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Successful Treatment of Aluminum Phosphide Poisoning with Digoxin: A Case Report and Review of Literature

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Abstract: Aluminum phosphide (AlP) is a pesticide which release phosphine gas when comes in contact with water or hydrochloric acid in stomach. Phosphine is a mitochondrial poison and interferes with protein and enzyme synthesis. Cardiogenic shock secondary to toxic myocarditis remains the most common cause of death in AlP poisoning. There is citable report on the use of digoxin for treatment of cardiac failure from ALP poisoning, although it has been used effectively for other causes of cardiac failure. Here an 18-years old female is introduced who referred to poisoning center with acute AlP poisoning and cardiogenic shock. Digoxin 0.5 mg was initially used and followed by 0.5 mg every 6 h during the first day. Digoxin was continued by 0.25 mg daily for management of cardiogenic shock until the effects of AlP resolved. The patient was discharged 10 days after admission, with full recovery. The conclusion is that administration of digoxin to ALP poisoning cases help manage to cardiogenic shock and prevent from death but needs to be confirmed by further studies.

Key words: Phosphine, poisoning, phosphide, digoxin

INTRODUCTION

There are two kinds of pesticide which are used to protect grains and rice from pests and rodents in household that are known as rice tablet. One of them is an herbal product and poisoning with it, is not dangerous but the other one is aluminum phosphide (AlP), a fumigant which release phosphine gas when comes in contact with water or hydrochloric acid in stomach (Mehrpour and Abdollahi, 2010). Phosphine is a mitochondrial poison (Abdollahi *et al*., 2004) and interferes with protein and enzyme synthesis (Mehrpour and Singh, 2010; Shadnia *et al*., 2005, 2009). Impairment of oxidative phosphorylation and shock due to AlP poisoning may lead to multi organ dysfunction especially hypoxic damages (Mehrpour *et al*., 2008a).

Reported mortality rate due to AlP poisoning is too high (60-80%) and it is an emergency situation in emergency departments (Pajoumand *et al*., 2002; Shadnia *et al*., 2009; Mehrpour and Abdollahi, 2010). Although, some compounds have been introduced as decontaminant from gastrointestinal tract (Shadnia *et al*., 2005) but there is no specific antidote for AlP poisoning (Nikfar *et al*., 2011). Cardiogenic shock still remains the most common cause of death in AlP poisoning (Shadnia *et al*., 2011), so theoretically; treatment of cardiogenic shock may result in recovery because of digoxin cardiotonic potential in this poisoning as hypothesized by Sanaei-Zadeh and Farajidana (2011). Here a case of severe acute AlP poisoning with major cardiotoxicity who was successfully survived by use of digoxin is reported.

CASE REPORT

An 18 years old female was admitted to emergency Department of Emam-Khomeini Hospital as the main referral hospital for poisoned patients located in Ardabil, west of Iran (Mehrpour and Singh, 2010), about 4 h post ingestion of one 3 g tablet of AlP. After intentionally ingestion of AlP at the home, she complained vomiting, epigastric pain and thirst, when she was transferred to a local hospital where received gastric lavage and 100 g charcoal. Then, the patient was referred to Emam-

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Table 1: Clinical and laboratory investigation of our patient with aluminum phosphide poisoning

