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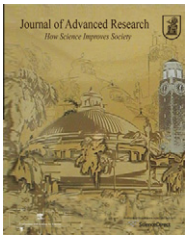

ORIGINAL ARTICLE

Zinc phosphide toxicity with a trial of tranexamic acid in its management

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KEYWORDS

Zinc phosphide;
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Psychosocial counseling

Abstract Zinc phosphide is a highly effective rodenticide used widely to protect grain in stores and domestically to kill rodents. Acute poisoning may be direct by ingestion or indirect through accidental inhalation of phosphine gas generated during its use. This study aims to identify the patterns of intoxication with zinc phosphide among Egyptian patients admitted to the National Egyptian Center of Clinical and Environmental Toxicological Research (NECTR); to study the role of antifibrinolytics in management of zinc phosphide toxicity; and to publish the results of the study, which include recommendations for action towards planning prevention and education programs. The study provides descriptive data and analysis of 188 cases admitted to the NECTR with acute zinc phosphide poisoning over a period of 22 months. Results show that poisoning is more common among females (60.6% of cases) than males (39.4%); the mean age is nearly 21 years old. The most common cause of poisoning is suicidal attempts (83.6%) followed by accidental exposure (16.4%). The most common causative factors that lead to self-poisoning are marital disharmony, economic hardship, social problems and scolding from other family members. Signs and symptoms of toxicity include gastrointestinal disturbances, respiratory compromise and changes in mental status. Other features include disseminated intravascular coagulation, hepatic and renal impairment. Metabolic disturbances had been reported. Death can result immediately due to pulmonary edema or delayed due to cardiotoxicity. Patients must be admitted to hospital and observed for at least 3 days. Symptomatic and supportive care is the mainstay of therapy. Zinc phosphide poisoning requires gastric lavage with excessive sodium bicarbonate solution. Tranexamic acid – an antifibrinolytic

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agent – was found to be of help in some cases. Psychosocial counseling in cases of intentional poisoning is an important aspect of overall management of the problem.

Introduction

It has been estimated that some form of poison directly or indirectly is responsible for more than one million illnesses worldwide annually. This figure could be just the tip of the iceberg since most cases of poisoning actually go unreported, particularly in Third World countries [1].

The problem of poisoning, both unintentional and intentional, is getting worse with time as newer drugs and chemicals are developing in huge numbers. Poisoning cases are increasing day-by-day due to changes in lifestyle and social behavior. Deliberate self-poisoning has reached epidemic proportions in parts of the developing world [2]. Moreover, the problem is not confined to developing countries; it frequently occurs in developed countries as well.

Pesticide poisoning from occupational, accidental and intentional exposure is a major developing world public health problem [3]. Millions of people are exposed to danger through hazardous occupational practices and unsafe storage of pesticides. Based on extrapolations from limited data, it was estimated that three million cases of pesticide poisoning occur world-wide annually with 220,000 deaths, the majority intentional [4].

In Egypt in 1996 Abdelmegid and Salem surveyed 5913 patients admitted to the Alexandria Poison Center (APC) during the previous year and recorded that pesticide poisoning accounted for 14.3% of admitted cases [5]. In 2006, at Ain Shams University, insecticide poisoning represented 51.0% of admitted cases (a total of 21,805 cases); of this number, organophosphorus insecticides accounted for 75.0%, zinc phosphide 20.0% and carbamates 5.0% [6].

Zinc phosphide is a highly effective rodenticide. It is a crystalline, dark grey powder mixed into food as rodent bait. It is also used widely to protect grain in stores and during transportation.

Acute poisoning with this compound may be direct due to ingestion of the salt or indirect from accidental inhalation of phosphine gas (PH3) generated during its use [7].

Phosphides are normally found as powders or pellets, usually in the form of zinc or aluminum phosphide (Zn_3P_2 and AlP, respectively); calcium and magnesium phosphides are also available [8]. Due to its low price and easy availability, zinc phosphide is emerging as a common self-poisoning agent in Egypt.

Zinc phosphide ingested orally reacts with water and acid in the stomach and produces phosphine gas, which may account in large part for observed toxicity. Phosphine is an extremely toxic gas, being highly irritating to the respiratory tract and also producing severe systemic toxicity [9].

