

Case Report

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Successful management of zinc phosphide poisoning: possible benefit of virgin olive oil

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Abstract

Metal phosphides in general and zinc phosphide, in particular, are potent insecticides and rodenticides. These are commercially used for protection of crops during storage, as well as during transportation. However, these are highly toxic substances. Zinc phosphide (Zn_2P_3) and other phosphides are generally misused intentionally for suicidal purpose in Turkey. While most fatal PH_3 exposures are unintentional, metal phosphide pellet ingestion has been used intentionally as a means of suicide in several Asian countries and in Europe. Once ingested, zinc phosphide is decomposed into highly toxic phosphine gas by the action of a dilute hydrochloric acid content of the stomach. Phosphine acts as a respiratory poison. Even 20:100,000 part of phosphine in the air is reported to be fatal. Their detrimental effects may range from nausea and headache to renal failure and death. Its poisoning has a high mortality and recent years have seen an increase in the number of poisoning cases and deaths caused by suicidal ingestion. In episodes of metal phosphide poisoning, the treatment depends on the route of exposure. We aimed to present an intentionally ingested Zn_2P_3 of 15 g patient on suicide purpose and our therapy with orally $NaHCO_3$, activated charcoal and virgin olive oil. In our case, we used repeated doses of virgin olive oil to induce antioxidant activity beside the recommended therapy regimens. Interestingly, the patient presented only mild symptoms of toxicity such as transient metabolic acidosis and hepatic dysfunction.

Keywords: Management, poisoning, zinc phosphide, virgin olive oil

Introduction

Metal phosphide rodenticides, such as aluminium (AlP), magnesium (Mg_3P_2) and zinc phosphides (Zn_3P_2), are used to protect food from insects and rodents [1]. Zinc phosphide (Zn_2P_3) has been used in rodenticide that commercially used for protection of crops during storage, as well as during transportation. Phosphides degrade under aqueous conditions, producing the deadly gas phosphine (PH_3) (1). Numerous studies have attempted to focus on the precise mechanisms of metal phosphide toxicity, particularly on the direct effects of the PH_3 gas. While most fatal PH_3 exposures are unintentional, metal phosphide pellet ingestion has been used intentionally as a means of suicide in several Asian countries and in Europe. A recent report of phosphine poisonings in Europe indicated that approximately 28% were by intentional ingestion and 65% were by accidental inhalation [2]. Renal failure and cardiac failure due to toxic cardiomyopathy were the commonest secondarily affected systems leading to rapid mortality [3].

Firstly; It blocks the enzyme cytochrome C oxidase as a result of which mitochondrial oxidative phosphorylation is inhibited. It also disturbs the mitochondrial morphology, inhibits oxidative respiration by 70% and

causes a severe drop in mitochondrial membrane potential, causing, in turn, the cells to die rapidly [3]. Mitochondrial cytochrome C oxidase inhibition may also lead to pulmonary and cardiac toxicity.

Secondly; Phosphine is responsible for the denaturation of oxyhaemoglobin molecule. It progressively converts oxyhaemoglobin to methaemoglobin and hemichrome species. The reaction of phosphine with oxyhaemoglobin leads to a formation of phosphite and phosphate ions [4]. Phosphine thus reduces the oxyhaemoglobin of blood. In episodes of metal phosphide poisoning, the treatment depends on the route of exposure. If the victim has ingested metal phosphide, the slurry of activated charcoal may be administered. Emetics should not be given orally. Metabolic acidosis must be treated by administering sodium bicarbonate. Activated charcoal, sorbitol suspension or sodium bicarbonate solution should be administered orally [3].

The main recommendation in most reported cases is that early recognition and treatment of phosphine/phosphide poisoning are of great importance and treatment of shock and metabolic acidosis together with the intensive care therapy of the cardiopulmonary effects are essential. Early vomiting is thought to improve the prognosis. Our recent experience of a 42-year-old man who had ingested 15 g of zinc phosphide and expected to have a fatal outcome, showed that early gastric lavage with serum physiologic solution, oral sodium bicarbonate solution, activated charcoal, oral virgin olive oil and intravenous magnesium contributed to survival.

