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Case Report of Suicide Attempt Using Zinc Phosphide in Nepal

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Abstarct

Zinc phosphide is an easily available rodenticide and a common mode of poisoning in the Indian subcontinent. It is highly toxic with a mortality rate ranging from 37-100 percent. The proposed mechanism of toxicity is due to the release of phosphine gas after contact with gastric acid. The gas thus liberated, inhibits cytochrome C oxidase and oxidative respiration. The affected systems are cardiovascular, respiratory, gastrointestinal, hepatobiliary, and hematologic systems and cause electrolyte imbalance. Additionally, metabolic acidosis and an increase in lactate levels can be correlated with the degree of toxicity. The onset of effects can be as early as 4 hours and the risk gradually decrease after 72 hours. There is no antidote to the poison.

Aggressive intensive care monitoring and supportive management are the only methods. Early gastric lavage with activated charcoal to induce vomiting is advised. Attempts to clear the zinc phosphide early from the lumen with evidence in the X-ray abdomen using Castor oil have been tried, showing a beneficial effect. Along with this, antioxidants such as alpha-lipoic acid and injectable magnesium sulfate can prevent oxidative injury. Early use of Vitamin K and use of N-acetyl-cysteine have been used to prevent and treat liver injury. However, these methods have not been incorporated in the standard treatment regimen but have shown positive results in preventing mortality. Further extensive studies and standardized treatment is needed for Zinc phosphide poisoning.

Introduction

Pesticides and rodenticides containing zinc phosphide (ZnP) are easily accessible chemicals worldwide. The prevalence of Zinc Phosphide poisoning is comparatively higher in Asian countries, where intoxications are mainly caused by the intentional intake of the substance for suicidal purposes (Bilics, Héger, Pozsgai, Bajzik, Nagy & Somosközi, 2020). The mortality rate of zinc phosphide poisoning is around 37–100% worldwide (Dogan, Güzel, Çiftçi, Aycan, Çelik, Çetin, 2014). Poisoning is the second most common method of suicide in Nepal after hanging. National data are available for 2017 and 2018. During these years, 5317 and 5819 suicides were reported to the police (a total of 11,136); 2535 (22.8%) suicides were due to poisoning of which more than 90% of cases are due to pesticides (Ghimire, Utyasheva, Pokhrel, Rai, Chaudhary, Prasad, 2022).

The toxicity of metal phosphides is due to phosphine liberated when ingested

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phosphides come into contact with gut fluids, the gas being absorbed through the alimentary mucosa and distributed to tissues (Proudfoot, 2009). Phosphine is a highly toxic gas in humans and exerts its effects by many proposed mechanisms, including inhibition of cytochrome C oxidase and oxidative respiration. Phosphine is responsible for the denaturation of oxyhemoglobin molecules. It progressively converts oxyhemoglobin to methemoglobin and Hemi chrome species. The reaction of phosphine with oxyhemoglobin leads to the formation of phosphite and phosphate ions (Altintop &Tatli, 2017). Phosphine mainly affects the cardiovascular, respiratory, gastrointestinal (GI), hepatobiliary, and hematologic systems and causes electrolyte and metabolic abnormalities (Trakulsrichai, Kosanyawat, Atiksawedparit, Sriapha, Tongpoo, Udomsubpayakul, 2017). The earliest symptoms are usually nausea, abdominal pain, chest tightness, excitement and agitation, and a feeling of chilliness and of being "cold all over." Vomiting is constant; if it follows within an hour, the prognosis is improved. Jaundice has been rarely noted in fatal cases, but has been a feature of survivors.

Shock, early dyspnea, thirst, oliguria, convulsions, or coma have been features of fatal cases. Most of the deaths had been due to refractory hypovolemia and prerenal kidney injury together with fulminant liver failure, acute pulmonary edema, and metabolic acidosis both high and normal anion gap due to lactic acidosis caused by hypoxia, distal renal tubular acidosis respectively. The majority of fatal cases die after about 30 hours, probably because of cardiac damage. Those who survive three days are out of danger (Stephenson,1967; Yogendranathan, Herath, Sivasundaram, Constantine, Kulatunga, 2017). No specific antidote has been identified; therefore, the main treatment is supportive care (Yogendranathan et al., 2017). Zinc with an atomic number of 30 is a potentially radiopaque material that is a constituent of the famous zinc phosphide rodenticide(Hassanian-Moghaddam et al., 2014).

Data and Methods

This case report is based the direct clinical trial of a patient who consumed Zinc phosphide poisoning and was admitted to the ICU. The various data and management protocols applied for the management were extracted from the literary articles from Google scholar, PubMed, and research papers from Nepal Health Research Council. The management protocols were mostly the case reports from various countries like Thailand, Hungary, India etc.

