Clinical manifestations and treatment management of hospitalized patients with zinc phosphide poisoning, Mazandaran Province, Northern Iran

Seyed Khosro Ghasempouri¹, Zakaria Zakariaei²*, Seyed Mohammad Hoseininejad³, Fatemeh Chinian⁴, Mostafa Soleymani⁵, Seyedeh Masoumeh Pashaei⁶ and Mahdieh Sadeghi⁴

Abstract
Background: Zinc phosphide (ZnP) is a dark gray crystalline compound used as a rodenticide against rodents such as mice. ZnP poisoning may be accidental or suicidal. The aim of this study was to investigate the clinical manifestations and treatment management of hospitalized patients with ZnP poisoning in Mazandaran Province, northern Iran.

Methods: Between 2013 and 2017, a cross-sectional study was performed on hospitalized patients with ZnP poisoning who were referred to two training hospitals in Mazandaran Province, northern Iran.

Results: A total of 127 patients participated in this trial, including 71 (55.9%) men and 56 (44.1%) women. The patients' average (standard deviation) age was 25.5 (±16.82) years, and it took 2.18 (±2.23) hours to refer them to the hospital. There were 42 (33%) cases with less than one package, 9 (7%) cases with several packages, and 76 (60%) cases with no particular usage.

Conclusions: This study has shown that ZnP poisoning may be asymptomatic initially or with mild clinical symptoms that may gradually worsen. Therefore, hospitalization and obtaining a history and a careful physical examination should be considered.

Keywords: Zinc phosphide, Poisoning, Suicide, Clinical manifestations

Introduction
Zinc phosphide (ZnP) and other compounds containing phosphine gas are effective fumigants and rodenticides that are widely utilized in many countries, particularly in developing countries. After consumption, phosphides are converted by gastric acid into phosphine gas, the main toxic substance. Phosphine gas then enters the bloodstream from the gastrointestinal tract. In humans, phosphine is a highly toxic gas that affects the body through a number of mechanisms, including inhibition of cytochrome c oxidase, oxidative respiration, the formation of free radicals via increased lipid peroxidation, and acetyl cholinesterase inhibition (AChE) [1, 2]. Phosphine gas released from refined grains in silos and other agricultural areas can be toxic by inhalation, and poisoning by it happens quickly (usually within 30 minutes of exposure) when it comes into contact with the skin [3, 4]. Phosphine gas generally affects organs such as the gastrointestinal (GI), cardiovascular, respiratory, hepatic, and hematologic systems, as well as causes...
electrolyte and metabolic disorders [1, 2]. Some of the serious symptoms of phosphine gas poisoning are hypotension, pulmonary edema, congestive heart failure, cardiac arrhythmia, cardiovascular collapse, and acute kidney injury [1, 5]. Hepatotoxicity and intravascular hemolysis with methemoglobinemia, as well as renal failure, are less common findings [6].

Since no specific antidote has been discovered, supportive care is the mainstay of management. Despite some efforts to develop more effective therapies and drugs for treatment, the fatality rate remains high, particularly for aluminum phosphide (AlP) toxicity. Although AlP and ZnP both produce phosphine gas in the human body, some symptoms and the mortality rate are different between these two metal phosphides [7, 8].

ZnP is a black powder or gray crystalline compound [1, 2]. Due to its low cost and widespread availability, ZnP is commonly used as a household rodenticide in developing countries due to its low cost. There are limited reports and clinical studies on ZnP poisoning in humans [5, 9–13]. The diagnosis of phosphide poisoning is made by history and clinical signs. Exposed patients may also show hypokalemia and elevated lactate levels, although these findings are not diagnostic. According to case reports, phosphide is radiopaque in x-ray imaging, so abdominal radiographs can help confirm the diagnosis [14]. Consequently, the current study was performed to investigate the clinical findings and early management of patients with ZnP poisoning who were referred to two training hospitals in Mazandaran Province, northern Iran.

