

Accidental Zinc Phosphide Poisoning among Population: A Case Report

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Abstract

The use of rodenticides in Gaza in the past years becomes easy due to rodent outbreak. The municipalities allow the use of rodenticides without quality control or technical supports. This situation leads to an easy purchasing of zinc phosphide or its analog. This resulted in acute poisoning among adults and children. Herein we reported an accidental zinc phosphide poisoning to an adult man and discussed the associated medical complications with this case. Gastric lavage followed by atropine and vitamin K gavage on the 1st day of poisoning (hospital admission) resulted in a slight improvement of the case. Clinical symptoms included severe abdominal colic without losing consciousness. Complete blood count (CBC) showed elevated levels of white blood cells (WBCs) and granulocytes (GRAN) levels indicating medical complication of the case. Biochemical analysis showed elevated levels of liver and cardiac biomarkers indicating potential liver and heart injuries. Continuous gavage of vitamin K, resulted in a gradual improvement of the case. On the 4th day of medical period, abdominal colic disappeared and CBC parameters became near the reference range. Consequently, the patient was set free from the hospital.

Keywords

Zinc Phosphide Poisoning, WBCs, GRAN, AST, ALT, CK

1. Introduction

Accidental poisoning of pesticides among general population rapidly increased in Gaza strip due to rodenticides application. So far an outbreak of rodents in Gaza enhanced the chemical control to reduce the populations of rats. Municipalities, ministry of health and ministry of agriculture approve rodent control even by participation of the local communities. This decision enhanced pesticide

marketing with less quality control. Zinc phosphide was the key product for fast rodent control using food poisoning techniques [1]. It is commercially available in different formulations containing of 320 g zinc phosphide/kg.

Accidental poisoning of pesticides may occur during field application [2] [3] [4] [5], suicidal attempts [6], occupational exposure [7] and other indirect ways of exposure [8]-[21].

Previous studies from Gaza [22]-[28] did not report zinc phosphide toxicity. The limitation is that they did not give considerable attention to zinc phosphide poisoning. To date, this is the 1st report from Gaza to highlight and discuss zinc phosphide poisoning. However, here below we presented a case report of zinc phosphide poisoning from Gaza with a young man, 31 years old and discuss its medical consequences.

So far Zinc phosphide is an inorganic pesticide, solid at room temperature, and has a grey color but often dark or even black. It is highly toxic in acute exposure to humans, its acute oral LD50 for rat 45.7 mg/kg [29]. It is classified as IB [30].

2. Materials and Method

Mr. Ann F. an adult man, 31 years old, married, has two children, was preparing food poisoning for rat control in his house garden in Khanyounis city using zinc phosphide as an active ingredient. He mixed the zinc phosphide with animal food and presented to the rat. He felt sick at the end of the preparation, hypoactive with abdomen colic, his parent brought him to the European hospital in the south part of Gaza.

During the interview with his parents, they claimed that he was preparing food poisoning for rats. They also brought with them the empty package of the used pesticide. It appeared to us that it was Zinc phosphide. This information made the medical treatment easier than other poisoned cases without historical information. As we elaborated above it is a rodenticide, very toxic according to WHO classification.

2.1. Medical Treatment

Following the international guideline described previously for pesticide poisoning [30], the clothes of Mr. Ann F. were removed and his skin was washed several time with water and soup to insure contamination free environment.

Immediately, the medical team performed gastric lavage several time to remove all zinc phosphide. This step repeated several time to insure complete removal of zinc phosphide. In one attempt, activated charcoal was used to enhance and insure optimal removal.

Mr. Ann was admitted in the intensive care unit for observation and complete medical treatment. Venous blood samples were drawn for complete blood chemical analysis, and for Heart enzyme and liver biomarkers determination. These steps were repeated every day to monitor the treatment weather in the right direction or not.

Mr. Ann received 10 mg atropine in 500 mL normal saline solution every 6 h on the 1st day (on admission) only then it was stopped, and replaced by vitamin K.

2.2. Analysis of Blood and Urine

Urine and blood samples 10 ml each were drawn on admission and repeated during the medical treatments for zinc phosphide analysis using previous methods [31] [32] [33]. In this procedure samples were digested with nitric acid at 65°C for 24 hr then temperature was raised up to 135 for several hr up to have a clear solution after words zinc concentrations in the samples were determined using Inductive coupled plasma analyzer (ICP).

