
Maii Farag Henaidy1, Ashraf A. Noah2, Mohamed Ayman El-Zahabi3, Hany Mustafa Gemeah4, Amal M. Shouair5, Reda R. Mabrouk4

1) Forensic medicine and clinical toxicology department, Faculty of medicine, Alexandria University, Alexandria, Egypt
2) Alexandria Clinical Research Administration, Directorate of Health Affairs, Egyptian Ministry of Health and Population, Alexandria, Egypt
3) Pharmaceutical Medicinal Chemistry and Drug Design Department, Faculty of Pharmacy, Al-Azhar University, Cairo, Egypt
4) Directorate of Health Affairs in Buhaira-Clinical Research Department, Ministry of Health and Population, Damanhur, Egypt

ABSTRACT:
Aluminum phosphide (AlP) poisoning presents a significant public health concern, particularly in developing countries where it is widely accessible. This case report presents successful management of acute AlP poisoning in a pregnant woman at 28 weeks gestation. The patient was presented with vomiting and abdominal pain but remained stable. Arterial blood gas analysis revealed metabolic acidosis, prompting bicarbonate administration. Dual therapy with N-acetylcysteine (NAC) and Coenzyme Q10 (CoQ10) effectively mitigated oxidative stress and stabilized the patient. Collaborative interdisciplinary care ensured maternal and fetal well-being, leading to a favorable outcome upon discharge. This case highlights effective therapeutic strategies and the importance of interdisciplinary collaboration in managing acute AlP poisoning.

Keywords: aluminum phosphide poisoning, pregnant woman, N-acetylcysteine, Coenzyme Q10, dual therapy

INTRODUCTION
Aluminum phosphide (AlP) is extensively utilized in agricultural settings to protect crops during storage and transportation, with applications spanning across silos, ships, and trains [1]. Particularly prevalent in developing countries, AlP is often distributed in tablet form, earning it the colloquial name “rice tablets” [2]. The popularity of these tablets is attributed to their affordability, potency, and easy accessibility, but they also carry a significant risk of poisoning and fatality[3].

In Egypt, AlP poisoning is emerging as a significant public health concern, with a predominant occurrence among individuals aged 18 to 45 years, mainly females from rural areas, and often associated with suicidal intent [4]. The toxicity of AlP stems from the release of phosphine gas upon contact with water or stomach acid, which is absorbed through the gastrointestinal tract and excreted primarily through the kidneys and lungs [5, 6].

Initial poisoning symptoms typically appear within 10-15 minutes and progress rapidly, affecting the cardiovascular and respiratory systems [7]. Ingestion may also cause gastrointestinal irritation, presenting as nausea, vomiting, epigastric and retrosternal pain, dyspnea, anxiety, irritability, and a distinctive odor resembling garlic or spoiled fish in the breath [1]. Gastrointestinal signs may include hematemesis, vomiting, and epigastric pain, with dysphagia as a common delayed complication [8]. Central nervous system manifestations include irritability, anxiety, dizziness, numbness, and tremor, with severe neurological signs such as delirium, seizure, and coma occurring later [9]. Hepatotoxicity often manifests as elevated liver enzymes and jaundice, with histopathological findings showing hepatocyte vacuolation and sinusoidal congestion [10]. Respiratory symptoms include tachypnea, dyspnea, crepitation, and rhonchi, often progressing to respiratory distress syndrome and pulmonary edema [1].

Cardiac symptoms involve ventricular enlargement, hypokinesia, arrhythmias, and hypotension, with electrocardiogram (ECG) changes indicating sinus tachycardia followed by conductive delays and arrhythmias [8]. Electrolyte abnormalities such as high or
low sodium, potassium, and magnesium levels, along with hypocalcemia, hyperglycemia, and changes in cortisol levels, may also occur and are associated with poorer prognosis [11]. Mitochondria, pivotal organelles abundant in cardiomyocytes, play a vital role in cellular energy production [12]. AIP disrupts mitochondrial function by inhibiting cytochrome-c oxidase and respiratory chain enzymes, leading to the generation of reactive oxygen species (ROS) and oxidative stress [13]. This oxidative damage manifests as lipid peroxidation, cell membrane disruption, and ultimately cell death, particularly affecting cardiomyocytes and contributing to cardiovascular complications [14].