Findings and Discussion

Case Presentation

A 51-year male ingested 3 packets of Commando (Zinc Phosphide) which is equivalent to 10 gram per packet, with the intention of suicide after a dispute with his son. According to the patient's party, he consumed the poison at his workplace when he was alone. After consumption, the patient vomited 3 times which mostly consisted of food particles. The patient presented to our Emergency Department after 4 hours of ingestion where a rapid initial evaluation was done. He was ill-looking and drowsy. He did not

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have any symptoms relevant to zinc phosphide poisoning except fast-shallow breathing. His pulse rate was 100 beats per minute, blood pressure was 130/98 mmHg, respiratory rate was 22 breaths per minute, blood oxygen saturation was maintained at 94% in room air and Glasgow Coma Scale(GCS) was 15/15. Initially intravenous access was secured with 20 Gauge cannula following which nasogastric and Foley's catheter were inserted. Gastric lavage was done with 2 liters of normal saline and 50 grams of activated charcoal. Intravenous medications included Pantoprazole, Ondansetron, Vitamin K and N-acetyl-cysteine were given prophylactically. Baseline investigations were sent. The total leukocyte count was 11,000 cells/cumm, Renal Function Test were within normal limits, along with Liver Function Test except for Alkaline Phosphatase(ALP) which was 370 U/L. PT/ INR 13 and 1.08. Arterial Blood Gas (ABG) was done which showed pH of 7.34, pCO2 of 29.9mmHg, Lactate of 3.4 and HCO3 of 16.9.

Subsequently, an X-ray abdomen was done which showed the presence of radio-opaque zinc phosphide poison in the abdomen. The patient was then shifted to the Intensive Care Unit(ICU) with informed consent and expected prognosis. In ICU, the patient's vitals, urinary output, blood sugar, PT/INR and ABG were monitored strictly. ABG, CBC, RFT, and LFT were done on a daily and on requirement basis. N-acetyl-cysteine was given as per the paracetamol poisoning protocol which was 10.5 gm in 200 ml D5W over one hour, then 3.5gm in 500ml D5 over four hours, and subsequently 7gm in 1000ml D5 over the next 16 hours Castor oil, which acts as a powerful laxative, helps in early removal of the compound from the bowel and was initiated at the dose of 60ml via nasogastric tube on a requirement basis till X-ray abdomen was clear of radio-opaque Zinc phosphide. On the first day, it was given 3 times, and on the second day it was given 2 times.

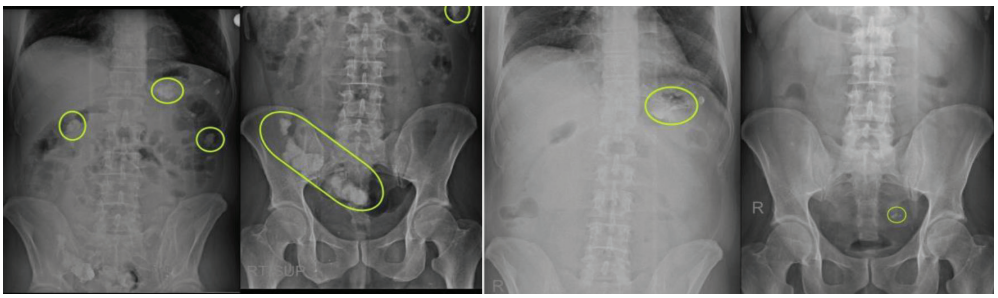
In addition, an injection of Metoclopramide was given to increase intestinal motility and treat nausea. Alpha-Lipoic Acid, an antioxidant, 600 mg by nasogastric tube once a day was initiated, which was changed to oral after 4 days and continued for a total of 7 days. On the day 4, Psychiatry consultation was done. Capsule Olanzapine and Tablet Clonazepam were added for Adjustment Disorder with a Brief Depressive Reaction.The patient was shifted to a ward after 24 hours of the asymptomatic period from the clearance in the X-ray abdomen. On the first follow-up CBC, RFT, LFT, Xray Chest, and Urine RE were repeated which were within normal limits.