2.3. Complete Blood Count (CBC) Measurements

Blood samples were drawn every day for CBC and enzymatic measurements. CBC measurement was performed according to the standard method of ministry of health [34]. As described recently [35], activities of ALT, AST, and ALP were taken as indicators of liver injury due to zinc phosphide poisoning. The activity of alkaline phosphatase (ALP) was determined according to Kind and King [36] using commercially supplied kits, ref number 10441 9910021, lot 60112654 purchased from DiaSys, Germany through Israeli company. AST and ALT activities were measured based on Reitman and Frrankel [37] using a commercially available kit for AST ref numbers 126019910021, lot 60112076 and ALT kit ref BXC0213D, lot 162254 from Bio-Merieux purchased from Israeli company.

Percentage of enzyme activation was calculated accord to Equation (1), [38]

$$\% \text{Enzyme activation} = 100 * \frac{(EA_t - EA_c)}{EA_c} \quad (1)$$

where EA_c and EA_t are the enzyme activity of the control group (reference range) and treatment (poisoned case) respectively.

3. Results

3.1. Blood Parameters

In **Table 1** we present the results of blood analysis of Mr. Ann F. It can be observed that WBC was higher than that of the reference range on the 1st day of poisoning (on admission). Then the level gradually reduced and became closer to the lower limit of the reference range. This result indicates that WBC was involved in the detoxification process of zinc phosphide. Furthermore, granulocytes (GRAN) level was several times higher than the reference range. Due to gastric lavage, the level was reduced but still in the cutoff range, indicating some damage was occurred. Hemoglobin level was 15.4 g/dl, closed to the upper limit of reference range. Then the level was reduced. PLT level was high on the 1st day of admission then severely reduced on the 2nd and 3rd days. On the 4th day PLT level went up indicating recovery.

Table 1. Blood analysis of the patient during the intensive care unit hospitalization.

Parameter	1 st day	2 nd day	3 rd day	4 th day	Reference range
WBC	15.9	10.6	7.2	5.7	4.5 - 13.5 (k/ μ L)
RBC	4.89	4.09	4.09	4.52	4.5 - 5.3 (m/ μ L)
HCT	45	38.2	37.7	41.4	37 - 49 (%)
MCH	13.5	30.6	30.3	30.3	25 - 35
RDW	13.9	13.5	13.3	13.5	11.5 - 14.5 (%)
LYM	1	1.4	1.4	1.3	0.6 - 4.1 (%)
GRAN	14.4	8.5	5.2	4	2.0 - 4.1 (%)
HGB	15.4	12.5	12.4	13.7	12 - 16 (g/dL)
MCV	92.1	93.5	92.1	91.6	78 - 102
MCHC	34.2	32.7	32.9	33.1	31 - 37
PLT	209	163	152	229	140 - 450 (k/ μ L)

where WBC = white blood count; RBC = red blood count; HCT = hematocrit; MCH = mean corpuscular hemoglobin; RDW = red blood distribution percent; LYM = lymphocyte cell percent; GRAN = granulocyte cell percent; HGB = hemoglobin; MCV = mean corpuscular volume; MCHC = mean corpuscular hemoglobin concentration; PLT = platelet count.

3.2. Responses of Liver and Heart Enzymes

Table 2 shows the influences of zinc phosphide on activities of liver function tests, and heart enzyme activities. It can be observed that on the 1st day (on admission) the levels of AST, CK total and CK-MB are above reference range and tended to increase higher than the reference range indicating hepatotoxicity and cardiac toxicity.

Furthermore, AST activity remained higher than reference range in the last three days of medical treatments. This indicates liver cell injury. It is well known in the literature that increasing AST and ALT levels often represent hepatocyte injury with altered cell membrane permeability, causing the excessive leakage of transaminases. This event may be appeared due to the interaction of PH3 with cytochrome oxidase as in reaction Equation (2) and causing mitochondrial damage. In addition CK Total remained several time higher than the reference range indicating high potential of cardiac toxicity and medical complications.

So far, elevation level of enzymes based on Ref [2] were in the range of 1.22 - 3.2 folds higher than the reference range. This indicates the magnitude of damage on different organs. Moreover, **Table 3** shows the concentrations of total and direct Bilirubin. It is obvious that both values enlarged several times above normal range on the 4th day of medical period indicating developmental toxicity. So far both values confirm liver cell damage and injury as indicated in **Table 2**.

3.3. Effects on Precipitation Parameters

In **Table 3**, we presented the value of INR, the important indicator of blood clotting as affected by zinc phosphide poisoning. Regardless to the apparent variations on the values in **Table 3**. Statistical analysis did not discriminate significant

Table 2. Activity of liver and heart enzymes profiles during poisoning.

