Acute Liver Failure and Intravascular Haemolysis in Zinc Phosphide Poisoning

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PRESENTATION OF CASE

A 37-year-old male presented with symptoms of nausea, vomiting, abdominal pain, jaundice, lacrimation and reddish brown urine discoloration since 2 hours after ingestion of 30 gms of zinc phosphide with suicidal intent 4 hours before arriving at the hospital. There was no history of hematemesis, melena, convulsions. On examination blood pressure: 140/90 mmHg, Pulse: 120 beat per minute, RR: 24 cycles/minute, temperature: 37.5°C and O_2 saturation: 91 percent in room air. Visible icterus was present. Diffuse tenderness was reviled by abdominal tests. Organomegaly was not present. The neurological examination was not important. There were flapping tremors. With 0.9 percentage of NaCl solution added with activated charcoal, the patient was given gastric lavage. Table 1 displays laboratory tests in the emergency department.

Zinc phosphide (ZnP) is a rodenticidal agent. The most common complications after ingestion are nausea, vomiting, hypotension, and metabolic acidosis. We present 37-year-old male patient presenting in this hospital's emergency department (ED), with nausea, vomiting, abdominal pain lacrimation, jaundice, and reddish brown urine discolouration. Medical studies identified symptoms of intravascular haemolysis and acute liver failure. The patient was managed successfully with transfusions of blood, fresh frozen plasma (FFP), N acetyl cysteine (NAC).

Rat shoot is a commercially available rodenticide that contains the active ingredient Zinc Phosphide (ZnP). It is a rodenticide which is low cost, accessible and very reliable.[1,2] It has been misused worldwide as a suicide poison. It contains 32 percent zinc phosphide that is highly toxic. For suicidal or homicidal attempts, it is typically ingested accidentally or intentionally.[3] It enters the body through skin, respiratory and gastrointestinal tracts. The gastric acid hydrolyses it, and converts it into phosphine gas.[4] The most serious complications associated with ZnP poisoning are non-specific gastrointestinal symptoms and cardiotoxicity. Phosphine inhibits the cytochrome C oxidase system that causes renal failure and hepatic failure.[5] Intravascular haemolysis is a reported complication of ZnP poisoning.

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Laboratory Parameters	Normal Range	Results	Laboratory Parameters	Normal Range	Results
BUN (mg/dl)	5-20	20	Platelet count (*10³/m³)	150-400	358
Creatinine (mg/dl)	0.5-1.5	0.8			
Serum Na (mEq/l)	135-145	145	PT (s)	11–13 s	16.1
Serum K (mEq/l)	3.5-4.5	3.5	INR	1-1.5	1.9
LDH (U/L)	225-500	1170	Bilirubin (mg/dl)		
CPK (U/L)	20-200	102	Total	0.2–1.3	6.0
Amylase (U/L) Urine for haemoglobin	30-100 Positive	60	Direct Indirect	< 0.2 0.3-1.0	2.0 4.0
Blood glucose (mg/dl)	70-110	92	AST (IU/L)	11–47	456
WBC (*10³/m³)	4-11	13.2	ALT (IU/L)	7–53	784
RBC (*10³/m³)	3.5-5.5	4.4	ALP (IU/L)	38–126	90
Haemoglobin (g/dL) G6PD	12.5-17.5 5.5 to 20.5 U/gram of Hb	9.5 10	Ph	7.35-7.45	7.32

Table 1. Laboratory Data of the Patient in Emergency Department

The patient was treated with blood transfusions due to acute hepatic failure and haemolysis, with 5 units of fresh frozen plasma (FFP), n-acetyl cysteine (NAC) 150 mg/Kg as loading dose in 15 minutes, followed by 50 mg/Kg (3 gr) in 500 cc DW 5% in 4 hours and then 100 mg/Kg (6 gr) in 1000 cc DW 5% in 16 hours as maintenance dose, Syp. Lactulose, Tab. Rifaximin. Taking into account the low haemoglobin level of 7.9 mg/dl, we transfused 2 units of packed red cells and it then reached 9.5 mg/dl. The laboratory parameters changed slowly over the next 5 days (pictured in Table-2). The patient was found to be healthy on the ninth day after admission, laboratory tests were found to be normal after which the patient was referred to department of psychiatry and discharged from department of toxicology.