Given mitochondria's significance, targeting them with therapeutic agents has gained attention in molecular pharmacology [15]. Coenzyme Q10 (CoQ10), a vital component of the mitochondrial electron transport chain, acts as an antioxidant, reducing cellular oxidative stress and potentially enhancing cardiac function [16]. Combining CoQ10 with paraffin oil has shown promise in improving outcomes in acute AIP poisoning cases [17]. N-acetylcysteine (NAC), another potent antioxidant, replenishes intracellular glutathione levels and has demonstrated protective effects against phosphate-induced oxidative stress in preclinical and clinical studies [18]. When administered alongside CoQ10, these antioxidants exhibit a remarkable cardioprotective effect, potentially serving as prophylactic agents against cardiotoxicity [19]. Thus, co-administration of CoQ10 and NAC emerges as a promising therapeutic approach to mitigate mitochondrial dysfunction, improve heart contractility, and enhance survival in patients with AIP poisoning.

Case presentation:
A 29-year-old pregnant woman, gravida 2, para 1, who had a previous normal vaginal delivery, presented to the emergency department at Kafr El-Dawwar hospital at 28 weeks gestation with a complaint of ingesting aluminum phosphate tablets approximately 4 hours prior to admission. She reported experiencing 4-5 episodes of vomiting and abdominal pain. Upon arrival, she was conscious, alert, and oriented. On general examination, her blood pressure was 100/60 mmHg, respiratory rate was 26 breaths per minute, pulse rate was 87 beats per minute, and temperature was 37.5°C. Arterial blood gas (ABG) analysis upon admission revealed a pH of 7.39, HCO₃ of 12.5 mmol/L, and CO₂ of 21 mmHg. She had no significant medical or surgical history. Obstetric and gynecological examination showed a lax abdomen with no uterine contractions or vaginal bleeding.

A comprehensive assessment of the patient's condition was conducted, including a complete blood count, blood glucose level, and liver and renal function tests (bilirubin, AST, ALT, urea, creatinine, BUN), which collectively indicated a stable state. Furthermore, troponin and MB-CK levels were within normal ranges, and an ECG was performed to verify the patient's cardiac function remained unaffected. Ultrasound confirmed a single viable fetus in breech presentation with adequate liquor at 28 weeks gestation, weighing 1468 grams, and a fundal placenta. Following consultation, it was decided to observe the patient closely and monitor her progress.

Discussion:
Clinically speaking, acute Aluminum phosphide (AIP) poisoning manifests as rapidly progressing cardiogenic shock and severe metabolic acidosis [20]. Despite appropriate supportive measures, patient survival often remains elusive, rendering the management of acute AIP toxicity an exceptionally daunting and challenging endeavor [21]. In our case, the initial assessment of the AIP-poisoned pregnant woman revealed critical vital signs, including hypotension, tachypnea, a normal pulse rate, and a slightly elevated temperature. ABG analysis indicated a metabolic acidosis state and a slight respiratory alkalosis, which are serious metabolic disturbances commonly associated with AIP toxicity [22].

Remarkably, despite these concerning clinical findings, the patient remained conscious, alert, and oriented, as evidenced by her Glasgow score and clinical assessment. This highlights the complex and unpredictable nature of AIP poisoning, where severe physiological disruptions can coexist with preserved cognitive function, at least in the early stages of intoxication [22]. Despite the absence of respiratory distress, continuous respiratory monitoring was upheld, obviating the need for intubation or ventilation. To rectify metabolic acidemia and maintain the patient's pH within an acceptable range, a regimen of 150 mEq of bicarbonate over 8 hours was administered, yielding subsequent ABG analyses showing resolution of the metabolic acidosis by the following day.

Apart from standard supportive care, medical practitioners were tried to improve AIP toxicity by either diminishing phosphine release in the stomach or mitigating phosphine-induced cellular dysfunction [23, 24]. Antioxidants like NAC and CoQ10 have also been clinically tested to alleviate phosphate-induced oxidative stress [16, 25].

A dual therapy approach was adopted to address AIP toxicity. NAC was administered at a dose of 150 mg/kg intravenously over 1 hour, followed by 50 mg/kg over 4 hours, and then 100 mg/kg over 16 hours in 5% dextrose. Furthermore, patients received 300 mg of CoQ10 as an antioxidant therapy, dissolved in the paraffin oil. Subsequently, CoQ10 was continued at a dose of 200 mg/day every 12 hours.