Phosphine acts by disrupting mitochondrial function through blocking cytochrome C oxidase. In addition to producing energy failure in cells, free radical generation increases, resulting in lipid peroxidation [10,11]. Phosphine also inhibits cholinesterases in rats [12].

Phosphides produce toxicity rapidly, generally within 30 min of ingestion; and death may follow in less than 6 h [13]. The ingestion of fresh unopened tablets consistently results in death [14]. Phosphide ingestions over 500 mg are often fatal [15].

Phosphides are potent gastric irritants; profuse vomiting and abdominal pain are often the first symptoms [14]. Respiratory signs and symptoms include tachypnea, hyperpnea, dyspnea, cough and chest tightness that may progress to acute lung injury over days [16–19]. Also, delayed onset non-cardiogenic pulmonary edema can develop and once incurred it should be managed aggressively using endotracheal intubation and positive end-expiratory pressure (PEEP) ventilation [20].

Tachycardia, hypotension and dysrhythmias may develop. Phosphine-induced dysrhythmias include atrial fibrillation, flutter, heart block and ventricular tachycardia and fibrillation [21]. Other effects include central nervous system toxicity manifested as coma, seizures, tonic-clonic convulsions and delirium [13,18].

Hepatomegaly, raised transaminases, hepatic failure, severe hypoglycemia or severe metabolic acidosis with acute distal renal tubular acidosis, have been associated with zinc phosphide ingestion [22,23]. Also acute pancreatitis has been reported [7,24].

The aim of this study is to identify the patterns of intoxication with zinc phosphide among Egyptian patients admitted to the National Egyptian Center of Clinical and Environmental Toxicological Research (NECTR); to study the role of antifibrinolytics in management of zinc phosphide toxicity; and to publish the results of the study, which includes recommendations for action towards planning prevention and education programs.

Subjects and methodology

This retrospective study provides descriptive data and analysis of 188 cases with a history of acute zinc phosphide poisoning admitted to the NECTR over a period of 22 months (from January 2007 to October 2008). Data of poisoning cases were collected and analyzed with respect to age, sex, geographic distribution, causes of poisoning, clinical picture, management procedures, outcome and length of hospital stay.

Results

There were 188 cases with a history of acute poisoning with zinc phosphide, of which 159 (84.5%) were zinc phosphide alone; 6 cases (3%) involved food contaminated with zinc phosphide; 19 cases (10%) involved zinc phosphide combined with organophosphorus poisoning; and 4 cases (2%) involved zinc phosphide combined with drugs. The last 23 cases were analyzed separately to illustrate the clinical picture of combined effects.

The amount of intentional ingested powder varies from 1/2 to two sachets (a sachet is 2–3 g).

Table 1 shows that the studied group comprised 100 females (60.6%) and 65 males (39.4%) and that age ranged

Table 1 Descriptive analysis of the studied group.

Sex	Number	%	Age incidence (in years)		Mean (in years)	SD
			Min	Max		
Males	65	39.4	1	55	21.9	±8.8
Females	100	60.6	1.6	45	19.8	±6.6
Total	165	100				

Min = Minimum.
Max = Maximum.

Table 2 Age group distribution among a total number of 188 patients admitted to NECTR.

Age groups (in years)	Number of patients	%
0–9	9	4.8
10–19	85	45.2
20–29	79	42
30–39	9	4.8
>40	6	3.2

from 1 to 55 years with a mean of 21.9 years ± 8.8 in males and from 1.6 to 45 years old in females with a mean of 19.8 years ± 6.6.

Table 2 shows that 45.2% of patients were 10–19 years old, 42% were 20–29 years old, 4.8% were less than 9 years old, 4.8% were 30–39 years old and 3.2% were more than 40 years old.

Table 3 shows reasons for exposure, which were intentional suicidal attempts in 83.6% of cases and accidental exposure in 16.4% of cases.

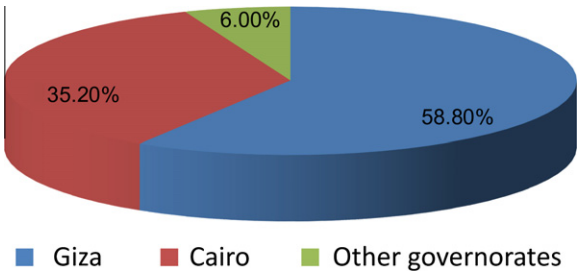
The geographic distribution shows that most cases were from the Giza district (58.8%), then the Cairo district (35.2%), then the other governorates including El-Fayoum, El-Dakahleya, Assuit, Benisweif, El-Menia, El-Kalyoubeya and El Behera at lower percentages up to 6% (Graph 1).

