055/a-1661-5439
7. Abd-Allah M, Abdalla A, Mohamed N, et al. Updates on toxicology of Aluminum Phosphide and different management protocols. Zagazig University Medical Journal. 2022. doi: 10.21608/zumj.2022.125913.2491
8. Armandeh M, Bameri B, Baeeri M, et al. The role of levosimendan in phosphine-induced cardiotoxicity: evaluation of electrocardiographic, echocardiographic, and biochemical parameters. Toxicology Mechanisms and Methods. 2021; 31(9): 631-643. doi: 10.1080/15376516.2021.1950248
9. A Farrar R, B Justus A, A Masurkar V, et al. Unexpected survival after deliberate phosphine gas poisoning: An Australian experience of extracorporeal membrane oxygenation rescue in this setting. Anaesthesia and Intensive Care. 2021; 50(3): 250-254. doi: 10.1177/0310057x211047603
10. Papp Z, Édes I, Fruhwald S, et al. Levosimendan: Molecular mechanisms and clinical implications. International Journal of Cardiology. 2012; 159(2): 82-87. doi: 10.1016/j.ijcard.2011.07.022
11. Gurjar M, Baronia A, Azim A, et al. Managing aluminum phosphide poisonings. Journal of Emergencies, Trauma, and Shock. 2011; 4(3): 378. doi: 10.4103/0974-2700.83868

12. Mathai A, Bhanu M. Acute aluminium phosphide poisoning: Can we predict mortality?. Indian Journal of Anaesthesia. 2010; 54(4): 302. doi: 10.4103/0019-5049.68372
13. El-Sarnagawy G. Predictive Factors of Mortality in Acute Aluminum Phosphide Poisoning: 5 Years Retrospective Study in Tanta Poison Control Unit. Ain Shams Journal of Forensic Medicine and Clinical Toxicology. 2017; 29(2): 70-79. doi: 10.21608/ajfm.2017.18211
14. Shadnia S, Rahimi M, Pajoumand A, et al. Successful treatment of acute aluminium phosphide poisoning: possible benefit of coconut oil. Human & Experimental Toxicology. 2005; 24(4): 215-218. doi: 10.1191/0960327105ht513oa
15. Aghebat-Bekheir S, Abdollahi M. Discovering the most impactful treatments for aluminum phosphide cardiotoxicity gleaned from systematic review of animal studies. Human & Experimental Toxicology; 2024. doi: 10.1177/09603271241290922
16. Heringlake M, Alvarez J, Bettex D, et al. An update on levosimendan in acute cardiac care: applications and recommendations for optimal efficacy and safety. Expert Review of Cardiovascular Therapy. 2021; 19(4): 325-335. doi: 10.1080/14779072.2021.1905520
17. Tycińska A, Gierlotka M, Bugajski J, et al. Levosimendan in the treatment of patients with acute cardiac conditions: an expert opinion of the Association of Intensive Cardiac Care of the Polish Cardiac Society. Kardiologia Polska. 2020; 78(7-8): 825-834. doi: 10.33963/kp.15551
18. Lelonek M, Stopczynska I, Koroscik E, et al. Multicenter experiences with levosimendan therapy and its safety in patients with decompensated advanced heart failure. Advances in Clinical and Experimental Medicine. 2020; 29(11): 1305-1312. doi: 10.17219/acem/126301
19. Li H, Duan Y, Chen B, et al. New pharmacological treatments for heart failure with reduced ejection fraction (HFrEF). Medicine. 2020; 99(5): e18341. doi: 10.1097/md.0000000000018341
20. Follath F, Cleland JGF, Just H, et al. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial. Lancet. 2002; 360(9328): 196-202. doi: 10.1016/S0140-6736(02)09455-2