Our approach to utilizing NAC aligns with previous instances where the drug was employed to combat oxidative damage caused by AIP toxicity, while also providing preventive measures against cardiovascular complications [26, 27]. Moreover, a prior investigation determined that administering NAC led to elevated blood pressure and decreased mortality rates in analogous scenarios [28].

We administered CoQ10, an antioxidant that enhances myocardial contractility by boosting energy production at the mitochondrial level in cardiomyocytes [16]. Prior research corroborates our method, as CoQ10, in addition to its antioxidant capabilities, can rejuvenate cellular energy production, thereby selectively enhancing cardiac systolic function [17].

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Following stabilization, decontamination and supportive care, the patient was transferred to the toxicology department for further evaluation and monitoring. Consultation with the obstetrics and gynecology department led to a decision to place the patient under observation and follow-up closely. Continuous fetal monitoring was initiated to assess fetal well-being.

Throughout the observation period, the patient remained hemodynamically stable with no signs of worsening clinical status. Repeat ultrasound confirmed the presence of a single viable fetus with stable parameters. The patient did not develop any cardiac symptoms during the hospitalization, and she was discharged with appropriate follow-up arrangements to monitor for potential delayed complications and ensure continued fetal well-being.

**Clinical significance:**
Our case report clinically proves that the dual therapy (NAC and CoQ10) approach is therapeutically effective against AlP poisoning as NAC replenishes intracellular glutathione levels, offering protection against phosphine-induced oxidative stress, while CoQ10 enhances mitochondrial function and myocardial contractility.

The successful outcome in our case emphasizes the importance of incorporating NAC and CoQ10 into treatment protocols for AlP poisoning. Supported by existing research, this therapeutic strategy presents a promising approach to managing life-threatening AlP intoxications, potentially improving clinical outcomes and survival rates.

**Strengths and limitations:**
The present case report is well documented, including specific clinical findings, vital signs, diagnostic tests, and treatment approach is well-supported by existing research on the efficacy of NAC and CoQ10, aligning with current scientific evidence. Additionally, our case showcased the involvement of multiple specialties, such as toxicology and obstetrics, underscores the importance of comprehensive, multidisciplinary care.

However, the report lacks information on long-term outcomes for both the patient and the fetus, which would be crucial for a full assessment of the treatment's impact. Also, the absence of a control group for the treatment regimen makes it challenging to definitively attribute patient outcomes to the administered therapies.

**Future recommendations:**
Longitudinal studies involving larger patient cohorts or randomized controlled trials comparing NAC + CoQ10 dual therapy against standard care protocol or placebo should be conducted to address the variability in treatment responses and to assess the long-term outcomes. Further mechanistic studies are warranted to elucidate the underlying pathophysiological mechanisms of AlP toxicity, which could lead to the identification of novel therapeutic targets and the development of more effective treatment strategies.

**Conclusion**
In conclusion, AlP poses a significant threat in regions where it is readily available and commonly used for self-poisoning. Its rapid onset of toxicity, characterized by cardiogenic shock and metabolic acidosis, presents a considerable challenge in clinical management. Despite the daunting nature of treating acute AlP toxicity, our case study demonstrates the successful application of a dual therapy approach involving NAC and Co Q10, aimed at mitigating oxidative stress and enhancing myocardial function.

The administration of NAC and Co Q10 aligns with previous research highlighting their efficacy in combating AlP-induced toxicity and improving cardiovascular outcomes. Through meticulous supportive care and targeted interventions, our patient showed significant improvement and remained stable throughout her hospitalization.

Continuous monitoring and collaboration between medical specialties, including toxicology and obstetrics, were essential in ensuring the patient's well-being and the safety of her fetus. With appropriate management and close follow-up, the patient was discharged with a favorable prognosis, underscoring the importance of comprehensive care and interdisciplinary collaboration in managing complex cases of AlP poisoning.

**Declaration:**
**Ethics approval:** Ethical approval obtained via the Egyptian Ministry of Health and Population – Cent. Direct. For Research and Health Development (Approval No.: 13-2023/21).

**Informed consent to participate:** The authors certify that they have obtained all appropriate patient informed consent forms. In the form, the patient has given her consent for their images and other clinical information to be reported in the journal.

**Informed consent for publication:** Informed consent has been obtained for the publication from the patient.

**Availability of data and materials:** Available upon request to corresponding author.

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**References**

**Effective Management of Acute Aluminum Phosphide Poisoning in Pregnancy: A Case Study of Dual Therapy Efficacy and Collaborative Care**