Measured enzyme	1 st day	2 nd day	3 rd day	4 th day	% E	Reference range
ALT	12 ± 3	18 ± 3	21 ± 3	19 ± 4	-	1 - 43 (u/l)
AST	47 ± 5	58 ± 5	82 ± 5	82 ± 12	1.27 - 2.22	0 - 37 (u/l)
ALP	259 ± 12	187 ± 15	ND	265 ± 25	-	100 - 300 (u/l)
CK TOTAL	374 ± 15	2073 ± 120	ND	ND	2.99 - 16.6	26 - 125 (u/l)
CK-MB	80 ± 6	45	44 ± 5	39 ± 6	3.2	up to 25 (u/l)
LDH	1378 ± 25	ND	ND	670 ± 30	3.1 - 1.49	225 - 450 (u/l)
Amylase	140 ± 13	94 ± 9	ND	43 ± 5	1.12	25 - 125 (u/l)

% E represents elevation of enzyme activity due to poisoning. Creatine kinase (CK), lactic acid dehydrogenase (LDH), alkaline phosphatase (ALP), Aspartate aminotransferase (AST), and Alanine aminotransferase (ALT).

Table 3. Precipitation parameters.

Measured parameter	1 st day	2 nd day	3 rd day	4 th day	Reference range
PT-Seconds	16.9 ± 2.5	Nd	Nd	16 ± 3	11 - 15 sec
INR	1.33 ± 0.22	Nd	Nd	1.26 ± 0.2	(0.8 - 1.2)
PT-Activity	62 ± 5	Nd	Nd	68 ± 8	

differences between the measured values and corresponding reference range.

It is obvious that prothrombin precipitation time (PT) is reduced from 16.9 ± 2.5 second (the 1st analysis after poisoning) to 16 ± 3 second after three days of ICU hospitalization (Vitamin K was given every day).

3.4. Zinc Residue Analysis

Inductive coupled plasma analyzer did not detect zinc in urine or blood. This was probably due to the fact that gastric lavage removed high fraction of zinc phosphide. Moreover, zinc phosphide may be excreted from the body throughout the feces path way not by urine.

4. Discussion

The idea behind using gastric lavage, atropine and vitamin K gavage, is that the medical protocol of poisoning cases includes performance of these steps immediately on arrival to the hospital unless the case is unconscious. Additionally, gavage of atropine to the poisoning cases is the 1st step of medical treatments regardless to the fact that poisoning case occurred through organophosphorus poisoning or zinc phosphide and its analogs.

4.1. Mode of Action and Toxicity

The presented results indicate acute poisoning of Mr. Ann due to accidental zinc poisoning. It was noticed that after accidental ingestion of zinc phosphide, Mr.

Ann began vomiting, abdominal colic, hypoactivity, headache. These symptoms appeared in the 1st day of poisoning. The appearance of these symptoms may be explained by the fact that zinc phosphide is being hydrolyzed in the stomach under acidic media to form hydrogen phosphide and zinc ion according to equation (Equation (2)).



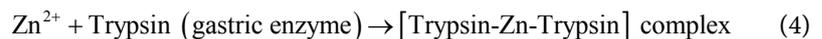
$$K_1 = \frac{(\text{Zn})(\text{PH}_3)}{(\text{Zn}_3\text{P}_2)(\text{H}^+)}$$

where K_1 is the reaction constant and represents formation of toxic molecules (PH_3) hydrogen phosphide in the stomach of human being. This reactive molecule tends to react with cytochrome c oxidase (mitochondrial enzymes responsible for respiration of cells) to form inhibited enzyme as in Equation (3).



$$K_2 = \frac{(\text{PH}_3 - \text{Cytochrome C oxidase})}{(\text{PH}_3)(\text{Cytochrome C oxidase})}$$

where K_2 is the inhibition constant and represents the magnitude of toxicity.



It can be observed that the quantity of zinc phosphide ingested, the potential toxicity increased as obvious from Equation (3), that shows, PH_3 production is a function with the initial concentration of zinc phosphide being ingested. In addition, the acidity of the stomach is a key factor on producing PH_3 , so far in a less stomach acidity or in alkaline stomach, reaction Equation (2) would not have occurred, consequently no production of active molecule (PH_3) and toxic symptoms neither appear on the live nor on the heart. Moreover, the reaction in Equation (4) can be responsible on the abdominal colic and other symptoms. The release of the clinical symptoms after the 1st day may be attributed to the fact that large fraction of zinc phosphide being removed by gastric lavage and the remaining part may be excreted throughout the feces pathway.

This discussion is a driving force towered developing medical treatment for gastric lavage that can immediately change the gastric media from sever acidic to neutral or slightly alkaline that can stop reaction in Equation (2). In addition, it can be suggested that adding activated charcoal, clay, and/or organo-clay may drastically reduce the toxicity due to possible adsorption between zinc phosphide and those materials. This suggestion is supported previous results of [39] [40] that revealed high adsorption between organo-clays and organic and inorganic molecules.