Investigations	Reference Range	At Admission	6 hrs	Day 1	Day2	Day 3	Day 4	Day 5	Day 6	At Discharge	1 week follow-up
Total Differential Count	4000-11000/cumm	11000		12,100	4300	5700	7100	7000	7500	8000	9000
Neutrophils	40-75%	68		82	51	63	57	55	55	60	66
Lymphocytes	20-45%	24		11	39	25	12	31	30	25	30
Monocytes	2-10%	7		6	1	10	7	10	5	8	6

Eosinophil	1-6%	1		1	9	2	1	4	4	1	1
Basophil	0-2	0		0	0	0	0	0	0	0	0
Hemoglobin	M13-18gram% F12-16%	16		15.2	14	12.9	13.1	12.5	12.5	12.6	13
Platelets	150000-450000/cumm	1,70,000		1,52,000	1,53,000	1,41,000	1,52,000	147000	146500	146000	147000
Sodium	135-145meQ/L	138		137.7	139.4	137	139	140	140	139	140
Potassium	3.5-4.5meQ/L	3.93		4.26	3.8	3.58	**3.4**	4	3.9	4	4.1
Urea	15-40mg/dl	23		21	17	20	20	21	25	20	26
Creatinine	0.4-1.3mg/dl	1		0.8	1.1	0.8	0.8	0.9	0.8	0.8	0.9
Bilirubin Total	0.2-1.2mg/dl	0.4			1		0.8		0.5	0.6	0.7
Bilirubin Direct	<0.3mg/dl	1			0.4		0.3		0.2	0.2	0.1
SGPT	0-45U/L	18			16		21		21	20	22
SGOT	0-35U/L	19			27		59		52	45	30
Alkaline	<270U/L	**370**			230				230	220	200
Phosphatase											
PT	10-14secs	13	15	12	14	14	13	14	12	13	12
INR	0.9-1.1	1.08	**1.2**	1	**1.16**	**1.16**	1.08	1.16	1	1	1.08
Magnesium	1.61-2.61 mg/dl	**1.6**		1.9							
ABG											
pH	7.35-7.45	7.34	7.37	7.44	7.49	7.46	7.45	7.5			7.4
pO2	83-108mmHg	81	49	60	77	82	68	60			90
pCO2	35-45mmHg	26.9	29.5	33.1	33.8	31.8	28.1	28.6			40
HCO3	20-25mmol/L	14	16.9	22.5	25.5	22.5	19.5	23.3			23
Lactate	0.7-2.5mmol/L	5.8	3.4	1	0.44	0.81	1.64	0.37			0.9

Abdominal Xrays showing radio opaque Zinc Phosphide particles in stomach and duodenum

Day 1:



Before administration of Castor Oil **Six hours after administration of Castor Oil**

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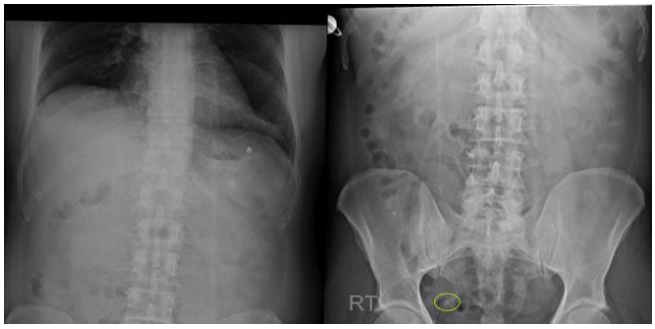
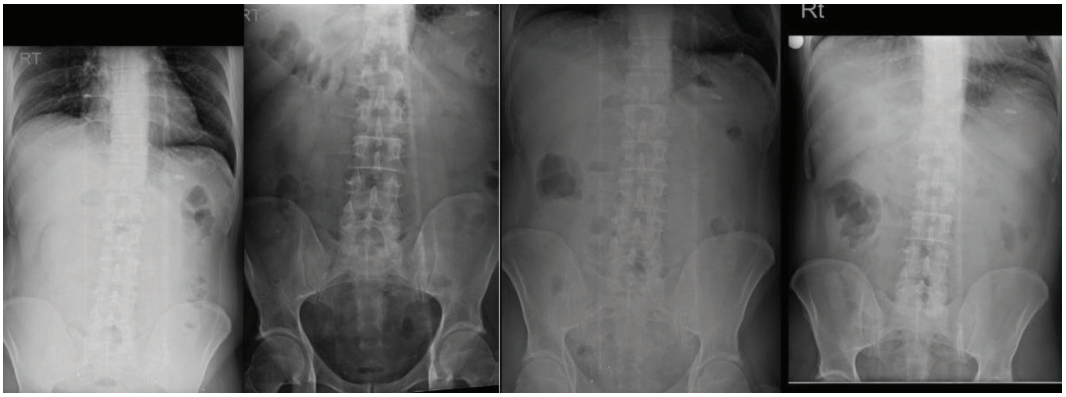


12 hours aftera dministration of Castor Oil

Day 2: **Day 3:**



Discussion

Zinc phosphide is a household rodenticide and its use for intentional suicide consumption is common in the Indian sub-continent. Nepal is an agricultural country where pesticides are widely used for pest control and easily accessible. Poisoning is the second most common method of suicide (Ghimire et al., 2022). Zinc phosphide (ZnP) is a heavy, dark gray, crystalline powder, which evolves phosphine rapidly in dilute acid or very slowly in water (Stephenson, 1967). A dosage of 4 to 5 g of zinc phosphide (55–70 mg/kg) had resulted in human deaths in acute toxicity (Yogendranathan, 2017). This dose is consistent with our patient who consumed approximately 30 gm of poison. The mortality rate of zinc phosphide poisoning is around 37–100%(2). It causes both metabolic and nonmetabolic toxic effects. The mechanism of phosphide poisoning has been explained as follows by various studies (Yogendranathan, 2017).

