CASE REPORT

Severe Hypoglycemia Following Acute Aluminum Phosphide (Rice Tablet) Poisoning; A Case Report and Review of the Literature

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Abstract- Aluminum phosphide (AlP) as 3 g tablet is widely used in Iran to protect stored food grains from pests. Hyperglycemia following its ingestion has been already reported in the recent years but severe hypoglycemia is uncommon. Here, we report a 19 year old male who attempted suicide with one tablet of AlP and demonstrated severe hypoglycemia. Despite restoration of blood glucose concentration to normal, he failed to respond to supportive treatment and died. The possible mechanisms leading to severe hypoglycemia are discussed. Though severe hypoglycemia is rare following AlP poisoning, physicians managing such patients should be aware of it.

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Keywords: Aluminum phosphide; Rice tablet; Poisoning; Hypoglycemia; Blood glucose level

Introduction

Two kinds of rice tablets one being herbal while other containing 3g aluminum phosphide (AlP) are available for use in Iranian households to protect stored food grains from pests and rodents (1). Self poisoning with AlP tablets is increasingly being reported from Iran in recent years (2,3). Its toxicity is due to the release of phosphine which occurs when it comes into contact with moisture or gastric juice (4). Phosphine is believed as a mitochondrial toxin though its exact mechanism of action is not known (5). Hyperglycemia following its ingestion has been already reported in the recent years also rarely mild hypoglycemia has been reported (3,6-10). Severe hypoglycemia as being reported in the present case is uncommon.

Case Report

A 19 years old male was admitted to emergency department (ED) of Firouzgar Educational Hospital (One of the referral hospital for poisoned patients located in Tehran (11), about 5 hours after ingestion of one 3 g tablet of AlP. Prior to admission, he has been healthy and was not taking any medication or illicit drugs. He didn't have any history of diabetes mellitus or insulin usage. At admission, he was confused with Glasgow consciousness scale (GCS) of 8. His Blood pressure was 80/60 mm Hg, pulse rate 116/min, respiratory rate 17/min, oral temperature 35.8^{o}C with cold and clammy extremities. Investigations revealed hemoglobin (Hb) 15.1 g/dl, hematocrit 58.3 with normal total and differential white cell counts. ABG analysis revealed ever metabolic acidosis with pH 6.99; O_2 pressure (PO_2) 57 mmHg; CO_2 pressure (PCO_2) 27.8 mmHg; arterial HCO_3 level 6.6 mM and O_2 saturation of 85%. His electrocardiogram was normal except for sinus tachycardia. Blood biochemistry revealed serum sodium 142 meq/l, serum potassium 3.9 meq/l, serum calcium 7.5 mg/dl, serum magnesium 1.3 mg/dl, aspartate aminotransferase (AST) 55 U/l; Alanine aminotransferase (ALT) 63 U/l; bilirubin 1.4 mg/dl; blood urea nitrogen (BUN) 19 mg/dl, creatinine 1.0 mg/dl and blood glucose 18 mg/dl (venous and estimated by autoanalyzer) (Table 1).

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Table 1. Vital signs and laboratory investigation of our patient with aluminum phosphide poisoning.

Dose of ALP (mg)	3000
Elapsed time (hours)	5
Glasgow consciousness scale (GCS)	10
Systolic Blood Pressure (SBP) (mmHg)	80
Pulse Rate (Beat/minute)	116
Respiratory rate	17
Oral Temperature (^oC)	36
O_2 Saturation (%)	85
Arterial Pressure (PO_2)(mmHg)	57
Arterial HCO_3 (mM); Normal: 22-26 mM	6.6
Serum CO_2 Pressure; Normal: 35-45 mmHg	27.8
Arterial pH (7.35-7.45)	6.99
Serum Potassium(K) (meq/l); Normal:3.5-5	3.9
Serum Sodium (Na)(meq/l); Normal:135-150	142
Hematocrite (%)	58
WBC Count (per mm)	12677
Hemoglobin (g/dl)	15.1
Blood glucose level at admission (mg/ml) (70-110mg/dl)	18
Blood glucose level 1 hour after admission (mg/ml)	126
Serum Calcium (mg/dl); Normal: 8-10 mg/dl	7.5
Serum Magnesium (mg/dl); Normal: 1.8-3 mg/dl	1.3
Alanine aminotransferase (ALT) (U/L) (7-56 U/l)	63
Aspartate aminotransferase (AST) (U/L)(5-35 U/L)	55
Total Bilirubin (mg/dl); Normal: 0.2-1.3 mg/dl	1.4
Serum creatinin (mg/dl)	1
Blood Urea nitrogen (mg/dl)	19