So far accidental swilling of a low concentration of zinc phosphide may be attached by WBC as shown by high level of WBC on the 1st day (on admission) and be prevented to reach the liver accordingly no anticoagulation may occur. Our explanation is supported by the results in **Table 1**, which showed a decrease in WBC during the ICU medication. Moreover, the data in **Table 3**, indicate

nearly a high value of INR above normal range (0.8 - 1.2). This suggests that prothrombin formation was inhibited, this is also obvious from the high value of prothrombin precipitation time (PT) **Table 3**. In due time a reduction in the value was obtained due to Vitamin K gavage to the patient. Our results agree with previous reports [2] [3] who found similar observation in medical treatment of Chlorpyrifos poisoning.

This disappearance of zinc phosphide in blood and urine samples may be attributed by the fact that zinc phosphide can be hydrolyzed as in Equation (2) not only in the stomach but also under acidic environmental conditions and producing phosphine (PH_3) which can be inhaled and reacted with cytochrome c oxidase as in Equation (3). Our explanation is in accordance with previous reports [41] [42].

4.2. Further Consequences of Zinc Phosphide Poisoning

In **Figure 1**, we presented the ratios of AST to ALT, AST and to platelet. It has been documented that AST/ PLT index is a reliable marker for prediction of liver fibrosis [43] [44]. Our calculated values for AST/ALT and AST/PLT at any point is above 1.5 suggesting severe liver injury. This suggestion is in accordance with [45].

4.3. Environmental Relevance of Pesticide Poisoning

It is well known in the literature that zinc phosphide poisoning is a significant cause of morbidity and mortality in poor countries where pesticide application occurred with caseless attention to the safety regulations. It has been shown that a dosage of 4 to 5 g of zinc phosphide which equivalent to LD50 value of (55 - 70 mg/kg) had resulted in human deaths in acute toxicity [46]. The presented case herein developed severe toxicity but finally with successfully medical treatment the patient recovered.

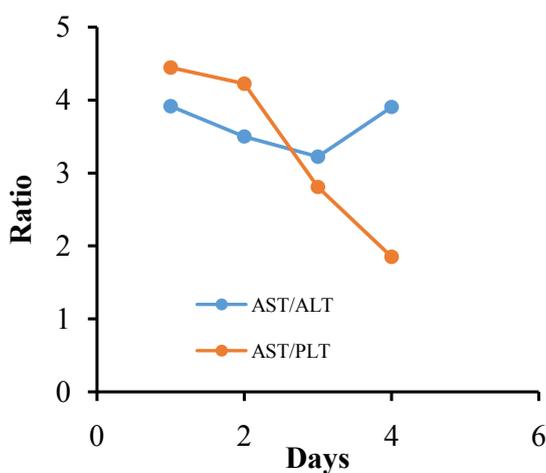


Figure 1. Aspartate aminotransferase (AST) to alanine aminotransferase (ALT) ratio, aspartate aminotransferase to platelet level during the medical period.

So far, the environmental relevance of this work emerges from the fact that poisonous cases among population may occur due to occupational exposure, swelling of contaminated food, drug poisoning, pesticides poisoning and poisoning of industrial chemicals. So far, previous investigations [47]-[57] revealed that poisoning among population may occur via ingestion of contaminated food and water and contaminated air.

Recent investigation reported poisoning cases among farm workers [58] [59] due to using pesticide containers as domestic tools. Recent survey [2] [3] indicated long term toxicity among farmers. So far long term toxicity of pesticides in Gaza Strip have been documented [9] [10] [11] [12] [13].

Furthermore, spraying pesticides in farms have been shown to damage non-target organisms such as cyanobacteria [22] [15], plants ([53], fish ([54] [55]). So far many authors devoted tremendous efforts to reduce the toxicity of farmers, this included clay based and/or organo-clay formulations [18] [19] [20] [21] [22] [60]-[68]. Regardless of these scientific reports accidental poisoning may not be stopped but it has to be reduced to the lowest level.

5. Conclusion

Accidental poisoning may be stopped throughout careful attention during pesticide application. Nevertheless, it may suddenly occur due to misunderstanding the rules and regulations and probably due careless attention during work. Nevertheless, accidental poisoning may occur due to environmental conditions. However, poisoning with zinc phosphide created liver damage and cardiac toxicity. Careful attention must be taken during work with organophosphorus pesticide. This should include mask during work to avoid breathing or ingestion of small amounts of zinc phosphide.

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Ethical Statement

This study was not funded by any organization.
Compliance with ethical standards.

Conflict of Interest

Author declares that he has no conflict of interest.

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