Endocrinology & Metabolic Syndrome
ISSN: 2161-1017

Arefi and Tabrizchi, Endocrinol Metab Synd 2012, 1:5
DOI: 10.4172/2161-1017.1000109

Hypothesis Open Access

# Could Glucagon be a Therapeutic Option in the Management of Acute Aluminium Phosphide Toxicity?

**Mohammad Arefi* and Narges Tabrizchi**

*Tehran University of Medical Sciences, Baharloo Hospital, Iran*

## Abstract

**Background:** Acute aluminum phosphide is a severe toxicity in Iran and the other countries such as India. Morbidity and mortality of this toxicity are high because of the absence of any antidote. Its mortality is related to releasing of phosphine gas after ingesting of this poison.

**Objective:** Cardiovascular collapse and hypotension are the main factors which result in death in this toxicity. Although serum therapy is essential in its management, the vasopressors play an important role too.

**Discussion:** Glucagon is a pancreatic polypeptide hormone that has diverse utility as both a therapeutic and diagnostic agent. It has been used as an effective therapeutic agent for beta blocker and calcium channel blocker toxicity and shock for many years.

**Summary:** We propose that glucagon can dominate the refractory hypotension and myocardial depression in combination with serum therapy and vasopressors in aluminum phosphide toxicity.

**Keywords:** Aluminum phosphide; Glucagon; Toxicity

## Introduction

Aluminum phosphide poisoning has high mortality resulting from cardiac impairment and hemodynamic disorders [1]. Aluminum phosphide is a rodenticide which is diffusely used in the world. Because of its severe toxicity, mortality is high. After ingestion, the phosphine gas is released on contact with stomach fluid. The released phosphine induces multi-organ failure. Circulatory failure and severe hypotension are common features .Free radicals have an important role in the pathogenesis of aluminum phosphate toxicity [2]. The high mortality of aluminum phosphide is due to cardiac impairment and hemodynamic disorders [1]. Although the majority of articles concentrate on the correction of side effects, nevertheless none of therapeutic planning was successful in improving the outcome of severe toxicity.

## The Hypothesis

We believe that the acute cardiovascular injuries that characteristically occurs in severe poisoning with beta blockers and calcium channel blockers also happens in aluminum phosphide poisoning. This injury may play an important role in morbidity and mortality of this toxicity. Refractory hypotension and cardiovascular collapse are common causes of death. We hypothesized that glucagon along with other supportive managements can dominate the refractory hypotension and myocardial depression and decrease of mortality and morbidity of aluminum phosphide toxicity.

## Evaluation of Hypothesis

Aluminum phosphide poisoning is one of the most severe poisoning with multi-organ systems of the body involvement. Unfortunately, because of absence of any antidote for this toxicity, its mortality is high. Aluminum phosphide is sold as the tablets in the grocery market in Iran and uses as a rodenticide. Its high mortality can be due to increased incidence of severe heart failure, pulmonary edema and liver failure. Due to its cheapness and ease of accessibility it is relatively used high for the suicide attempt. Phosphate gas (phosphine) will be released after aluminum phosphate ingestion because of stomach acids. Released phosphine is rapidly absorbed and cause systemic toxicity through inhibition of oxidative phosphorylation, resulting in cellular hypoxia. Release phosphine affects primarily heart, lungs, gastrointestinal tract and the kidneys, although all organs can be involved. If there is any clinical suspicion for this toxicity diagnosis is made by the silver nitrate which is added to the stomach secretions. [3]. In the study of aluminum phosphide poisoning was reviewed in a 7-years study and early gastric lavage, oxygen, sufficient fluids and vasopressors, ventilator support and other supportive care have been proposed for treatment. It was reported that magnesium sulfate can be used as an antidote to stabilize the cell membrane and prevents heart conduction problems. One of the most frequent manifestations was cardiovascular (78.12%). Stomach decontamination with potassium permanganate and the use of gluconate calcium, magnesium, sodium bicarbonate and charcoal in many patients were considered [4]. There were ECG abnormalities in (65.6 %) cases [3]. In the study of Lourize et al. the mortality rate was 49 percent, with the association of shock and decreased levels of consciousness [5]. The mechanism of shock and myocardial damage is unclear. In some case reports myocardial necrosis and vacuolation is seen in myocardial biopsy. Frequency of hypotension and shock varied from 76% to 100% [6]. Hypovolemia due to vomiting associated with acute poisoning can also reduce blood pressure. Dysrhythmia encountered in phosphorus poisoning. The most common disorders are a bundle branch block, atrio-ventricular block, atrial fibrillation, ventricular and atrial extrasystoles, ventricular tachycardia and rarely sinoatrial block. Re-polarization abnormalities like depression or elevation of ST segment and T wave inversion are also noted. Echocardiography in many reports shows hypokinesia. [6,7].