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Case Report

A 42-year-old male presented to emergency department approximately 1 h after consumption of about 15 g of Zn₂P₃. His history was proved by his wife showing the package of Zn₂P₃. On arrival, he was conscious but irritable, with a pulse rate of 96/min, blood pressure (BP) of 95/75 mmHg, respiratory rate of 18/min, and temperature of 36.8°C. There was a slight flushing of the face, but he was otherwise asymptomatic. The patient had a Glasgow Coma Score of 14-15/15. The first venous blood gas analysis normal. Per abdominal physical examination revealed normal. An intravenous access was established and monitoring with an electrocardiogram (ECG), BP, and pulse oximetry. An abdominal X-ray showed radiopaque material throughout the gastro-luminal tract. In the emergency room, the patient was given gastric lavage with 0.9 NaCl solution (total 2000 mL) followed by oral administration of activated charcoal (1 g/kg of 30% suspension) plus oral sodium bicarbonate solution (8.4%, 100 mEq). The patient was given 50 ml of virgin olive oil to antioxidant activity. Then the second dose was given 50 ml 15 min later by nasogastric way. After then 50 ml was given following every 30 minutes he was given total 300 ml every 50 ml. During this period, pulse oximetry, BP, and ECG monitoring were normal. Slight metabolic acidosis, which was recovered to normal levels after the treatment, without administration of alkalization agents. During his examination in ED, he once vomited heavily. After vomiting to minimise the risk of intoxication due to the inhalation of phosphine patient was immediately decontaminated by washing and putting on a new dress. The patient was subsequently admitted to the Intensive Care Unit for cardiovascular and respiratory support

On the day of hospital admission, the patient experienced abdominal pain. Bedside ultrasound was normal. Afterwards, the pH and bicarbonate levels remained stable, indicating that the patient did not develop severe systemic toxicity.

In the 2nd day of admission, the patient developed slight metabolic acidosis (pH = 7.30, PCO₂ = 31.1 mm Hg, HCO₃⁻ = 14.2 mEq/L), as well as marked aminotransferase elevations (aspartate aminotransferase (AST): 62 IU/L, alanine aminotransferase (ALT): 32 IU/L). He was treated with the following intravenous drugs: sodium bicarbonate (for metabolic acidosis); magnesium sulphate (20%, 20 mL every six hours because of an antioxidant effect of magnesium); and pantoprazole (40 mg every 12 hours to suppress stomach acid secretion). He was treated with virgin olive oil (50 ml every 6 hours to increase antioxidant activity), activated charcoal (0.5 g/kg of 30% suspension every three hours) plus sodium bicarbonate (8.4%, 50 mL) every two hours) were administered via nasogastric tube. Administration of the charcoal, sodium bicarbonate and virgin olive was stopped after 48 hours. No arrhythmias were detected. Serum magnesium levels could not be measured on admission because in our hospital laboratory it is not included in the list of emergency tests. After 2 days his liver function tests (LFTs)

components changed to AST: 64 IU/L and ALT: 87 IU/L. Conservative treatment and supportive therapy were continued during hospitalisation. The patient was discharging from the hospital 3 days after poisoning. A follow-up liver function test was normal 2 weeks after discharge from a hospital.

Discussion

Metal phosphides are highly effective insecticides and rodenticides. These are frequently used to protect grains in stores and during its transportation. Poisoning by suicidal or accidental ingestion of zinc phosphide is a frequent medical emergency seen all over the world. On exposure to moisture, zinc phosphide liberates the highly toxic gas, phosphine. Generally, in phosphine poisoning, symptoms of toxicity usually develop rapidly, sometimes within 15 min. Our patient had admitted after about 60 min of ingestion. As early as an admission the more successful the treatment occurs. Early admission might be effective on this patient's survival. The majority of deaths occur within the first 12-24 hours, usually due to cardiovascular arrest. Deaths occurring after 24 hours are often due to liver failure [5].

The current recommended treatment protocol mentioned in textbooks includes lavage with sodium bicarbonate (3-5% solution) and administration of activated charcoal. We also applied these therapies. Activated charcoal can decrease the absorption of phosphide particles, which are thought to be responsible for delayed toxic effects [5]. Calcium gluconate and magnesium sulphate have been used with good results, presumably due to their membrane-stabilizing effects and also probably due to the antioxidant effect of magnesium. Acute phosphide poisoning produces hypomagnesaemia with or without ECG changes. However, the mortality rate is significantly higher in those patients with hypomagnesaemia who have ECG changes. A positive correlation has been demonstrated between mortality and lower magnesium concentrations in serum and red blood cells.