Parameter (normal range)	On admission	6 h	12 h	18 h	24 h	2nd day	3rd day	4th day	5th day	6th day
Blood Pressure (BP) (mmHg)	50/pulse	70/50	70/50	90/60	100/70	105/70	110/70	115/75	110/70	115/70
Pulse Rate (beat/minute)	120	124	118	106	96	84	76	72	74	70
Respiratory rate	17	20	24	20	18	16	16	18	16	16
Oral temperature (°C)	35.8	36.7	36.5	36.9	37	36.9	36.9	36.9	37	37
O_2 saturation (%) (>85%)	92	92	88	94	98	98	95	97	98	95
Serum O_2 pressure (PO_2) (80-100 mmHg)	59	56	53	58	59	65	74	80	81	80
Serum HCO_3 (22-26 mmol L^{-1})	11.1	7.6	9.3	11.4	15.5	20.6	23.2	23.5	23.2	23.7
Arterial serum CO_2 pressure (35-45 mmHg)	31.7	17.4	28.5	25.7	32	36.5	39.2	38.7	37.9	38.5
pH (7.35-7.45)	7.162	7.035	7.10	7.26	7.31	7.37	7.39	7.38	7.39	7.38
Serum potassium (3.5-5 meq mL^{-1})	3.9	4	3.8	3.8	3.7	3.8	3.9	4.1	3.9	4.2
Serum sodium (135-150 meq mL^{-1})	142	146	146	146	145	142	147	145	141	145
Hematocrite (mg mL^{-1})	40	38	38	37	38	37	36	37	38	38
WBC count (per mm)	11500	12800	12600	12800	11300	10800	9200	9700	8800	8200
Prothrombin time (12-14 sec)	13.3	13.3	13.4	13.6	13.4	16.1	28	24	14	13.7
Partial thromboplastin time (25 to 35 sec)	30	32	30	30	30	30	36	32	24	22
INR* (0.8-1.2)	1	1.2	1.1	1.1	1.2	1.2	2	1.6	1.2	1.1

*International Normalized Ratio (INR)

Khomeini Hospital for better management. The patient did not have history of chronic disease or taking any medications or illicit drugs. At admission, she was agitated with Glasgow Consciousness Scale (GCS) of 14. Her Blood Pressure (BP) was not detected but others were as follow: pulse rate: 120 min^{-1} and filiform, respiratory rate: 17, oral temperature: 35.8°C with cold and clammy extremities. Investigations revealed hematocrit: 40 and white blood cell counts: 11500. Arterial Blood Gas (ABG) analysis revealed ever metabolic acidosis with pH: 7.162; serum O_2 pressure (PO_2): 59 mmHg; serum CO_2 pressure (PCO_2): 31.7 mmHg; serum HCO_3: 11.1 mmol L^{-1} and O_2 saturation of 92%. Her electrocardiogram was normal except for sinus tachycardia. Blood biochemistry revealed serum sodium (Na): 142 meq mL^{-1}, serum potassium (K): 3.9 meq mL^{-1}, serum calcium (Ca): 7.9 mg dL^{-1}, serum magnesium (Mg): 1.5 mg dL^{-1}; Blood Urea Nitrogen (BUN): 18 mg dL^{-1}, creatinine: 1 mg dL^{-1} and blood glucose: 212 mg dL^{-1} (Table 1). Electrocardiogram (ECG) showed sinus tachycardia with no ST-T changes. Troponin I (TPI) was negative. Her bedside echocardiogram showed severe Left Ventricular (LV) systolic dysfunction (EF = 25%), global hypokinesia, mitral valve regurgitation (MR) and increased mean pulmonary artery pressure (PAP = 26). End-diastolic size of LV was 55 mm and end-systolic size of LV was 45 mm. Left atrial size was 37 mm. Then when she was transferred to ICU, she received endotracheal intubation and mechanical ventilation and gastric decontamination with sodium bicarbonate (44 mEq, orally), permanganate potassium (1:10,000) and activated charcoal (1 g kg^{-1}, orally). Then she was treated with magnesium sulfate 6 g by IV infusion daily, calcium gluconate 4 g by IV infusion daily and adequate hydration. Due to severe metabolic acidosis she received 6 vials of sodium bicarbonate (44 mEq) stat that continued by 6 vials daily. Due to acute left heart failure and severe hypotension, dopamine (10 μg kg^{-1} min^{-1}) was started. Additionally, she received digoxin 0.5 mg initially followed by 0.5 mg every 6 h during the first day. Digital continued by 0.25 mg daily. At day 2, her blood pleasure and pH significantly increased (Table 1). At day 3, INR were increased till 2. Echocardiography on day 3 was normal. At that time due to better condition of patient she was extubated. At day 4 of admission, she was transferred to the poisoning ward. At day 6, infusion of digoxin was stopped. She was discharged 10 days after admission, with full recovery.

