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Review Article

Novel Therapeutic Strategies in Managing Aluminum Phosphide Poisoning: A study based on Human Randomized Controlled Trials

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ABSTRACT

Background: Aluminum phosphide is a very lethal fungicide. It has serious complications, and there is no approved antidote. Therefore, this study investigated the novel therapeutic strategies in managing Aluminum Phosphide poisoning.

Methods: In this review, studies were identified using the keywords "aluminum phosphide poisoning" and "Randomized Controlled Trial" in the PubMed and Google Scholar databases from 2016 to 2025.

Results: In this investigation, the mechanism of toxicity, Clinical and Laboratory abnormalities, Complications, Diagnostic tests, Prognostic factors, and early management of Aluminum Phosphide poisoning were studied. Then, novel therapeutic strategies for aluminum phosphide poisoning were evaluated.

Conclusion: Although there is no effective antidote for aluminum phosphide poisoning, numerous therapeutic strategies, both previously reported and novel, have been proposed to manage it. However, their effectiveness has not yet been confirmed. For these reasons, preventing poisoning remains the most important priority. It is recommended to use fungicides less toxic than aluminum phosphide or to prevent easy access to it.

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Introduction

Pesticide poisoning can occur accidentally, intentionally, occupationally, or even as a suicidal attempt. This poisoning is a major health problem and is claimed to estimated 300,000 lives annually [1]. Aluminum phosphide (AlP) is a highly toxic substance used as a pesticide for grain storage, known in Iran as "Rice tablets" [2, 3]. In Iran, this substance is available in tablet form (3 grams) containing 1 gram of AlP [4]. Due to its cheapness, wide availability, and high toxicity, it causes many mortalities. Even one-sixth of this substance is fatal to humans, and the mortality rate is 70–100% [5, 6]. The duration of the poison's effect ranges from 1 to 48 hours (average 3 hours) [7]. Treatment of ALP poisoning is supportive, and there is no effective antidote [8]. However, previously recommended treatments for ALP poisoning include gastric lavage with sodium bicarbonate and charcoal, as well as magnesium sulfate, sodium bicarbonate, digoxin, Norepinephrine, and vitamin C. Also, poor-prognosis conditions in ALP poisoning include abnormalities in Electrocardiography, Acute Renal Failure, increases in blood sugar, leukocytes, and Uric Acid, and losses of consciousness, Blood Pressure, pH, and Prothrombin time [9, 10].

Type of study

In this investigation, the mechanism of toxicity, Clinical and Laboratory abnormalities, Complications, Diagnostic tests, Prognostic factors, and early management of Aluminum Phosphide poisoning were studied. Then, novel therapeutic strategies for aluminum phosphide poisoning were evaluated.

Evidence Acquisition

In this review, the required studies were searched using the keywords "aluminum phosphide poisoning" and "Randomized Controlled Trial" in the PubMed and Google Scholar databases from 2016 to 2025.

Discussion

Toxicodynamic: (the absorption, distribution, and mechanism) of toxicity

Aluminum Phosphide poisoning usually occurs by inhalation (usually unintentional) or oral ingestion (usually intentional in a suicide attempt). While poisoning by inhalation is rarely fatal, ingestion can lead to very serious consequences [7]. Also, Water, air humidity, or hydrochloric acid in the stomach release phosphine gas (PH3), which is colorless, flammable, and rapidly absorbed through inhalation, skin, or the gastrointestinal tract. Cardiomyocytes are a main target of PH3 [2]. Figure 1, shows the mechanisms of aluminum phosphide poisoning.

Clinical and laboratory findings and complications

The main features of Aluminum Phosphide poisoning include nausea, vomiting, epigastric pain,