Patients and methods
This cross-sectional study was approved by the Mazandaran University of Medical Science Ethics Committee (IR.MAZUMS.REC.1398.1717) and was carried out in accordance with the Helsinki Declaration Principles.

The current research is a cross-sectional study that was performed on patients with ZnP poisoning who were referred to two training hospitals (Imam Khomeini and Razi) in Mazandaran Province, northern Iran, from 2013 to 2017. Inclusion criteria included all patients with a history of ZnP ingesting, laboratory tests such as arterial blood gases and abdominal and pelvic x-rays. Exclusion criteria included incomplete information registration, dissatisfied patients, and those who did not cooperate.

Statistical analysis
The study’s statistical population included 127 ZnP poisoning patients, and data collection procedures included a checklist that contained personal and social information such as age, gender, and marital status. The amount of ZnP consumed, the time to refer to the emergency room, vital signs and clinical manifestations such as nausea, vomiting, abdominal pain, dyspnea, drowsiness, respiratory distress, palpitations, and level of consciousness were all recorded, as were diagnostic and therapeutic processes such as pulse oximetry, serum electrolyte levels, blood biochemistry, and the need for intubation.

The software used in this study was SPSS v.20, and a P value < 0.05 was considered a significant level. Frequency was used to show qualitative variables, and mean and standard deviation were used to express quantitative variables. A Pearson or Spearman coefficient was calculated to examine the correlation between quantitative variables, and a Chi-Square test was used to correlate the qualitative variables.

Results
This cross-sectional study was performed to investigate the clinical manifestations of patients with ZnP poisoning, and 127 patients were studied, in which

| Table 1 | Demographic index of evaluated patients |
| --- | --- |
| Variables | Frequency (%) |
| Gender |  |
| Men | 71 (55.9) |
| Women | 56 (44.1) |
| Marital status |  |
| Single | 48 (37.8) |
| Married | 79 (62.2) |

| Table 2 | Mean and standard deviation of patients’ vital signs |
| --- | --- |
| Variables | Lowest | Highest | Mean (SD) |
| Temperature | 37.00 | 38.20 | 36.70 (1.43867) |
| Systolic blood pressure | 75.00 | 160.00 | 116.0 (19.40022) |
| Diastolic blood pressure | 50.00 | 90.00 | 72.20 (11.96543) |
| Number of breaths | 12.00 | 33.00 | 18.93 (3.7245) |
| Heart rate | 65.00 | 175.00 | 88.74 (18.35112) |
| Spo2 | 88.00 | 100.00 | 98.10 (2.75462) |

| Table 3 | The frequency of the signs and symptoms during hospitalization in evaluated patients |
| --- | --- |
| Variables | Frequency (%) |
| Signs and symptoms |  |
| Nausea & Vomiting | 61 (48) |
| Abdominal Pain | 33 (25.9) |
| Respiratory Disorder | 3 (2.36) |
| Drowsiness | 5 (3.9) |
| Palpitation | 1 (0.787) |
| Abdominal pain, Nausea and Vomiting | 18 (14.1) |
Table 4  Pearson correlation was performed between different variables in patients, the results of which are shown in the table below