DISCUSSION

AlP is a highly toxic pesticide that is often used for suicide in many countries as a cheap, easily available and effective grain fumigant and rodenticide (Proudfoot, 2009; Shadnia *et al*., 2005, 2008). After ingestion, it produces serious systemic effects within an hour. The toxic effects and prognosis is highly dependent on dose, freshness of tablets, immediate vomiting after the onset of poisoning, lower GCS, hypotension, acidemia, existence of abnormality in ECG, hematocrit, leucocytosis, hyperglycemia, BUN and SAPS-II at the time of admission in the hospital (Shadnia *et al*., 2010). The most common signs and symptoms in AlP poisoning are gastrointestinal symptoms and profound circulatory collapse which results in congestive cardiac failure and acute respiratory arrest (Shadnia *et al*., 2009). Profound cardiogenic shock and circulatory collapse is the result of direct effects of AlP on cardiac myocytes (Shadnia *et al*., 2005; Proudfoot, 2009). Supporting by previous reports, the present case showed severe hypotension, hyperglycemia, acidemia, low ejection fraction and LV systolic dysfunction confirmed by echocardiography. Echocardiographic performance in the present case showed marked LV systolic dysfunction. Follow-up of cardiac function by echocardiography in few cases of AlP poisoning revealed

dysfunction of the left ventricle (Bhasin *et al*., 1991; Gupta *et al*., 1995). In fact cardiotoxicity of this agent varies from minor electrocardiographic abnormalities such as a sample sinus tachycardia to severe cardiac contractility depression secondary to toxic myocarditis (Sanaei-Zadeh and Farajidana, 2011). Other surveys on cardiotoxicity of AlP poisoning showed an increased left ventricular dimension, left ventricle hypokinesia, akinesia, low ejection fractions, severe hypotension, increased systemic venous pressure, normal pulmonary artery wedge pressure and ECG abnormalities (Gupta *et al*., 1995; Bhasin *et al*., 1991).

After treatment with digoxin in the present case, the echocardiography on day 3 became normal. It has been reported that patients who survived AlP poisoning have normal echocardiographic findings on day 5 (Gupta *et al*., 1995).

Till now, researchers are trying to reduce mortality rate with different agents such as N-acetylcysteine and trimetazidine (Proudfoot, 2009), but none of them have been effective yet. In addition, some surveys have tried to show efficacy of magnesium in AlP poisoning and although its efficacy in other pesticides such as organophosphate poisoning was proved (Pajoumand *et al*., 2004), but its advantage in AlP poisoning is in debate. Intra-aortic balloon pump has been used to mechanically support the heart in toxic myocarditis and refractory shocks in AlP poisoning (Gurjar *et al*., 2011; Siddaiah *et al*., 2009), but these are too invasive.

Although, our cases had a severe poisoning with AlP with marked LV dysfunction and reduced capillary wedge but after using digital, she significantly improved. In systolic dysfunction, intravenous administration of digoxin increases cardiac output and reduces pulmonary capillary wedge pressure and heart rate (Sanaei-Zadeh and Farajidana, 2011). Although, in non-toxic cases of acutely decompensated heart failure, alternative therapies with superior short and/or long-term safety and efficacy profiles are available (e.g., angiotensin converting enzyme inhibitors, intravenous diuretics and other intravenous inotropes), but in cases of AlP, these treatments are less effective (Gurjar *et al*., 2011; Siddaiah *et al*., 2009), thus digoxin can be used as adjustment therapy in addition to specific treatments for the stabilization of patients with acutely decompensated heart failure. In patients with heart failure, digoxin may be the preferred drug for slowing the ventricular rate, due to an improvement in left ventricular function. Rapid intravenous digitalization can be performed by giving 0.5 mg initially followed by 0.25 mg or 0.5 mg every 6 h until digitalization is achieved. Digoxin can be continued by 0.25 mg daily.

The present patient showed hyperglycemia that is suggested as a poor prognostic factor in AlP poisoning (Mehrpour *et al*., 2008b, 2009). Treatment of hyperglycemia throughout management of the poisoning should be considered within treatment, which may improve the outcome such as that of organophosphates (Rahimi and Abdollahi, 2007). The blood glucose concentration of our case became normal after treatment and continued to remain normal.

CONCLUSION

Clinical significance of digoxin in the management of AlP poisoning should be considered in further cases to optimize the management protocol.

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