Table 4 shows the different clinical presentations of poisoned patients who were classified according to an internal protocol applied in our centre as either asymptomatic or with minor, moderate or major symptoms. Accordingly, 24.2% of the patients were asymptomatic on arrival at the emergency department, while 36.4%, 29.1% and 10.3%, presented with minor, moderate and major symptoms, respectively.

Minor symptoms were in the form of GIT manifestations (epigastric pain, nausea or vomiting); moderate symptoms included respiratory manifestations in addition (dyspnea and excessive secretions); and major symptoms involved signs of effects on other systems (tachycardia and hypotension, agitation, hallucinations and depression).

Table 3 Causes of poisoning.

Sex	Cause of poisoning			
	No. of suicide attempts	%	No. of accidental poisoning	%
Males	54	83	11	17
Females	84	84	16	16
Total	138	83.6	27	16.4



Graph 1 Geographic distribution.

Table 4 Analysis of recorded symptoms.

Initial presentation	No. of females	No. of males	Total number	%
Asymptomatic	30	10	40	24.2
Minor symptoms	38	22	60	36.4
Moderate symptoms	20	28	48	29.1
Major symptoms	12	5	17	10.3
Total	100	65	165	100

Asymptomatic = without any symptom or only dizziness.
Minor symptoms = in the form of GIT manifestations (epigastric pain, nausea/or vomiting).
Moderate symptoms = included respiratory manifestations in addition (dyspnea and excessive secretions).
Major symptoms = involved signs of other system affection (tachycardia and hypotension, agitation, hallucinations and depression).

Table 5 shows that 33.3% of cases were metabolically stable on admission; 11.5% of cases presented with metabolic acidosis, of which 9.2% were in a compensated state; 10.3% presented with respiratory acidosis, of which 5.7% were in a compensated state; 18.4% presented with respiratory alkalosis, of which 10.3% were in a compensated state; 26.5% of cases presented with mixed metabolic acidosis and respiratory alkalosis, of which 19.6% were in a compensated state.

Table 6 shows that 30% of patients had elevated ALT levels; 45% had elevated AST levels. Kidney function tests were nearly within normal range; only 2.4% had an elevated urea level. There were some electrolyte disturbances; 50% of patients had low sodium levels; 25% had low potassium levels. Synthetic liver functions were performed in 1/3 of patients so as to assess the condition of the liver and the need for treatment with antifibrinolytic or anticoagulation therapy. Results revealed that 33% of them had prolonged PT, 10% had low prothrombin concentration while INR and platelet count were within normal range on admission.

The majority of cases (50%) presented to the emergency department within 2 h of exposure; meanwhile 20% of cases presented within 1 h, 10% after 4 h and the remaining 20% within 6–12 h of exposure.

As regards management procedures, Table 7 shows that patients who presented within 2 h of exposure underwent gastric lavage with sodium bicarbonate solution (61%); 32.7%

Table 5 Metabolic status of patients.

Metabolic status	Number	%
Normal	58	33.3
Metabolic acidosis (uncompensated)	4	2.3
Compensated metabolic acidosis	16	9.2
Respiratory acidosis (uncompensated)	8	4.6
Compensated respiratory acidosis	10	5.7
Respiratory alkalosis (uncompensated)	14	8.1
Compensated respiratory alkalosis	18	10.3
Mixed metabolic acidosis and respiratory alkalosis	12	6.9
Compensated mixed	34	19.6
Total	174	100