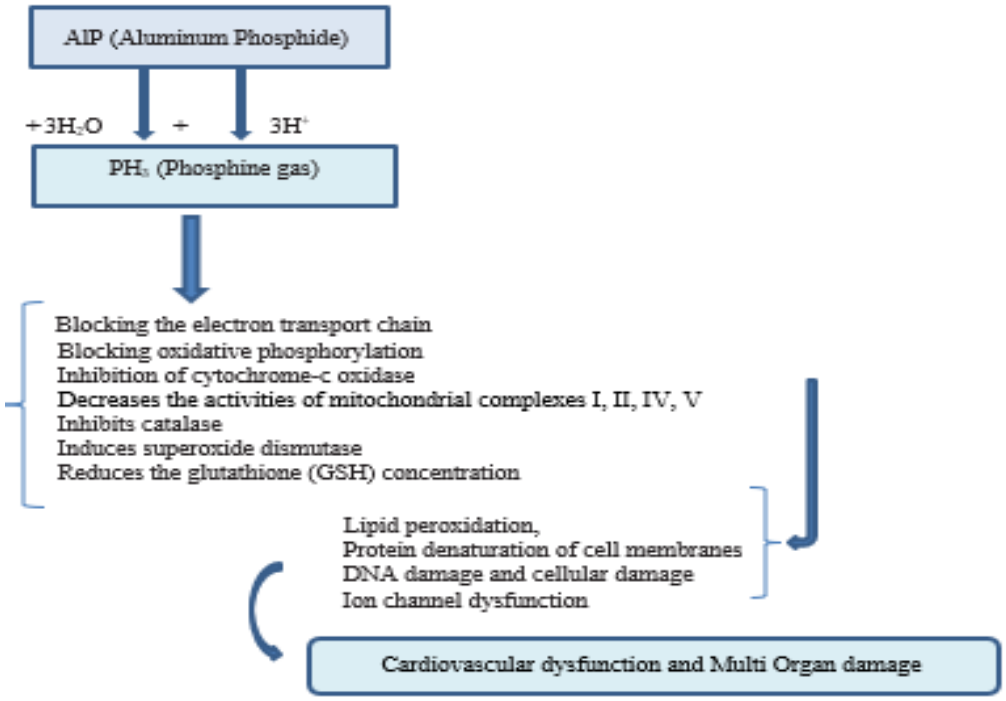

Figure 1. Mechanisms of action of Aluminum Phosphide poisoning [11].

Table 1. Novel Management of Aluminum Phosphide (ALP) poisoning, their mechanisms of action, and dosages based on Human Randomized Controlled Trials.

Studies	The number of patients	Novel Managing and dosages	Mechanisms of action
Goharbari et al (2)	24	**Oral liothyronine** 50 µg in the first 6 h	1. Improve (systolic blood pressure, arterial blood pH, and total thiol molecules) 2. Decrease (lipid peroxidation) 3. Increase (catalase activity) 4. Prevent (further decline in total antioxidant capacity)
El-Ebiary et al (5)	30	**N-acetyl cysteine (NAC)** 140 mg/Kg IV in the first, then 70 mg/Kg IV every 4 hours up to 17 doses	1. Antioxidant capacity
Mousavi et al (1)	24	**Triiodothyronine (T3)** 75 µg in the first, then 25 µg every 8 hours up to 3 doses	1. Maintain a higher range of SBP 2. Control cardiogenic shock 3. Regulate metabolism 4. Improve acidosis and blood pressure 5. Enhance recovery in patients 6. Cardio-protective effects
Abdelhamid et al (6) and Faraji Dana et al (7)	96 and 44	**Acetyl-L-carnitine (ALC)** 1g infusion of ALC upon arrival at the hospital, then every 8 hours	1. Enhances mitochondrial function 2. Inhibits mitochondria-dependent apoptosis 3. Reduces intracellular ROS levels by affecting ROS-catalyzing enzymes 4.Binds to Fe2+, leading to its deactivation
Abdelhamid et al (6), Elbastawesy et al. (12), Helal et al. (13)	96, 60, 62	**Paraffin oil** Mix of 50 ml paraffin oil added to 50 ml of Na HCO3 8.4% for lavage then 50 ml of paraffin oil was administered and left in the stomach.	1. Effective at suppressing phosphine release from ALP
Rahimi et al (8)	82	**Fresh-packed RBC Infusion** 2 units (250-300 ml per unit) were infused for 60-90 minutes with sixty minutes intervals.	1.Improved cardiac function 2.Balanced arterial blood gas profile, plasma electrolytes, and cardiac troponin levels 3.Normalize the body's buffering capacity 4.Improve the oxygen carrying-capacity and intravascular volume
Rasha et al (14)	84	**Coconut oil and Coenzyme Q10** 600 mg CoQ10 dissolved in 50 ml coconut oil; and repeated 12 hours later	1.Antioxidant capacity 2.Cardio - protective
Nelson et al (11), Adel et al (15) and Pannu et al (16)	- 108 60	**Insulin-euglycemia therapy** **Glucose-insulin-potassium (GIK)** Regular insulin: The first 1 IU /kg, then 1 IU /kg/h Bolus of dextrose: The first 0.5-g/kg then 0.5-g/kg/h	1.Improve survival and hemodynamics
Nelson et al (11) and Hafsa et al (17)	64 -	**Intravenous lipid emulsion (ILE, IFE), 20%** The first 1.5 ml/kg, then 0.25 ml/kg/min for 30 – 60 minutes	1.Improvement in the survival time, the mean arterial blood pressure, arterial blood gases 2. Significant reduction in serum lactate levels.
Halvaei et al (4)	36	**vitamin E** 400 mg, IM, every 8 hours	Antioxidant capacity

