Phosphine induced acute cardiototoxicity in children: A need for health awareness
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Abstract
Aluminum Phosphate (AP) is a cheap and highly effective pesticide. Phosphine is the active pesticidal component which is highly toxic. Mortality is high and ranges between 40-70%. There is a desperate need for creating awareness. We report a case series with a mortality of 40% and emphasize the need for public awareness.

Keywords: Phosphine, Aluminum Phosphate, Cardiotoxicity.

Introduction
Phosphine is the active gaseous ingredient of the pesticide aluminum phosphate (AP) and is liberated upon contact of AP with moisture in the environment. Accidental exposure is by inhalation but ingestion is also a route of toxicity. Phosphine gas is highly toxic with symptoms occurring within first 2 hours of exposure and mortality rates ranging from 40-70%. For workers in agricultural storage and handling, respiratory protection to prevent toxicity is mandatory. In Pakistan, this pesticide has been misused in houses for bed-bug eradication because of its high potency. We report a case series in children admitted between February 2014 and April 2015 in whom the mortality was 40% when this chemical was used for fumigation at homes. The purpose of this report is to create awareness that this toxic pesticide is not for domiciliary use. This report has been made with parental consent.

Case 1 and 2
Two children belonging to the same family, aged five years and 8 months respectively, presented in July 2015 with drowsiness, irritability and bouts of cough occurring at midnight. They slept with their parents in one room which was fumigated the same evening with AP to kill bed bugs. The five year old became drowsy and developed severe respiratory distress and died on the way to the emergency. The 8 month old was also rushed in the emergency. He had vomiting and respiratory distress. He had tachycardia with a heart rate of 130 bpm, blood pressure 100/60 mmHg, had poor perfusion.

His cardiac enzymes were elevated and he had severe lactic acidosis. Electrocardiogram showed non-specific ST-T wave changes (Figure-1). Echocardiography showed moderate to severe left ventricular systolic dysfunction, with an ejection fraction of 35%. The child was treated with inotropes (milrinone, epinephrine), enalapril and furosemide. Within 48 hours his cardiac function improved and he was shifted out of intensive care unit. He was discharged with a left ventricular ejection fraction of 70%.

Case 3
A seven year old girl was brought to emergency in September 2015 with nausea, vomiting and abdominal pain for one day. Her father had put few AP tablets for fumigation in the room where she had slept. She became drowsy and was brought to the emergency room. She had a pulse rate of 117bpm, blood pressures were 95/55 mmHg, and oxygen saturations were 97% on 2 liters of facial oxygen. She had gallop rhythm and hepatomegaly. Electrocardiogram was unremarkable. Echocardiogram showed depressed left ventricular function with an ejection fraction of 45%. She was given intravenous infusion of dobutamine and dopamine. She was discharged after 2 days on oral captopril and diuretics. The left ventricular function had improved, ejection fraction being 57%.

Case 4
Three year old boy was brought to the emergency department in February 2016 with persistent vomiting, tachypnea and drowsiness for 3 hours. Fumigation was done with AP in this child’s room where he slept with his
parents. He was in severe respiratory distress, poorly perfused with low volume thread pulses, blood pressure 71/42 mmHg, heart rate 190 bpm, and gallop rhythm was heard. He was diagnosed to have cardiogenic shock and managed aggressively with endotracheal intubation, correction of severe metabolic acidosis (pH=6.98, serum bicarbonate 9 meq/l) and multiple inotropic (dopamine and epinephrine) infusions. He was drowsy (Glasgow coma scale 4/15). His echocardiogram showed a very poor bi-ventricular function with a left ventricular ejection fraction of 20% and right ventricular ejection fraction of 30%. He was shifted to the intensive care unit, managed for cardiac failure but within one hour started to have hypotension and bizarre electrocardiographic changes with broad QRS complexes. Finally he went into ventricular fibrillation and could not be revived.

**Case 5**

Two year old girl was taken to a local hospital in April 2016 for vomiting and abdominal pain. She was diagnosed to have gastritis and discharged. At home she became drowsy and the vomiting persisted and so was brought back to the emergency room. She was found to be in cardiogenic shock with a heart rate of 160 beats per minute, very poor perfusion, low volume pulses and a very pale sweaty skin. Her electrocardiogram showed diffusely broad QRS complexes and ST-T changes (Figure-2) suggestive of severe myocardial disease. Cardiac enzymes were elevated. Echocardiogram showed mildly enlarged left ventricle with severe systolic dysfunction with an ejection fraction of 15% and moderate right ventricular dysfunction, TAPSE (tricuspid annular plane systolic excursion) of 8mm, s wave velocity on tissue Doppler of tricuspid annulus was 0.06 m/s. The child was managed aggressively in the intensive care unit with mechanical ventilation and multiple inotropes (milrinone and dopamine). The child improved after 48 hours with an improvement in ejection fraction to 35% and was discharged after 2 days with an ejection fraction of 60%.

**Discussion**

Aluminum Phosphate (AP) is a cheap and highly effective pesticide used widely in the storage of grains and other agricultural products. Phosphine is the active pesticide component released upon contact of AP with moisture. Inhalation is the common route of absorption followed by gastrointestinal. After rapid absorption, it is distributed throughout the body with adverse effects mainly on cardiovascular, respiratory, and nervous system, and to a lesser extent on liver, kidney and gastrointestinal tract. Phosphine is highly toxic with a very precipitous concentration-response curve. With a few hours of exposure, cardiovascular collapse, congestive cardiac failure and death. Most of the cardiovascular deaths occur with the first few hours to days of exposure. Death due to the damage of liver and kidneys may occur late.

Children exposed to phosphine are at a greater risk of poisoning compared to adults due to a higher lung surface area to body weight ratio and faster respiratory rates. Exposure to 7-14 mg m-3 (5-10 ppm) of phosphine for several hours may cause serious effects. The four hour inhalation of phosphine gas has been measured to be 11 ppm (approximately 0.014 mg/L) in animal (rat) studies, which places it in the highest toxicity category.

Phosphine, being a strong reducing agent, is capable of interacting with and inhibiting cellular enzymes such as mitochondrial cytochrome c oxidase resulting in generation of superoxideradicals and cellular peroxides. These cause lipid peroxidation leading to cellular injury. The most common early symptoms are related to respiratory tract due to direct cellular injury to the respiratory epithelium. In the myocardium it causes depression of cellular metabolism and myocardial necrosis.

Electrocardiographic abnormalities have been noted in 38-91% of cases and include bundle branch block (right, left) in 25%, atrioventricular block in 8%, atrial fibrillation in 2-6%, extrasystole (atrial and ventricular) in 18% and ventricular fibrillation in 2%. In the above series, case 3 died of ventricular fibrillation and case 5 had extensive conduction block.

Management of acute cardiotoxicity has to be aggressive because mortality is high, reported up to 67%. Controlled mechanical ventilation, management of cardiogenic shock and myocardial dysfunction with inotropes and diuretics is indicated. Intravenous magnesium has shown good results in some reports.

In Pakistan, AP is cheaper than other pesticides and is...
therefore frequently used for household fumigation. There is no public awareness regarding its lethal toxic effects and manufacturers also have not disseminated this information. Such cases of phosphine poisoning have been reported from India where cheaper household pesticides are used without being aware of its severe toxic effects.2

**Conclusion**
Aluminum Phosphate is a cheap and a very effective pesticide used for storage of grains and other agricultural products. Its routine use as domestic pesticide has to be strictly prohibited by creating awareness among public. Manufacturers have to label the product accordingly.

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**References**