Differences recorded in the total number of cases were due to some data missed in history taking.
Normal ABG values:
pH = 7.35–7.45.
PO2 = 95–100 mm Hg.
PCO2 = 35–45 mm Hg.
HCO3 = 24–28 mmol/L.
Diagnosis is based on the following criterion according to the Henderson–Hasselbach parameters:
If the pH is within normal range but associated with respiratory or metabolic disturbance, the patient is in a compensated state; if not the case is uncompensated.
A respiratory disturbance alters the arterial PCO2, while metabolic disturbance alters the HCO3:
Metabolic acidosis = pH value, PCO2 and HCO3 are below normal ranges.
Metabolic alkalosis = pH and PCO2 and HCO3 are above normal ranges.
Respiratory acidosis = pH is below normal range, HCO3 and PCO2 are above normal ranges.
Respiratory alkalosis = pH is above normal range, HCO3 and PCO2 are below normal ranges.
Mixed types = is diagnosed by Winter's formula Expected $PCO2 = (1.5 \times HCO3) + 8 \pm 2$.
This means that if a metabolic acidosis is present, we use Winter's formula to determine the respiratory response; in cases of simple metabolic acidosis, the measured PCO2 will fall within the range determined by the equation; if a respiratory disturbance is coexisting, then PCO2 varies outside the range; if below the range, a respiratory alkalosis is also occurring; if above the range, there is respiratory acidosis.
N.B. The diagnosis did not depend upon measuring the anion gap, as the studied cases were of ZP poisoning, so there was no need to measure the anion gap as it would be essential only to differentiate between the causes of metabolic acidosis.

Table 6 Analysis of different laboratory investigations.

Other investigations	Patient values	Normal values	Number (%)
ALT	> 40 U/L	Up to 40	30 (28.5)
AST	> 38 U/L	Up to 38	45 (42.8)
Urea	> 50 mg/dL	Up to 50	3 (2.4)
Creatinine	> 1.5 mg/dL	Up to 1.5	0 (0)
Sodium	< 135 mmol/L	136–145	72 (50)
Potassium	< 3.5 mmol/L	3.5–5	36 (25)
Prothrombin time	> 12.3 s	Control 12.3	55 (33)
Prothrombin concentration	Out of range	80–100%	10 (6)
INR	< 1	1–1.2	0
Platelet count	< 150	150–450	0

Aspartate aminotransferase (AST) = up to 38 U/L.
Alanine aminotransferase (ALT) = up to 40 U/L.
Urea = 15–50 mg/dl.
Creatinine = 0.5–1.5 mg/dl.
Sodium (Na) = 136–145 mM/L.
Potassium (K) = 3.5–5.0 mM/L.
Prothrombin time (PT) = 12.3 s.
Prothrombin concentration (PC) = 80–100%.
International normalized ratio (INR) = 1.0–1.2.

Table 7 Analysis of management procedures.

Procedures	Number of patients	%
Gastric lavage with sodium bicarbonate	100	61
Oral sodium bicarbonate	54	32.7
Activated charcoal	122	74
Others (fluids, antispasmodic, antiemetics, sedatives, antibiotics, cathartics, etc.)	138	83.6
Tranexamic acid	16	9.7

Table 8 Analysis of medical outcome.

Medical outcome	Number of patients	%
Completely cured	59	35.7
Discharged with residual effects	12	7.2
Discharged on consent	93	56.3
Death	1	0.6
Total	165	100

received oral sodium bicarbonate solution; activated charcoal was given to 74% of patients; other symptomatic treatment used according to the condition of the patient included fluid administration, antispasmodics, antiemetics, sedatives, antibiotics and cathartics. Tranexamic acid as an antifibrinolytic agent was found to be of help in 9.7% of patients.

Table 8 shows the medical outcome of the studied cases: complete cure was recorded in 35.7% of cases; 7.2% were discharged with some residual effects such as mild abdominal pain; 56.3% were discharged before 48 h on personal consent for social or financial reasons but most of these were completely cured as revealed on follow up in the outpatient clinic, a percentage which should be added to the completely cured figure; death was recorded only in 0.6% of cases due to delay in reaching the hospital, deterioration of the patient's general condition and development of pulmonary complications. Depression was the commonest residual outcome in most cases of intentional poisoning and these needed psychological assessment and follow up with a specialist.

The length of hospital stay varied from 2 h to up to 2 days with a mean of 13.36 h according to clinical condition and other factors related to agony, social factors or economic causes.

Patients who accidently ingested food contaminated with zinc phosphide (3%) showed milder manifestations compared with other cases; this could be explained by ingestion of a small amount of poison, early presentation to the emergency department and the performance of gastric lavage; there was one

exception, a case that came late and showed the full picture of toxicity.