Laboratory Parameters	Normal Range	12 hr	Day 1	Day 2	Day 3	Day 4	Day 5	Day 9
Lactate dehydrogenase	225-500 U/L	1170	2025	2571	1440	668	420	409
Creatinine phosphokinase	20-200 U/L	350	525	606	400	109	100	100
White blood cells (WBC)	4-11*10³/m³	12.3	19.1	18.4	9.2	7.6	8.0	6.8
Red blood cells (RBC)	3.5-5.5 *106/m3	3.4	2.04	3.9	3.5	4.9	3.6	4.1
Haemoglobin	12.5-17.5 g/dL	7.9	6.9	7.9	9.5	12	12.1	12.3
Platelet count	150-400 *10³/m³	201	100	94.0	150	252	243	354
Prothrombin time (PT)	11–13 s	18.8	21	16.0	11.2	13.1	12.1	11.1
International normalized ratio (INR)	1-1.5 s	1.9	2.9	1.9	1.2	1.4	1.3	1.2
Total bilirubin	0.2-1.3 mg/dL	6.0	8.2	8.0	4.6	2.0	1.9	1.1
Indirect bilirubin	0.3-1.0 mg/dL	4.0	5.2	5.1	3.1	1.3	1.3	0.9
Direct bilirubin	<0.2 mg/dL	2.0	3.0	2.9	1.5	0.7	0.6	0.2
Aspartate aminotransferase (AST)	11–47 IU/L	90	155	100	60	25	30	24
Alanine aminotransferase (ALT)	7–53 IU/L	140	185	150	100	70	64	57
Alkaline phosphatase (ALKP)	38-126 IU/L	139	150	140	150	155	140	130
pH	7.35-7.45	7.51	7.54	7.42	7.49	7.35	7.34	7.37
PCO_2	33-45 mmHg	36	37.1	36	35.1	34.9	35.1	35.5
HCO_3	22-28 mEq/L	29.8	33.1	32.1	39.1	24.6	24.9	24.3

Table 2. Laboratory Results of the Patient during Hospitalization

DISCUSSION

Zinc phosphide is a chemical compound of inorganic origin. It is gray solid while commercial samples are often dark or even black and have been used as rodenticides, and also as a human toxin in suicidal attempts in under developed countries.[6] A do se of 55-70 mg/Kg which is approximately 4 to 5 grams of ZnP may lead to mortality.[3] The average age of patients who attempt to commit acute toxicity in humans was found to 27 years.[7] ZnP is similar to aluminium phosphide as both of them contain hydrogen phosphine (PH3) gas that is harmful to the human body.[8] After ingestion, it is hydrolysed by gastric acid and is converted into phosphine gas that spreads through the stomach and intestinal vessels in the bloodstream.[3,9] In the respiratory chain, phosphine inhibits cytochrome C oxidase enzyme that leads to phosphine gas formation in the bloodstream. Bleeding diathesis is caused by the direct toxic effect of phosphine on the vessel wall, leading to haemorrhage of the gastrointestinal tract, eyes and extremities. [10] Clinical symptoms include extreme hypotension, myocarditis, pericarditis, acute pulmonary oedema, gastrointestinal symptoms (such as nausea, vomiting and diarrhoea), metabolic acidosis, congestive heart failure and acute kidney failure. In addition, there may be retrosternal pain, shortness of breath, cyanosis, hepatic failure, extreme hypoglycaemia, delirium and tonic-colonic seizure.

No specific treatment for phosphine gas poisoning has currently been identified. Mortality rate ranges from 37 to 100%.[9] There is no antidote available and the recommended treatment for ZnP poisoning is supportive and symptomatic. It is recommended that activated charcoal be administered as soon as the patient is admitted.[11] For patients with irreversible acute liver failure liver transplant is the final recommendation.[12] Several studies have shown the advantages of using NAC in patients with hepatic damage caused by phosphine poisoning.[13] Jaundice, which is triggered by hepatic damage or intravascular haemolysis, is also seen in organ phosphorus toxicity.[14,15] Jaundice in this case was due to intravascular haemolysis and acute hepatic failure as shown by indirect hyperbilirubinemia, elevated liver enzymes, reticulocytosis, haemolytic anaemia, elevated serum LDH. No signs of OP poisoning were present in patient. Haemolysis occurs as a result of G6PD deficiency but in our case, the level of G6PD was found to be within normal range [16, 17] Morphological changes in erythrocytes after in vitro incubation with PH3 gas were documented in one study. All cells showed crenation, however, and no haemolysis or Heinz body formation was reported, so haemolysis was ruled out to be due to the direct effects of PH3 on red blood cells.[18]

CONCLUSIONS

ZnP is a rodenticide widely used, and is also commonly used as a social poison. There may be a variety of clinical presentations raging from acute fulminant hepatitis, extreme hypotension, serious metabolic acidosis, or mixed metabolic acidosis, respiratory alkalosis, and acute renal failure. The treating clinician should be alert to all these clinical possibilities when treating these cases.

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