Review Article

Review of aluminum phosphide poisoning

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ABSTRACT

Agricultural revolution and increasing pesticidal use have brought its share of downsides in the form of pesticidal poisoning. Every year approximately 300,000 deaths happen worldwide due to pesticide poisoning. Organophosphates, chlorates, and aluminum phosphide are the commonly used pesticides. Alkaline phosphatase (ALP) is the most lethal among the available pesticides and no antidote is available and aptly called as suicide poison. The common use and easy availability of ALP is causing acute and chronic health effects which have reached major proportions in Asian and Middle Eastern countries such as India, Bangladesh, Iran, Jordan, and Sri Lanka. Toxicity of ALP is related to prompt release of lethal phosphine gas as ALP tablet absorbs moisture. Phosphine gas mainly affects cardiovascular system gastrointestinal tracts, lungs, and kidneys. The clinical features of poisoning include nausea, vomiting, abdominal pain, pulmonary edema, cyanosis shock arrhythmias, and alter sensorium. Diagnosis of ALP poisoning largely depends on history and clinical setting and treatment is usually initiated without waiting for silver nitrate paper test or gastric aspirate analysis. Treatment includes early gastric lavage symptomatic supportive therapy and palliative care. There has been greater understanding about the mechanism and pathophysiology of ALP toxicity over the years, although that cannot be commented about the treatment modalities. Government efforts to restrict sale have been offset by the lack of strict enforcement by regulatory agencies. Case fatality rates from ALP poisoning have shown some decline over the years due to early supportive management. Different treatment modalities and protocols have been tried at various centers with variable success; however, further research for an antidote is the need of the hour.

KEY WORDS: Aluminum Phosphide; Phosphine; Phosphide; Pesticides; Poisoning; Silver Nitrate Test; N-acetylcysteine; Magnesium Sulfate

BACKGROUND

Pesticide has been increasing tremendously in recent years and has contributed in improving agricultural produce all over the world. Because of the common use of these toxic substances, cases of intentional and accidental poisoning have led to significant morbidity and mortality. These have far reaching psychological and socioeconomic burden on societies, especially in low- to middle-income countries. Long-term exposure resulting in chronic poisoning has also been reported with alkaline phosphatase (ALP).[1]

Metal phosphides are a group of pesticides and fumigants that are being used quiet commonly for the past few decades, which include aluminum, magnesium, and calcium phosphite. They are cheap, potent, and free of adverse effects on agricultural produce, which makes them a popular choice in developing world. Aluminum phosphide (AIP) is most lethal among phosphides, which is used for safe transportation and storage of grains, especially in Asian, Middle Eastern, and African countries. India and Iran report a very high incidence of ALP poisoning although government efforts to control their widespread use has so far been futile due to poor enforcement.[2]

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LITERATURE SEARCH

We searched for keywords "AIP," "phosphine," and "phosphide" in PubMed, Google Scholar, and SCOPUS databases and selected all the relevant articles published between 1990 till date. The selected articles were reviewed for pathophysiology, clinical features, and management of ALP poisoning and articles with outdated and duplicated information were excluded.

EPIDEMIOLOGY

Barbiturate, organophosphate, and copper sulfate used to be the predominant causes of poisonings and deaths between 1970 and 1990. However, since l990, the number of poisoning cases secondary to ALP toxicity started to rise dramatically and became the leading cause of poisoning, being directly related to free availability of this cheaper alternative in the market.[3]

Every year approximately 300,000 deaths happen worldwide due to pesticide poisoning.[4] The number of poisoning cases in many regions of world is underreported as they are largely based on hospital records. The most commonly affected demography is of rural Asian adults.[5] The availability and usage of ALP is restricted in European countries under the respective national pesticide acts.[6] In fact, most cases of ALP poisoning in developed countries are accidental.[7] However, same is not true in developing nations such as India and Iran, with largest burden of pesticide and fumigant poisoning.