|                      | Age   | Referred time | Usage rate | Temperature | Blood pressure | Respiratory rate | Heart rate | Hypernatremia | Hyperkalemia | Acidosis |
|----------------------|-------|---------------|------------|-------------|----------------|------------------|------------|---------------|--------------|----------|
| Age                  | 1.000 |               |            |             |                |                  |            |               |              |          |
| Sig. (2-tailed)      | .     |               |            |             |                |                  |            |               |              |          |
| Referred time        | 0.001 | 1.000         |            |             |                |                  |            |               |              |          |
| Sig. (2-tailed)      | .     | .             |            |             |                |                  |            |               |              |          |
| Usage rate           | −0.05 | 0.180         | 1.000      |             |                |                  |            |               |              |          |
| Sig. (2-tailed)      | 0.996 | 0.111         |            |             |                |                  |            |               |              |          |
| Temperature          | −0.15 | −0.097        | −0.175     | 1.000       |                |                  |            |               |              |          |
| Sig. (2-tailed)      | 0.287 | 0.213         |            |             |                |                  |            |               |              |          |
| Blood pressure       | 0.270 | −0.162        | 0.020      | −0.025      | 1.000          |                  |            |               |              |          |
| Sig. (2-tailed)      | 0.730 | 0.211         |            |             |                |                  |            |               |              |          |
| Respiratory rate     | −0.38 | −0.207        | −0.066     | −0.053      | −0.223         | 1.000            |            |               |              |          |
| Sig. (2-tailed)      | 0.007 | 0.149         |            |             |                |                  |            |               |              |          |
| Heart rate           | −0.35 | −0.134        | −0.270     | −0.053      | −0.223         | 0.621            |            |               |              |          |
| Sig. (2-tailed)      | 0.014 | 0.352         |            |             |                |                  |            |               |              |          |
| Hypernatremia        | 0.127 | 0.032         | 0.110      | 0.117       | 0.127          | −0.201           | −0.201     | 1.000         |              |          |
| Sig. (2-tailed)      | 0.378 | 0.824         |            |             |                |                  |            |               |              |          |
| Hyperkalemia         | 0.035 | 0.174         | 0.124      | −0.020      | −0.025         | −0.053           | −0.053     | 0.117         | 1.000       |          |
| Sig. (2-tailed)      | 0.811 | 0.227         |            |             |                |                  |            |               |              |          |
| Acidosis             | −0.07 | −0.142        | 0.040      | 0.062       | 0.213          | −0.168           | −0.003     | 0.316         | 0.062        | 1.000    |
| Sig. (2-tailed)      | 0.627 | 0.326         |            |             |                |                  |            |               |              |          |
only one death was seen among the patients. Among the patients, 71 (55.9%) were male and 56 (44.1%) were female. The mean (standard deviation) age of patients was 25.5 (±16.82) years, with a minimum age of 2 years and a maximum age of 81 years. Also, 48 cases (37.8%) were single and 79 cases (62.2%) were married (Tables 1, 2 and 3).

The average (standard deviation) time of referring to the hospitals was 2.18 (±2.23) hours, with a minimum of half an hour and a maximum of 10 hours. In 42 cases (33%), the consumption amount was less than one package (each package of ZnP is 10 g) and more than one package in nine cases (7%). In addition, in 76 cases, it was unclear (60%).

Vital signs and serum electrolyte levels were evaluated, the results of which are shown (Tables 3, 4). Also, 5 cases (3.9%) of patients had dizziness, 1 case (0.787%) had diarrhea, 1 case (0.787%) had weakness and lethargy, 1 case (0.787%) developed a seizure, 4 cases (3.15%) had headaches, and 2 cases (1.57%) of patients were pregnant. In terms of symptoms and laboratory findings, one case (0.787%) had a temperature of more than 37.8 °C, two cases (1.57%) had blood pressure below 90 mmHg, and eight cases (6.29%) had blood pressure (BP) above 140 mmHg. More than 20 breaths/minute were recorded in 15 patients (11.8%), and a heart rate (HR) of more than 100 beats/minute was reported in 15 cases (11.8%). Hypernatremia was observed in 7 (5.5%) of the patients, whereas hyperkalemia was found in 1 (0.787%).

**Discussion**

In our study, with the exception of one case that died due to multiple organ failure, most patients had gastrointestinal symptoms, and no hepatic or renal failure was reported. The clinical manifestations in patients were as follows: nausea and vomiting in 61 cases (48%), abdominal pain in 33 cases (25.9%), nausea and vomiting with abdominal pain in 18 cases (14.1%), five patients had drowsiness, and three patients developed respiratory disorders. Hydration, insertion of a nasogastric tube, administration of charcoal-sorbitol, pantoprazole ampoule, and correction of acidosis with sodium bicarbonate were among the treatments provided to the patients.