The patients who presented with suicidal ingestion of zinc phosphide combined with carbamazepine overdose (1%) (20–30 tablets), an enzyme inducer [25], exhibited a rapid appearance of the toxic effects of poisoning with zinc phosphide in the form of severe vomiting and epigastric pain; one of them presented to the emergency unit within 1 h; the other presented after 12 h with deterioration of his general condition in the form of drowsiness, hypotension, hypokalemia, hallucinations from the effects of carbamazepine overdose with metabolic acidosis and pneumonic patches revealed on X-ray, and so needed prolonged hospital stay and close monitoring.

A patient with suicidal ingestion of zinc phosphide combined with alcohol, an enzyme inducing agent, presented with severe metabolic acidosis, increased levels of liver enzymes, hypokalemia and bradycardia, a picture that necessitates aggressive therapy.

Patients who presented with suicidal ingestion of zinc phosphide combined with theophylline (1%) presented with their combined effects on the GIT in the form of severe and repeated vomiting, which was not relieved by the usual antiemetic drugs and so needed aggressive management; also, metabolic acidosis was reported with tachycardia, hypotension and hypokalemia, which necessitated intravenous fluid and electrolyte replacement and prolonged hospital stay compared with other cases.

Ten percent of patients presented with ingestion of zinc phosphide combined with organophosphorus compounds; 90% of them were suicide attempts and 10% were accidental exposure. Most cases (80%) presented with severe vomiting and abdominal pain in addition to muscle twitches and diarrhea, which indicated the combined effects of toxicity that required antidotal therapy (pralidoxime); 10% of cases needed endotracheal intubation and artificial ventilation due to late arrival, development of metabolic acidosis and deterioration of the respiratory functions.

Discussion

Acute poisoning with pesticides is a global public health problem. The easy availability of highly toxic pesticides in the homes of farming communities has made pesticides the easiest means of suicide with an extremely high case fatality. Similarly, the extensive use of pesticides exposes the community to both long-term and acute occupational health problems [26].

In Egypt most farmers outside Cairo use phosphide tablets extensively in grain stores, allowing the phosphine to be released once the storage sites are sealed. Phosphine exposure and toxicity from phosphide salts occurs during grain fumigation in both transport and storage areas, causing inhalation of the gas and reported cases of sudden death [13]; an important event occurred in June 2009, when death was reported in nine workers who were engaged in grain transportation in the Kalyoubeya governorate; the condition was not discovered at the time and caused a lot of controversy until diagnosed. Similarly, an agricultural health study (AHS) cohort study performed in Iowa and North Carolina (a cohort that included 52,629 private applicators) revealed that 16% of workers who apply pesticides in agriculture experienced a serious pesticide exposure event. Fifty major type of pesticides were included, falling into four main classes; herbicides, insecticides, fungicides and fumigants. The most frequent were alachlor, trifluralin, atrazine and phorate [27].

Our study was limited to admissions to the NECTR that represent only a small percentage of hospital admissions of cases of zinc phosphide poisoning in Egypt; other cases would present to other poison control centers such as the Ain Shams hospital or general hospitals; in addition there are calls received at the information unit and missed cases due to misdiagnosis or to finding difficulty in reaching any centre due to scarcity of specialized centers in other governorates.

Unfortunately, it is not currently possible to link all the databases to provide a more comprehensive overview of poisoning with zinc phosphide in our country; we think it is important therefore to highlight our views on this type of poisoning and to call for the publishing of statistical records of all cases of poisoning in specialized and other general hospitals.

A total of 10,638 cases attended the NECTR during the period of our study: 11.8% were pesticide poisoning and zinc phosphide poisoning represented 15% of this percentage. These results had not been previously published elsewhere since our reference was the information unit of the NECTR.

The diagnosis is usually made from the history since phosphine tissue concentrations are not routinely available.

The results of this study show that oral ingestion was the main route of poisoning, which is in agreement with other publications [28,29]. Most cases were teenagers and younger adults, as in the majority of centers across the world, which also record that the highest incidence of poisoning is in younger age groups [30–32] (Tables 1 and 2).

The differences recorded in geographical distribution might be attributable to the easier access to the centre; the culture; and to the magnitude of the problems encountered in overcrowded rural areas, where easy access to toxic pesticides turns many impulsive acts of self-poisoning into suicide.