- Phosphine inhibits the oxygen uptake in the rat liver mitochondria.
- It inhibits ADP uncoupled site and ion stimulated respiration thus affecting pyruvate malate, succinate, glycerophosphate, and ascorbate cytochrome biomolecules in liver mitochondria. However, the exact target site is a contentious issue.

- It alters mitochondrial morphology, inhibits oxidative respiration by 70%, and causes a large drop in mitochondrial membrane potential within 5 h of exposure.
- Phosphine and hydrogen peroxide can interact to form the highly reactive hydroxyl radical that causes lipid peroxidation which is the main mechanism of oxidative damage to cell structures that lead to cell death.
- Cytochrome C oxidase system is inhibited.
- There is decreased activity of cytochrome oxidase along with altered NADH and succinic dehydrogenase activities.
- It increases the lipid peroxidation in the central nervous system while reducing the antioxidant defense system such as superoxide dismutase, catalase, and glutathione reductase.
- It inhibits protein synthesis and enzymatic activity.
- It has anti-choline esterase effects and also causes denaturation of oxy-hemoglobin molecules.

Phosphine mainly affects the cardiovascular, respiratory, gastrointestinal (GI), hepatobiliary, and hematologic systems and causes electrolyte and metabolic abnormalities. The severe clinical symptoms in patients with phosphine poisoning include circulatory collapse, hypotension, pulmonary edema, congestive heart failure, cardiac arrhythmia, and acute renal failure. No specific antidote has been identified; therefore, the main treatment is supportive care (Trakulsrichai et al., 2017; Jamshed, Ekka, Aggarwal, Narayan, 2014). The case in the study vomited immediately after ingestion and had no severe symptoms except tachypnea and drowsiness.

Initially, if the patient presents within a few hours of ingestion gastric lavage is recommended (14) for patients with phosphide intoxication, and the use of charcoal (Dogan et al., 2014) is also advised. In line with these reports, gastric lavage was done and charcoal was used in our patient. Activated charcoal can decrease the absorption of phosphide particles, which are thought to be responsible for delayed toxic effects (Altintop, 2017). The toxicity of the poisoning is mainly manifested in lungs, liver,kidney and heart (Stephenson, 1967). As per the review, baseline investigations CBC, RFT, LFT, PT/INR, Elcetrolytes (Calcium,Magnesium), Arterial blood gas analysis were sent daily as determination of acidosis can reflect the severity of PH3 toxicity (Marashi, Arefi, Behnoush, Nasrabad, Nasrabadi, 2011). Recently, Hassanian-Moghaddam et al. suggested performing abdominal X-ray in the case of suspected ZnP poisoning, even if the patient is asymptomatic. They indicated that a positive abdominal radiography could be considered as poor prognostic factor. This fact can confirm the idea of PH3 absorption through luminal mucosa (Shakoori et al., 2016).

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As suggested by Shaakori et al., forceful decontamination with castor oil, a powerful laxative, with aim to remove zinc phosphide particles from the abdomen have been proven beneficial as it can reduce toxin absorption(Shakoori et al., 2016).The removal of the phosphide particles was , monitored by the abdominal Xray which was clear after 48 hours. Apart from castor oil injection N-acetyl-cystine (Proudfoot, 2009; Bhat & Kenchetty, 2015), Alpha lipoic acid (ALA) (Bilics et al., 2020), were used as a measure to prevent liver injury and as an anti-oxidant respectively. As the synthetic function is determined by PT/INR, there was slight increase in the parameter for which Vitamin K was used for maintenance of this function (Yogendranathan et al., 2017). On day 4, the vitals were stable and the patient was shifted to general ward. The patient was later discharged on day 7. With the above-mentioned novel approaches and vigilant monitoring, the patient survived the highly toxic poisoning with no antidote.

Conclusion

Zinc phosphide is an easily available rodenticide with high mortality and no antidote. Intensive monitoring with symptomatic management is the mainstay of treatment. Measures to decrease absorption with the use of gastric lavage, increase clearance with castor oil aided by abdominal X-ray, use of antioxidants such as Magnesium sulfate and Alpha-lipoic-acid, and injectable Vitamin K have shown to be beneficial in preventing mortality. Furthermore, a more extensive study is required for the confirmation of the above approaches.

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