In India, most extensive epidemiological and research work on ALP poisoning has been done by Chugh and Siwach *et al*.[8-10] ALP has been found to be the most commonly used suicide poison in Northwest India as per one autopsy study.[11] ALP accounted for 27% of all poisoning cases (second to organophosphorus compounds) admitted in an Indian hospital over a period of 15 years. There was no seasonal variation in cases of ALP poisoning unlike anticholinesterase poisoning.[12] However, another study from a government teaching hospital in North India reported ALP to be most common poison (38% of all cases from poisoning) followed by followed by organophosphorus compounds (18%). Almost 80% of total cases were suicidal in nature and rest being accidental and homicidal.[13]

Iran is another country with significant number of ALP poisoning cases with suicide being the most common mode of poisoning.[14] Large number of epidemiological data has been published by researchers from Iran, highlighting the public health concerns posed by ALP misuse.[15-17] According to Hosseinian *et al*., 146 deaths due to ALP poisoning were reported in Iran between 2000 and 2007, out of which 90% was suicidal.[18] A retrospective study over 7 years by Shadnia *et al.* reported ALP poisoning to be a significant cause of death with mortality rate of 31% in Tehran.[3]

PHYSICAL AND CHEMICAL PROPERTIES

ALP is a solid fumigant and is physically formulated as granules, pellets, or tablets. It is commonly available as dark grey tablet of 3 g each, by the commercial name of Celphos, Alphos, Quickphos, Synsele, Phostek, etc., each consisting of 56% ALP and 44% carbamate. ALP is the active ingredient of these preparations which liberates phosphine gas on absorbing environmental moisture. This is the reason why ALP tablets or pellets lose their potency overtime due to gradual release of phosphine gas on contact with atmospheric moisture leaving behind non-toxic aluminum hydroxide residue.[19]

Equation

$$ALP + 3H_2O \rightarrow Al(OH)_3 + PH_3$$

$$ALP + 3HCl \rightarrow AlCl_3 + PH_3$$

Pure phosphine gas (PH_3) is odorless but smells of foul decaying garlic due to the presence of phosphine and diphosphine. Diphosphine gas is the by-product of reaction between phosphine and moisture. Phosphine gas is inflammable and may ignite spontaneously in air at concentrations above 1.9% v/v. To prevent combustion of the ALP tablets during fumigations and storage, ammonium carbamate is added to the preparation which decomposes phosphine to ammonia, carbon dioxide, and diphosphine gas.[20,21]

MECHANISM OF TOXICITY

The most common cause of toxicity in humans is due to ingestion of ALP. Inhalational and absorption through eyes and dermal surfaces are other modes of toxicity although uncommon. Phosphine gas is released from ALP molecule on contact with either moisture or gastric hydrochloric acid. Phosphine is rapidly absorbed in systemic circulation through gastrointestinal mucosa leading to adverse effects. Phosphine is widely distributed to all body tissues and is oxidized to oxyacids which are excreted as urinary hypophosphites and exhaled unchanged through lungs. Unhydrolyzed ALP gets eliminated in unchanged form in the urine.[22]

Cellular injury is common in cardiac, hepatic, renal, and pulmonary tissues which are sensitive to oxygen depletion. At cellular level, phosphine leads to inhibition of cytochrome C oxidase and lipid peroxidation and forms highly reactive oxygen and hydroxyl radicals.[23] It also increases the activity of superoxide dismutase and decreases the levels of glutathione, resulting in cellular injury secondary to oxidative stress.[24] The adverse effect of phosphine on these cellular enzymes lasts for approximately 5 days. Changes in myocardial proteins due to mitochondrial toxicity cause increased permeability of sodium, potassium, magnesium, and calcium

across the cellular membranes, leading to change in cell wall potential and increased propensity for arrhythmias.[25] Apart from damage to cellular membrane and organelles, phosphine causes cellular vacuolation, degeneration, and apoptosis.[26] Phosphine inhibits cholinesterase enzyme in humans but is not found to have any clinical significance.[27]

Phosphides interact with hemoglobin to produce a methemoglobin moiety, called hemachrome, and denaturated hemoglobin aggregates known as Heinz bodies.[28,29] Phosphine gas also interacts with oxyhemoglobin to form carboxyhemoglobin, which can be measured by pulse CO-oximetry.[30]

TOXIC LEVELS

The recommended workplace exposure limit for phosphine gas is below 0.3 ppm (parts per million). Levels beyond 400 ppm are lethal with 30 min. These numbers are important for individuals working in grain storage warehouses, on ships, and manufacturing facilities of ALP.[31] Lethal dose of ALP in an average human is between 150 and 500 mg depending on the exposure of tablet to moisture and expiry date.[32]

CLINICAL MANIFESTATIONS

Acute Poisoning

Clinical features of ALP poisoning are non-specific and depend on dose, route of entry, and duration of exposure. Clinical features of ingestion poisoning manifest as nausea, vomiting, and epigastric pain within 15 min. Inhalational exposure causes respiratory irritation, cough, and dyspnea almost immediately. Organ toxicities lead to respective system manifestations and organ failure which, in turn, has worsen clinical outcomes.[33]