The incidence of attempted suicide in females was greater than in males (a ratio of 1.5:1) (Table 3), due to marital disharmony, economic hardship, social problems and scolding from other family members, which is in agreement with other studies [30,33–35].

Due to their easy availability, pesticides have become the most commonly used agent for suicide in the developing world [36,37]. Since intentional self-poisoning is often impulsive and simplified by easy availability of the poison, a proportion of self-poisoning by pesticides can be prevented by reducing its access. So regulating availability of pesticides and improving medical management may reduce fatality from pesticide poisoning and also reduce the number of suicide attempts in younger age groups [38].

Most patients in the study presented with abdominal pain and vomiting (75.8%), followed by respiratory manifestations (29.1%); systemic affection, which was evident in those who did not seek medical help immediately or to their ingestion of large amounts, presented to a lesser extent.

Initially asymptomatic patients (24.2%) attended the centre because they feared death even though no symptoms had manifested. Their actions were the result of a transient period of distress, they did not have the actual desire to kill themselves; they were only giving a cry for help to gain sympathy from their relatives and help with their problems whether social or economic.

Nearly 33% of cases were metabolically stable on admission so they were put under observation in the intermediate care unit (ICU). The rest (67%) required admission to the intensive care unit (ICU) for adjustment and careful monitoring; 11.5% of them presented with metabolic acidosis, which is in agreement with other studies [23,39–41]; 26.5% presented with mixed metabolic acidosis and respiratory alkalosis in accordance with other studies [39,42] (Table 5); patients with severe respiratory compromise (20%) required intubation and artificial ventilation.

With regard to systemic toxicity encountered with phosphine, it has been proved that the major targets of PH3 poisoning in the human body are the lungs, heart, brain, gastrointestinal tract, kidney and liver [43,44], in our study, 30% of patients showed elevated ALT levels, 45% had elevated AST levels without history of previous liver affection, which reflected the hepatotoxicity [7,42]. Saleki et al. in 2007 [45] stated that PH3 can cause liver dysfunction, especially after the first day of poisoning, and that the main histopathologic changes found were fine cytoplasmic vacuolization of hepatocytes and sinusoidal congestion. Similar condition was recorded in the case presentation of Khurana et al. in 2009 [46] who found elevated transaminases levels; also Karanth and Nayyar in 2003 [47] recorded severe hepatic dysfunction in their cases. Congestion, oedema and centrizonal necrosis of the liver were found on histopathological examination in the study of Musshoff et al. in 2008 [48].

No kidney affection was recorded in our study; kidney function tests were nearly within normal range; only 2.4% had an elevated urea level.

There were some electrolytes disturbances; 50% of patients had hyponatremia, similar to the case study of Khurana et al. in 2009 [46]; it is caused most probably by excessive vomiting and diarrhea or may be related to adrenal insufficiency. Twenty-five percent suffered hypokalemia, which may be related to repeated vomiting; Proudfoot [39] also attributed its occurrence to catecholamine release.

Zinc phosphide poisoned patients were carefully evaluated with complete history and physical examination. Symptomatic and supportive care was the mainstay of therapy. Some toxicology references suggest induction of emesis within 30 min post ingestion [41]. Gastric lavage with water or 3–5% sodium bicarbonate (to reduce gastric acid and production of phosphine) [39], or 1:5000 potassium permanganate (to oxidize phosphine to less absorbable phosphide) has been advised; however, other researchers stated that its effectiveness is unproven [49]. Each of these decontamination techniques carries its own risks and physicians must be aware of these dangers before undertaking any decontamination measures, taking into consideration the importance of airway protection.

Gastrointestinal decontamination with administration of sodium bicarbonate solution was performed in nearly 61% of our patients who presented within 4 h of poisoning; they showed better outcome than cases who presented later and who did not receive gastric lavage (Table 6).

Those who came late (32.7%) received oral sodium bicarbonate solution in a trial to oxidize any remnants in the gastrointestinal tract; activated charcoal as adsorbent was given in 74% of patients; other symptomatic treatments were used according to the condition of the patient as follows: fluid administration, antispasmodics, antiemetics, sedatives, antibiotics and cathartics (Table 7).

During the observation period, patients were closely monitored for cardiac affection by ECG monitoring, with assessment of hepatic and renal functions as well as fluid and electrolyte status.