The mortality rate in our study was 0.787% (1 patient), and this patient was an 81-year-old man (the oldest case in the study) who had an underlying disease. The cause of low mortality can be due to the humidity of the air in the study area, the low quality of the powder or its improper packaging, as well as the following early access to hospital care and the possibility of consuming small amounts of ZnP powder.

In 2017, Trakulsrichai et al. identified 455 poisoned people, 60.5% of whom were male, with a mean age of 39.91 years. The most common method of consumption was oral (99.3%). Most patients initially had normal vital signs and oxygen saturation with no altered mental status. Three of the most common clinical symptoms were gastrointestinal (68.8%), cardiovascular (22%) and pulmonary (13.8%). Most patients initially had normal blood test results and normal chest radiographic findings. The average hospitalization was 2 days, and the mortality rate was 7%. Approximately 70% of patients underwent gastric lavage and single-dose activated charcoal. A total of 31 cases underwent intubation and mechanical ventilation. Inotropic drugs were prescribed in 4.2% of cases [7].

Also, Nekoukar et al. reported a young man who, after intentional consumption of an unknown amount of ZnP powder, developed symptoms of nausea, vomiting, palpitations, jaundice, and liver and kidney failure, and died a few days later. They have concluded that in patients with a history of ingestion of rodenticide compounds, particularly ZnP, an arterial blood gas (ABG) and an abdominal x-ray are required, and GI decontamination with polyethylene glycol (PEG) should be considered in the presence of radiopaque substances [14, 15].

In 1998, Chugh et al. studied 20 cases in a study called “Symptoms of ZnP poisoning.” The most common manifestations were vomiting, abdominal pain, palpitations, sweating, dyspnea, tachypnea, metabolic acidosis, shock, and hypotension. There have been five deaths [5].

Gunaratne et al. reported severe ZnP poisoning in a 14-year-old girl who attempted suicide with phosphide and was referred for vomiting, then developed metabolic acidosis, acute pulmonary edema, acute renal failure, acute hepatic failure, and coagulopathy. She also had hyperglycemia, which is rare and is a poor prognostic indicator of exposure to phosphate gas. Upon admission to the hospital, the patient was conscious with a Glasgow Coma Scale (GCS) of 15, a HR of 80 beats/minute, and a BP of 70/100 mmHg [16].

In 2018, Hassanzadeh et al. reported a case of acute renal failure (ARF) and cardiac arrest following the consumption of ZnP rodenticide in Yasuj city. The patient was an 18-year-old man who used the rodenticide to commit suicide. They concluded that ZnP intoxication could lead to ARF [17].

**Conclusion**

Although many studies have shown that ZnP poisoning can be asymptomatic or cause mild clinical symptoms at first, it is associated with a poor prognosis and a variety of complications, including multi-organ failure and mortality, in some cases. To prevent undesirable consequences, timely and appropriate diagnosis and treatment are recommended in cases of phosphide compound poisoning.
Abbreviations
ZnP: Zinc phosphide; AChE: Acetyl cholinesterase inhibition; GI: Gastrointesti-
nal; AlP: Aluminum phosphide; ABG: Arterial blood gas; PEG: Polyethylene glycol; GCS: Glasgow Coma Scale; HR: Heart rate; BP: Blood pressure; ARF: Acute renal failure.

Acknowledgments
Not applicable.

Author contribution
SKG and SMH designed the study, wrote the manuscript. FC and SMP analyzed and interpreted the data. ZZ and MS involved in interpretation and editing the manuscript. MS is responsible for collecting data and submitting the manuscript. All the authors reviewed the paper and approved the final version of the manuscript.

Funding
The study was funded by the Mazandaran University of Medical Sciences. The funder has no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Availability of data and materials
The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
This research was approved by the Mazandaran University of Medical Science Ethics Committee (NO: IR.MAZUMS.REC.1398.1717) and was carried out in accordance with the Helsinki Declaration Principles. Written informed consent was obtained from each patient to enter the study.

Consent for publication
Not Applicable.