Chronic Poisoning

Chronic low-grade inhalational poisoning occurs in workers employed in silos and storage facilities. They develop predominantly respiratory symptoms of cough, dyspnea, and chest pain. Mandibular necrosis, also known as phossy jaw, is another complication commonly reported in literature. Long-standing skin exposure of 0.4 ppm of phosphine gas causes dermatitis changes.[34]

Organ Toxicity

Any organs could be affected by ALP poisoning. Earliest organ system to get involved is gastrointestinal tract in case of ingestion and lungs in case of inhalational poisoning.

Gastrointestinal toxicity

Early clinical features include nausea, vomiting, and abdominal pain. Serious manifestations are hematemesis, melena, esophagitis, gastroduodenitis, and esophageal strictures.[35] Rare complications are acute pancreatitis, ascites, and tracheoesophageal fistula.[36,37]

Cardiovascular toxicity

It is the most common cause of morbidity and mortality in patients with ALP poisoning. The usual cardiac symptoms are chest pain, dyspnea, palpitation, and syncope. Cardiac manifestations include congestive heart failure, arrhythmias, myocarditis, pericarditis, pericardial effusion, subendocardial infarction, and cardiogenic shock.[38] Sinus tachycardia is most common rhythm abnormality on electrocardiogram (ECG) in the first 3–6 h, and later ST-T changes and arrhythmias predominate.[39] Malignant arrhythmias include supraventricular tachycardia which constitutes half of the cases. Ventricular tachycardia was shown to occur in 40% of all cases of tachyarrhythmias in a study by Siwach *et al*. ECG changes normalize within 3 weeks if patient survives.[40] Echocardiographic features include dilated cardiomyopathy, poor ejection fraction, regional wall motion abnormalities, septal hypokinesia, pericardial effusion, and increased pulmonary capillary wedge pressure.[41] Postmortem examination reveals myocardial fiber destruction, myocyte vacuolation, neutrophilic infiltration, and cell necrosis. vascular toxicity associated with ALP poisoning manifests predominantly as refractory hypotension, which is multifactorial and refractory to inotropic and support.[42]

Respiratory toxicity

The common respiratory features are cough, dyspnea, tachypnea, cyanosis, rhonchi, and crepitations. Release of inflammatory cytokines causes exudative effusion and pulmonary edema which worsens the clinical condition. Pulmonary hemorrhage, respiratory failure, and acute respiratory distress syndrome (ARDS) are serious manifestations which require mechanical ventilation and intensive care support. Case report of serositis with pleural effusion has also been reported.[43]

Hepatic toxicity

Most common liver manifestation of ALP poisoning is jaundice and transaminitis. Mild-to-moderate hepatitis is frequently observed, although cases of fulminant hepatic failure are not infrequent.[44] These patients should also be screened for hepatic encephalopathy as subtle early features are missed commonly and mortality is quite high in such cases. Histopathology findings include hepatocyte vacuolation, sinusoidal congestion, and nuclear fragmentation.[45]

Electrolyte and metabolic abnormalities

Dyselectrolemia in the form of hypokalemia, hyperkalemia, hyponatremia, hypernatremia, and hypomagnesemia is common. Hypokalemia is mainly related to vomiting and metabolic alkalosis, whereas metabolic acidosis occurs

due to inhibition of oxidative phosphorylation and poor tissue perfusion.[46] Other metabolic abnormalities include metabolic acidosis, respiratory acidosis, and respiratory alkalosis. Hypoglycemia is seen more commonly as ALP affects the glucose metabolism, although hyperglycemia is associated with worse prognosis.[47,48]

Neurological toxicity

Neurological manifestations are seen in both acute poisoning and chronic exposure, which include dizziness, paresthesia, numbness, nystagmus, ataxia, delirium, seizures, altered sensorium, and coma. The reasons for these manifestations are unknown, although cerebral anoxia secondary to hypotension is thought to play an important role. Degeneration of Nissl granule in brain cytoplasm is seen on microscopic examination.[49,50]

Other effects

Renal involvement results in metabolic acidosis, uremia, oliguria, acute tubular necrosis, and glomerulonephritis. Other infrequent manifestations include serositis, adrenocortical insufficiency, thyroiditis, microangiopathic hemolytic anemia, rhabdomyolysis, methemoglobinemia, and disseminated intravascular coagulation.[51,52]