Hypoglycemia was immediately treated with 2 boluses of 50% dextrose (50 ml each) intravenously followed by 10% dextrose as a continuous infusion. In addition, the patient received gastric decontamination with sodium bicarbonate (44 mEq, orally), permanganate potassium (1:10,000), and activated charcoal (1 g/kg, orally), magnesium sulfate 4 g by IV infusion, calcium gluconate 4 g by IV infusion and adequate hydration. Though his blood glucose concentration became normal (100 mg/dl) shortly after bolus of dextrose and continued to remain normal i.e. 126 mg/dl after 1 hour of admission, he failed to respond to supportive treatment and died 2 hours later due to refractory hypotension leading to cardiac arrest. The autopsy on gross examination revealed generalized visceral congestion especially marked in liver, kidneys and lungs. Microscopic examination of liver revealed congestion, microvacoualization, hydropic degeneration of hepatocytes, centrilobular necrosis and mononuclear infiltration. Adrenal examination showed fat depletion and hemorrhagic necrosis. All other organs revealed only congestion.

Discussion

AlP is available in Iran as 3 g tablets and is marketed under brand names Celphos, Quickphos, Phostoxin. Each tablet contains 56% AlP and 44% of ammonium carbonate. Its toxicity is due to phosphine which is a mitochondrial toxin interfering with enzyme and protein synthesis via mechanisms which are poorly understood (4). Changes in blood glucose levels are known following its ingestion both in animal studies and humans (3, 7,9). In a study by Mehrpour *et al*. non-survivors had significantly higher blood glucose concentration than survivors and authors concluded that hyperglycemia prognoses higher mortality (7). Mild hypoglycemia has been already reported in two patients following AlP ingestion (10, 12). The possible mechanism for changes in blood glucose levels are complex and depend on the balance of factors which increase its concentration and those which reduce it. The former include stimulation of cortisol, glucagon, and adrenaline secretion and inhibition of insulin synthesis whereas hypoglycemia is probably the result of inhibition of neoglucogenesis in liver along with failure of hepatic glycogenolysis as reported in an experimental study in rats (4, 7, 9). Liver damage in humans in AlP poisoning has been reported in autopsy studies and was present in the present case at necropsy (13,14). Chugh *et al*. reported low levels of cortisol in these patients as a result of damage to adrenal cortex and in our patient, adrenal examination showed fat depletion and hemorrhagic necrosis at necropsy (15). Cortisol promotes gluconeogenesis and inhibits the peripheral utilization of glucose and lower cortisol levels could have contributed hypoglycemia. Other factors which could have contributed are failure of glucagon secretion and epinephrine synthesis (4). Further release of insulin-like growth factor (IGF-1) in response to shock may be another contributory mechanism (16).

AlP poisoning has been postulated to stimulate cortisol which leads to increasing blood level of cortisol, also it may cause stimulation of glucagon, and adrenaline secretion; in addition, it can inhibit insulin synthesis which may lead to hyperglycemia (7). Another suggested mechanism of hyperglycemia is rennin

activity in some cases, an increase in magnesium level of plasma and that of tissues, and high phosphate level (17). Moreover, pancreatitis and also a mild to moderate adrenal damage due to this poisoning may lead to hyperglycemia while sever adrenal damage may result in hypoglycemia (7,15). Although hyperglycemia is most frequent in this poisoning and also is known as a marker of poor prognostic, hypoglycemia in aluminum phosphide poisoning is a rare finding which may be so dangerous. Liver and adrenal damage when combined with inconsistency in biochemical changes in aluminum phosphide poisoning may affect blood glucose level.

Our case showed hypomagnesemia and hypocalcemia. It was in accordance with the results reported in Abder-Rahman *et al*. study which revealed that hypomagnesemia, hypocalcemia, high plasma phosphate level, or inhibition of citrate synthesis and 1, 6-biphosphatase activity in this poisoning may lead to hypoglycemia (17).

Our patient showed severs hypotension and sever acidosis in addition to sever hypoglycemia. Other studies also showed that the presenting features of AlP intoxication are rapid onset of shock, severe metabolic acidosis, cardiac dysrhythmias and adult respiratory distress syndrome (ARDS) (4). There are also proofs of direct damage to blood vessels and erythrocyte membranes (7). AlP poisoning if not treated causes death within 24 hours, presumably due to cardiogenic shock (4). In conclusion, though severe hypoglycemia is rare following AlP poisoning, physicians managing such patients should be aware of it. Though hypoglycemia was corrected, our patient still died as a result of intractable shock which is an important manifestation of severe AlP poisoning.

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