Competing interests
The authors have no conflicts of interest to declare.

Author details
1 Department of Forensic Medicine and Toxicology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran. 2 Toxicology and Forens-
ic Medicine Division, Orthopedic Research Center Communicable Diseases Institute, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, P. O box: 48166-33131Sari, Mazandaran, Iran. 3 Gut and Liver Research Center, Mazandaran University of Medical Sciences, Sari, Iran. 4 Student Research Committee, Mazandaran University of Medical Sciences, Sari, Iran. 5 Iranian National Registry Center for Lophomoniasis and Toxoplasmosis, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran. 6 Department of Emergency Medicine, Mazandaran University of Medical Sciences, Sari, Iran.

References
1. Proudfoot AT. Aluminium and zinc phosphide poisoning. Clin Toxicol. 2009;47(2):69–100.
2. Bumbrah GS, Krishan K, Kanchan T, Sharma M, Sodhi GS. Phosphide poisoning: a review of literature. Forensic Sci Int. 2012;214(1–3):1–6.
3. Kambayashi K. Early diagnosis and treatment of heavy metal poisoning. Naika Internal medicine. 1969;23(6):1285–92.
4. LeWitt PA. The neurotoxicity of the rat poison vacor. A clinical study of 12 cases. N Engl J Med. 1980;302(2):73–7.
5. Chugh SN, Aggarwal HK, Mahajan SK. Zinc phosphide intoxication symp-
toms: analysis of 20 cases. Int J Clin Pharmacol Ther. 1998;36(7):406–7.
6. Dogan E, Guzel A, Ciftci T, et al. Zinc phosphide poisoning. Case Rep Crit Care. 2014;2014:589712.
7. Trakulsrichai S, Kosanyawat N, Atikasawedparit P, et al. Clinical char-
acteristics of zinc phosphide poisoning in Thailand. TherClin Risk Manag.2017;13:335–40.
8. Hassanian-Moghadam H, Shahnazi M, Zamani N, et al. Plain abdominal radiography: a powerful tool to prognosticate outcome in patients with zinc phosphide poisoning. ClinRadiol. 2014;69(10):1062–5.
9. Marashi SM. What really happens after zinc phosphide ingestion? A debate against the current proposed mechanism of phoshpine liberation in zinc phosphide poisoning.Eur Rev Med Pharmacol Sci. 2015;19(22):4210–1.
10. Kamal Ael A, Abd el-Hamid DM, Hatch DL, Ahmed Ael N. Epidemiological study of the claimed zinc phosphide intoxication in Komombo district April 1996. J Egypt Public Health Assoc. 1999;74(1–2):175–91.
11. Frangides CY, Pneumatikos IA. Persistent severe hypoglycemia in acute zinc phosphide poisoning. Intensive Care Med. 2002;28(2):223.
12. Sangle SA, Thomas A, Verma S, Wadia RS. Zinc phosphide poisoning. J Assoc Physicians India. 1987;35(8):591–4.
13. Rodenberg HD, Chang CC, Watson WA. Zinc phosphide ingestion: a case report and review. Vet Hum Toxicol. 1989;31(6):559–62.
14. Patial RK, Bansal SK, Kashyap S, Sharma AK, Sharma B. Hypoglycemia following zinc phosphide poisoning. J Assoc Physicians India. 1990;38(4):306–7.
15. Nekoukar Z, Moghimi M, Rasouli K, et al. Suicide attempt using zinc phosphide rodenticide: A case report and literature review. Clinical case reports. 2021;9(10).
16. Gunaratne W, Wijeratne A, Pilapitiya S, Siribaddana S. A case of severe zinc phosphide poisoning. 2016.
17. Hasanadeh S, Tahrhasebi M, Aya A, Rohani M, Masnavei E, Jokar S. A case report: acute kidney injury and cardiac arrest after poisoning with the uncommon type of rodenticide (zinc phosphide) in Yasouj. Armaghane danesh. 2018;22(6):804–11.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.