headache, dizziness, hypotension, loss of consciousness [3, 9]. AlP poisoning can cause myocardial infarction and various cardiac abnormalities, such as supraventricular tachycardia, ventricular tachycardia, sinus tachycardia, fibrillation, atrial fibrillation, and flutter, within the first 3 to 6 hours after ingestion. Other important complications of AlP poisoning are Cardiac arrhythmia, congestive heart failure, pulmonary edema, Hematologic abnormality, metabolic acidosis, cardiogenic shock, and acute Renal and Hepatic failure, even death [7, 12]. In one investigation, some of the results of blood chemistry analyses included Metabolic acidosis, Leukopenia, Leukocytosis, Hypokalemia, Hyperkalemia, Hypoglycemia, Hyperglycemia, Hyponatremia, Hypernatremia, Thrombocytopenia, and Abnormalities in Liver, Kidney, Pancreas, and coagulation function tests [9].

Diagnosis

The diagnosis of Aluminum Phosphide poisoning, including clinical features, initial and routine laboratory tests (especially Liver and Kidney function tests), Cardiac monitoring, and ultimately confirmation of the diagnosis by Silver Nitrate testing [9, 11, 12].

Prognostic factors

Previous studies have shown that conditions with poor prognosis in ALP poisoning include abnormalities in Electrocardiography, Acute Renal Failure, increases in (Blood Sugar, Leukocyte, and Uric Acid), and losses of (Consciousness, Blood Pressure, pH, and Prothrombin time) [9, 10].

Treatment

Some articles have suggested some treatments such as gastric lavage with Coconut oil, Sodium Bicarbonate, or Potassium Permanganate, and the use of Activated Charcoal. In addition, some specific treatments for ALP poisoning, including intravenous administration of Magnesium Sulfate, Calcium Gluconate, Sodium Bicarbonate, Digoxin, Vasopressor, Hydroxyethyl Starch, Glutathione, Beta-Carotene, Melatonin, Vasopressin, Milrinone, Iron, Sucrose, Glucagon, and Vitamin C, have been suggested [1, 2, 9, 10, 12]. Table 1 shows novel management options for Aluminum Phosphide (ALP) poisoning, their mechanisms of action, and dosages based on Human Randomized Controlled Trials.

Conclusion

Although there is no effective antidote for aluminum phosphide poisoning, many therapeutic strategies, both previously reported and novel, have been proposed to manage it [15]. Therefore, in recent years, new therapeutic strategies have been developed based on human randomized controlled trials for the management of Aluminum Phosphide poisoning (Table 1). Since the mechanisms of action of Aluminum Phosphide poisoning are cardiovascular dysfunction, severe metabolic acidosis, and multiorgan damage, resulting from the blockage of Oxidative Phosphorylation, inhibition of Cytochrome -C oxidase, and reduction of Glutathione concentration, most of the proposed treatments are based on Anti-oxidative therapy, Cardio-protective, and improve hemodynamics, although their efficacy has not been confirmed (Table 1). For these reasons, preventing poisoning remains the most important priority. It is recommended to use other fungicides that are less toxic than Aluminum Phosphide, or to prevent easy access.

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Conflicts of Interest

The author reports there are no competing interests to declare.

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