Phosphine blocks the enzyme cytochrome C oxidase as a result of which mitochondrial oxidative phosphorylation is inhibited. It also disturbs the mitochondrial morphology, inhibits oxidative respiration by 70% and causes a severe drop in mitochondrial membrane potential, causing, in turn, the cells to die rapidly [6]. Mitochondrial inhibition may also lead to pulmonary and cardiac toxicity [6]. Commonly to reduce mitochondrial inhibition 10% Ca gluconate and 25% magnesium sulphate are used as antioxidants. We preferred virgin olive oil as an antioxidant beside the recommended therapy protocol.

Virgin olive oil is high in saturated fatty acids and can be combined with other oils. Actually, it is believed that olive oil consumption could reduce oxidative damage, not only for its richness in oleic acid, and, but also for its minor components, particularly the phenolic compounds [7]. Natural olive oil has a long shelflife compared to other vegetable oils [8]. This should be attributed to its

fatty acid composition as well as to the presence of antioxidants [9]. Phenolic acid is a strong antioxidant. The more phenolic acid olive oil included the more effect seen as an antioxidant. Hydroxytyrosol, the major representative phenolic compound of virgin olive oil, is a dietary component. Its possible protective effect on hydrogen peroxide (H₂O₂)-induced oxidative alterations was investigated in human erythrocytes [9]. So it could play a role on major therapy protocols in phosphine poisoning. Extra virgin olive oil, characterised by a high DPE content, may be helpful to maximise the antioxidant potential in humans [9].

The antioxidant activity of virgin olive oil extracts, shown in vitro by their ability to inhibit the effect of oxygen radicals on salicylic acid, is apparent at concentrations much lower than those of the single antioxidant compounds tested individually; this is probably due to the presence of other polyphenolic compounds, some of which are still unknown [10]. Another potential effect of virgin olive oil is increasing the bowels motility so that the absorption of the phosphine can be reduced.

Calcium gluconate 10% and magnesium sulphate 25% have also been advocated [5]. The main difference between the treatment protocol done in the present case and those recommended in the literature is the use of virgin olive oil.

The most important phenolic compounds that may be divided into different groups: phenolic acids, phenolic alcohols, Seco iridoids, lignans, and flavones [11]. In addition, a qualitative and quantitative profile of these compounds has been used, in recent years, to classify olive oils in terms of their stage of maturation, varietal and geographical origin [12]. Protocatechuic and syringic acid were also found to have antioxidant activity. There is an interest in the level of phenols in olives, olive oil and the so-called rape, a major by-product of the extraction process, because of the antioxidant activity of the total phenolic fraction.

Hepatotoxicity due to Zn₂P₃ has been occasionally reported from India [13]. By the way, in our case, despite ingestion of large amounts of toxin, after forceful intestinal decontamination, this complication was provisional, and could not take the patient to a fatal outcome.

However, there are many reports of fatal outcome due to cardiovascular collapse or hepatic failure; it seems that we have more time to use decontamination techniques in the case of Zn₂P₃ poisoning compared to other metal phosphides. In our case, we used virgin olive oil to induce antioxidant activity. According to an article published in 2016, more aggressive gastrointestinal decontamination is necessary for patients [4]. Different studies in rats [14] and humans [15] have revealed that N-acetylcysteine can help as it replenishes cellular glutathione and magnesium, in addition to its antioxidant properties. In rats exposed to AIP, N-acetylcysteine

increased survival time and reduced myocardial oxidative injury [15].

There are reports of the positive clinical effects of coconut oil against AIP poisoning in humans. Its mechanism of action is unclear, but it may form a protective layer around the gastric mucosa and prevent the absorption of phosphine gas. In addition, coconut oil may dilute HCl in the stomach and reduce the breakdown of phosphide. Sweet almond oil considerably reduced the mortality of rats poisoned with AIP. It also significantly lowered plasma cholinesterase levels. The authors suggested that sweet almond oil should be given orally immediately after AIP ingestion, but this has yet to be confirmed in humans.

Conclusion

As a result; Measures of possible benefits include early gastric lavage with oral administration of sodium bicarbonate, activated charcoal, virgin olive oil, and intravenous administration of magnesium. Gastric lavage should be applied persistently with a large amount of fluid. Virgin olive oil exacts as a supporter to the therapy regimen. The administration of virgin olive oil by intervals with low doses is important to reduce the risk of potential vomiting caused by virgin olive oil. Diagnosis and therapy should be done as immediately as possible.

Finally, we confirm the clinical significance of this treatment protocol in the management of acute phosphide poisoning and encourage clinical doctors to start clinical trials to optimise this protocol.

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