DIFFERENTIAL DIAGNOSIS

Manifestations of ALP poisoning could be misdiagnosed as due to sepsis, inflammatory, or metabolic causes. Zinc and other metal phosphides cause similar but less severe features compared to AIP. Differentiation requires tactful history and biochemical testing using hydrochloric acid, ammonium chloride, and ammonium hydroxide.[53,54]

DIAGNOSIS AND DETECTION OF PHOSPHINE

The diagnosis of ALP poisoning is based on clinical suspicion and appropriate history. No further confirmatory tests are required to initiate treatment. In case of any clinical doubt, a simple breath test using silver nitrate (0.1 N $AgNO_3$) impregnated paper can be performed to diagnose ALP poisoning. The presence of phosphine in breath turns silver nitrate paper black due to the formation of silver phosphate, which is easily detected at bedside.[55] Phosphine is also released on heating the viscera and body fluids above 50°C. These fumes are then detected using silver nitrate paper on the mouth of flask. This test is performed by forensic experts on post mortem examination; although it can also be performed on gastric aspirate samples in patients bedside.[56] Estimation of phosphine in blood or urine is not recommended due to its oxidization to phosphite and hypophosphite metabolites. However, these metabolites can be tested in urine if required. Gas chromatography using nitrogen phosphorus detector is the most sensitive and specific quantitative test available for phosphine detection. Arsine and ammonium detectors are also capable of phosphine estimation on expiratory samples but are not preferred due to validity issues.[57]

TREATMENT OF ACUTE POISONING

The treatment should be initiated immediately once clinical diagnosis of ALP poisoning is established. Basic principles of management are aimed at initial resuscitation, decreasing toxic exposure, increasing toxic excretion, and managing organ failure. Supportive therapy is the cornerstone of management in these patients in the absence of specific antidote. Clinical outcome improves with early resuscitation, intensive care management in specialized units with standard protocols in place. Toxicological advice may also be sought if available.

Initial Evaluation and Resuscitation

Primary clinical survey by a trained healthcare professional should be done immediately after wearing appropriate personal protection. Airway, breathing, and circulation parameters are assessed immediately, and appropriate management decisions should be taken without any delay. The medicolegal nature of these cases and intense emotional environment makes the whole situation quiet challenging for health-care staff and sometimes delay the treatment. Relatively younger age group of these patients with lesser comorbidities makes them suitable for full resuscitation and organ support therapies. Hence, the role of prompt management with early assessment by intensive care team cannot be stressed more. Initial investigations include routine blood tests, electrolytes, glucose, troponins, blood gases, and ECG.[58]

Decrease the Exposure of Toxin

Victim should be immediately removed from offending environment, especially in case of inhalational exposure taking necessary precautions. The attending medical staff should use appropriate personal protective equipment. Patient's clothes should be removed to prevent reabsorption of toxins through skin followed by thorough skin and eye wash using sterile water. Vomitus should be cleaned immediately from the vicinity as it may release phosphine gas.[59]

Gut Decontamination

Gut decontamination in the form of gastric lavage should preferably be done within 1 h of toxin ingestion. It is very important to make sure that patient's airway is protected. Water is avoided for gastric lavage due to the formation of phosphine gas from ALP, so various other agents could be used for gastric lavage. A gastric lavage protocol using potassium permanganate in 1:10,000 dilution, which oxidizes

phosphine to non-toxic potassium phosphate and aluminum permanganate, followed by activated charcoal in the dose of 1 g per kg body weight is advised to neutralize and reduce absorption of ALP.[60] Gastric lavage with 3–5% sodium bicarbonate solution has been tried with some success. Bajwa *et al*. recommended simultaneous gastric irrigation and aspiration with sodium bicarbonate and coconut oil in a 1:1 mixture of 50 ml each and demonstrated a survival rate of 42% in case series of 33 patients.[61] Vegetable oils act as a mechanical barrier over the gastric mucosa and reduce phosphide breakdown, preventing absorption of phosphine in systemic circulation. Gastric lavage using coconut oil has shown to be successful in the management of ALP poisoning patient.[62] Saidi *et al.* reported sweet almond oil to considerably reduce cholinesterase levels in rats and shown to be beneficial if given immediately after ALP ingestion.[63] Hassanian *et al*. proposed gastric ventilation for evacuation of phosphine gas from stomach after ALP ingestion. Air is insufflated through nasogastric tube using air pump and the contaminated air with phosphine escapes through orogastric tube.[64] Retrograde rectal lavage following three cycles of gastric lavage has been suggested in one study using nasogastric tube. Sorbitol solution can be used as cathartic.[65]

Excretion

Phosphine excretion through urine can be achieved by adequate intravenous hydration and dopamine infusion in renal dose. Increasing respiratory rate and minute ventilation while patient is on mechanical ventilatory support enhances phosphine excretion through the lungs.[19]

Early Identification and Managing Organ Failure

Phosphine affects all organ systems in the body and prompt supportive therapy is paramount in preventing organ failure and further complications.