Death was recorded in one case only who presented after 24 h of poisoning with bad general condition; he received basic therapy but unexpectedly developed sudden repeated hemoptysis suggesting the development of a hemorrhagic diathesis; intubation and artificial ventilation was performed but the patient's condition deteriorated rapidly and before receiving any corrective therapy he developed respiratory failure and died.

This case raised our attention to the possibility of the development of disseminated intravascular coagulopathy (DIC) as recorded in previous studies [39,42,46,50–52]. Proudfoot in 2009 [39] attributed its occurrence to the highly toxic phosphine gas not to the metal phosphides. Sood et al. in 1997 [50] stated that metabolic acidosis accompanying aluminium phosphide poisoning could have been responsible for the acute hemolytic episode recorded in their patient; a picture similar to that observed in our patient. Srinivas et al. in 2007 [51] described a patient with ALP poisoning presenting with intravascular hemolysis secondary to G6PD deficiency. However, Aggarwal et al. in 1999 [42] had proved the occurrence of intravascular hemolysis with aluminium phosphide poisoning in a patient with normal G-6-PD levels. Khurana et al. in 2009 [46] proved in addition the occurrence of microangiopathic hemolytic anemia (MAHA) in a patient who ingested aluminum phosphide. They stated that aluminum phosphide, being a redox substance, can theoretically cause hemolytic anemia. Aluminum phosphide could be associated with DIC, which is a well-recognized cause of MAHA. From this research, we can justify the possibility of the occurrence of DIC in phosphide poisoning.

Some patients presented with the usual picture of zinc phosphide poisoning (profuse vomiting, abdominal pain); then the condition deteriorated rapidly, from drowsiness, pallor, restlessness, irritability, tachycardia, hypotension, bleeding from gums or at the site of injection, to a disturbed conscious level, and shock and respiratory distress in some patients. Close clinical monitoring was done with full investigations that revealed the development of metabolic disturbances, elevated transaminases, low hemoglobin levels, prolonged prothrombin times and thrombocytopenia in most of them. Although not routinely used in management, but owing to the development of DIC, we began our trial using tranexamic acid, an antifibrinolytic agent, which competitively inhibits the activation of plasminogen to plasmin, a molecule responsible for the degradation of fibrin, which is the basic framework for the formation of a blood clot in hemostasis [53]. Tranexamic acid was started by a loading dose of 10 mg/kg intravenously followed by a maintenance dose of 10 mg/kg three times daily for 2–8 days according to the condition; two cases needed blood transfusion in addition due to low hemoglobin level; 2 days later, with continuous supportive care, patients showed a gradual improvement in their general condition with progressive improvement in liver function tests, coagulation profile and platelet count. Complete cure occurred within 1–2 weeks in all cases.

The use of steroids in the management of such patients was also greatly recommended for several reasons including stressful situations and hypotension [54,55], to minimize the possibility of pulmonary injury [54,56], as well as of

adrenocortical insufficiency, which might develop due to hemorrhage in the adrenal cortex as recorded in the study of Chugh et al. in 1989 [57] who detected severe adreno-cortical involvement in some patients; histopathological examination revealed severe changes in the adrenal cortex (complete lipid depletion, hemorrhage, necrosis, etc.) and all these patients died. They attributed these changes to shock or to the cellular toxic effect of phosphine, a finding also recorded by Arora et al. in 1995 [58] where histopathological changes were observed in various body organs such as lungs, liver, kidneys, heart, brain, stomach and adrenals, including varying degrees of congestion, edema and leucocytic infiltration changes suggestive of cellular hypoxia. Even adrenal gland damage can occur, as recorded by Proudfoot in 2009 [39].

Recommendations

Our recommendations focus on the importance of providing awareness to medical and paramedical staff of the manifestations of zinc phosphide poisoning especially in rural areas, to improve case management and to raise public awareness so as to limit the unregulated sale of this toxic compound.

Collaboration between different poison control centers for data-gathering about cases of zinc phosphide and other pesticide poisonings will help to create a solid database and a full picture of the actual condition in our country and will subsequently assist us to assess the magnitude of the problem and to perform the required actions.

Further research including studies on a larger scale should be considered concerning the use of antifibrinolytics and steroids in the management of poisoned patients, to improve their prognosis.

Another important issue is psychosocial counseling, which is an important aspect of the overall management of the problem of attempted suicide.

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