Cardiovascular Support

Myocardial dysfunction and hemodynamic instability are the leading causes of death in ALP poisoning. The aim of therapy is to maintain oxygenation and adequate tissue perfusion till poison levels are reduced. Continuous cardiac monitoring and 12-lead ECG are required in all patients. Malignant arrhythmias are treated with anti-arrhythmic drugs and cardioversion. Ventricular dysrhythmias were shown to be resolved in a case report by administering oral trimetazidine, a common antianginal medication.[66] Temporary pacing through transcutaneous or transvenous route is required in patients who develop bradyarrhythmia with adverse signs such as hypotension, syncope, and heart failure. Vasopressors and inotropes are required commonly in refractory shock to maintain tissue perfusion and mean arterial pressure and are administered as per central venous pressure or pulmonary capillary wedge pressure readings.[67] Rapid digitalization helps increase myocardial contractility and blood pressure and counters effect of ALP on myocardium preventing cardiogenic shock.[68] There is some published literature supporting the use of digoxin with dopamine in patients with cardiogenic shock and left ventricular dysfunction.[69] Myocyte contraction is improved using hyperinsulinemia euglycemic and hyperventilation protocols as described by Hoassainian *et al*. This effect is attributed to energy production and calcium availability using this treatment.[70] Hydroxyethyl starch is a colloid preparation which prevents fluid shift out of intravascular space, thereby helps maintaining blood pressure. Routine use of these preparations in ALP poisoning cannot be strongly recommended in the absence of hard data.[71] Measures such as intra-aortic balloon pump and left ventricular assist devices like Impella are used in refractory cardiogenic shock.[72] The use of extracorporeal membrane oxygenation in patient with hypoxemia and intractable circulatory collapse has shown benefit but is available in specialized centers.[73]

Respiratory Support

Development of ARDS is the most common respiratory complication and requires management with mechanical ventilation in intensive care unit (ICU). Efficacy of hyperbaric oxygen in humans with ALP poisoning has not been investigated.[74] Pulmonary edema may warrant use of diuretics in fluid overloaded patients. Patients with cyanosis not responding with oxygen therapy need CO-oximetry or plasma methemoglobin measurements. Symptomatic patients with methemoglobinemia usually benefit from 1% intravenous methylene blue (1–2 mg/kg body weight) over 5 min. Combination therapy with addition of intravenous Vitamin C (1 g 6 hourly) facilitates further decrease in methemoglobin concentration. Treatment of methemoglobinemia occasionally worsen acidosis.[51]

Role of Magnesium Sulfate

Magnesium sulfate acts as cell membrane stabilizer and reduces the incidence of malignant arrhythmias. It also acts as antiperoxidant and free radical scavenger, thereby decreasing the oxidative stress induced by phosphine.[75] Many different dosage protocols have been suggested, but the most common intravenous infusion protocol is 3 g magnesium sulfate ($MgSO_4$) over 3 h followed by 6 g over 24 h for 3–5 days. Bolus protocol of administering 4 g intravenously stat, 2 g after 1 h, and then 1 g every 4 hourly can be employed if continuous infusion is not possible.[76] In a meta-analysis by Siwach *et al*., mortality in patients who received magnesium sulfate did not significantly differed from the ones who did not receive it. Hence, the routine use of magnesium sulfate in these patients is questionable. Best approach would be to administer magnesium sulfate in patients with low or normal serum levels of magnesium and monitor daily serum levels to prevent adverse effects of hypermagnesemia.[77]

Antioxidant Therapy

N-acetylcysteine (NAC) is a well-studied compound which is commonly used in the treatment of paracetamol poisoning. It has shown to replenish cellular glutathione stores in addition to the strong antioxidant properties. NAC has shown to reduce mortality, hospitalization time, and need for mechanical ventilation in ALP poisoning.[78] A cohort study by Agarwal *et al*. reported survival benefit in patients who received treatment with NAC compared to the control group. The treatment protocol they used was intravenous infusion of NAC 150 mg/kg body weight in 200 ml of 5% dextrose over 1 h, followed by 50 mg/kg body weight in 500 ml of 5% dextrose over 4 h, and then 100 mg/kg body weight in 1000 ml of 5% dextrose over 16 h.[79] Vitamin B complex, Vitamin C, and beta-carotene seem to be theoretically beneficial secondary to their antioxidant properties, although there are no clinical data available. Vitamin E has shown to prevent destruction of hepatocytes secondary to phosphine-induced lipid peroxidation.[80]

Renal Support

Hemodialysis is helpful in patients with acute kidney injury who develop renal failure, fluid overload, and metabolic acidosis, but it does not remove phosphine form circulation. Patients with hypotension are not a candidate for conventional dialysis and are treated by continuous renal replacement therapies. Moderate-to-severe metabolic acidosis is managed aggressively with intravenous sodium bicarbonate before hemodialysis could be initiated as it results in improved patient outcomes.[81]

Other Treatments

Glucose levels should be monitored regularly to avoid hyper- or hypoglycemia. Dyselectrolemia is managed with established treatment protocols to reduce morbidity and mortality as these abnormalities are associated with worse outcomes. Calcium chloride stabilized cell membranes and is more potent in treating hypocalcemia.[65] Patient with adrenal insufficiency should receive steroids in appropriate dosage to prevent adrenal crisis and support blood pressure. Seizures should be managed accordingly with benzodiazepines. Phosphine is shown to inhibit acetylcholinesterase in rats; therefore, pralidoxime and atropine may prove effective in these patients, although there are no clinical data at present.[82] Baruah *et al*. reported successfully management of two cases with intravenous administration of lipid emulsion to entrap the absorbed phosphine molecules.[83]

MORTALITY AND PROGNOSTIC INDICES

Mortality in the first 12–24 h is primarily due to cardiovascular collapse. After 24 h, causes such as persistent shock, severe acidosis, ARDS, and fulminant hepatic failure are the common culprits.[84] Patient without any clinical features 6 h post-ingestion has good prognosis. Mortality rate reaches 100% in patients who have ingested of 500 mg or above of ALP.[85] There are case reports wherein patients survived even after consuming more than 9 g of ALP, with no exact reasons found. Survival is more likely in patients who have consumed expired or already exposed tablets. Poor prognostic markers include presence of cardiac arrhythmias, hypotension, dyselectrolemia, acidosis, methemoglobinemia, low prothrombin time, and organ dysfunction.[84]

Acute physiology and chronic health evaluation (APACHE II) and simplified acute physiology score (SAPS II) are common ICU scoring systems, which can be used to measure severity and predict mortality in these patients. Both APACHE II and SAPS II scores should be calculated on admission to ICU, utilizing certain physiological and clinical parameters of patient.[86,87]

Before Discharge

Jain *et al*. described dysphagia and esophageal strictures in survivors 1 month after ALP exposure.[88] All survivors with dysphagia should be offered upper gastrointestinal endoscopy for early detection of esophageal complications, which is seen in one-third of survivors at 40 days. Barium swallow is an alternative in centers where endoscopy is not available.[89] Role of psychological support is important in vulnerable individuals with a history of deliberate self-harm.

Long-term Complications

Dysphagia secondary to esophageal strictures and tracheoesophageal fistula has also been reported in literature.[37] Chronic neurological complications such as peripheral neuropathy, paresthesia and ataxia have been reported in case reports.[90]

PREVENTION

In the absence of specific antidote, the most important management strategy is restricting the misuse of ALP tablets by general public. Limiting sale to each individual, appropriate documentation, and replacing ALP with other non-fatal alternatives are some measures worth considering. A novel way is to make hard spikes on surface of ALP tablets preventing its ingestion. Education of general public and training of health-care professionals is paramount in fighting this epidemic.

CONCLUSION

The pathophysiology and clinical understanding of ALP poisoning has improved over the years. Case fatality rates have also declined due to early and improved management

but further research for an antidote is the need of the hour. There have been multiple management protocols reported in literature, although none of them have been validated in a larger clinical setting. To reduce the overall incidence of suicide, the Food and Agriculture Organization of United Nations has urged all nations to ban the sale of pesticides. Various countries across the globe have implemented pesticide safety regulations to reduce misuse with variable success. Much needs to be done in terms of implementation of stricter measures to tackle this epidemic of pesticide poisoning, especially in developing countries such as India and Iran.

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