***Corresponding author:** Mohammad Arefi, Tehran University of Medical Sciences, Baharloo Hospital, Iran, E-mail: marefi@sina.tums.ac.ir

**Received** October 12, 2012; **Accepted** November 02, 2012; **Published** November 27, 2012

**Citation:** Arefi M, Tabrizchi N (2012) Could Glucagon be a Therapeutic Option in the Management of Acute Aluminium Phosphide Toxicity? Endocrinol Metab Synd 1:109. doi:10.4172/2161-1017.1000109

## Discussion

### Why glucagon?

Glucagon is given as a first antidote treatment for beta blocker overdose [8,9]. It activates adenylate cyclase at a site independent from beta-adrenergic agents, causing an increase in adenosine 3'-5'-cyclic monophosphate (cAMP). Elevations in cAMP increase the intracellular pool of calcium available for releasing during depolarization; augmenting contractility [10]. Glucagon appeared to consistently increase the heart rate at least transiently but appeared to have no effect on mean arterial pressure even though it possibly increases cardiac output. Its effect on the survival rate in animal models of beta-blocker overdose was unclear. In the six studies of animal models of calcium channel blocker overdose included, glucagon appeared to have increased the heart rate and cardiac output and reverse second and third degree AV blocks, all at least transiently [8,11]. Glucagon may decrease vasopressor requirements in calcium channel blocker toxicity [12]. Its infusion significantly increases mean blood pressure and heart rate in severe amitriptyline toxicity [13]. Comparing the efficacy of vasopressin and glucagon no overall differences were noted in mean arterial pressure, systolic blood pressure, cardiac output, heart rate, pH, or glucose levels, although vasopressin treatment yielded higher MAP and systolic BP early in resuscitation [14]. It is necessary to emphasize that in some studies of animal models of beta-blocker overdose included; glucagon appeared to have no effect on mean arterial pressure even though it possibly increased cardiac output. The effect of glucagon on calcium channel blocker overdose included is researched too and it is shown that heart rate and cardiac output are increased and second and third degree AV blocks are reversed, all at least transiently by glucagon. There appear to be no effect of glucagon on mean arterial pressure although it did increase in one model. Glucagon appeared to have no effect on survival rate [8]. The hyperglycemic effect of glucagon is transient and is virtually impossible if the stores of liver glycogen are depleted. It is suggested to eat some sugar or food to stop reactive hypoglycemia. The most common side effects are nausea and vomiting. Glucagon has been used in the treatment of spasticity associated with radiology, magnetic resonance imaging acute diverticulitis and biliary tract and sphincter of Oddi dysfunction. It is contraindicated in pheochromocytoma. This hormone is used as the treatment for shock, cardiac inotropic agent, especially when there is previous use of β-adrenergic receptor antagonists and adrenergic receptor agonist may be ineffective [15].

## Conclusion

Because of effectiveness of glucagon on hypotension and myocardial contractility it may be useful in treating some aluminum phosphide toxicity side effects.

### Consequences of the Hypothesis

This concomitant evidence could lead to new therapeutic options in the management of acute phosphine toxicity.

### References

1. Akkaoui M, Achour S, Abidi K, Himdi B, Madani A, et al. (2007) Reversible myocardial injury associated with aluminum phosphide poisoning. Clin Toxicol (Phila) 45: 728-731.
2. Anand R, Binukumar BK, Gill KD (2001) Aluminum phosphide poisoning: an unsolved riddle. Jof Appl Toxicol.
3. Shadnia S, Sasanian G, Allami P, Hosseini A, Ranjbar A, et al. (2009) A retrospective 7-years study of aluminum phosphide poisoning in Tehran: opportunities for prevention. Hum Exp Toxicol 28: 209-213.
4. Shadnia S, Rahimi M, Pajoumand A, Rasouli MH, Abdollahi M (2005) Successful treatment of acute aluminium phosphide poisoning: possible benefit of coconut oil. Hum Exp Toxicol 24: 215-218.
5. Louriz M, Dendane T, Abidi K, Madani N, Abouqal R, et al. (2009) Prognostic factors of acute aluminum phosphide poisoning. Indian J Med Sci 63: 227-234.
6. Shah V, Baxi S, Vyas T (2009) Severe myocardial depression in a patient with aluminium phosphide poisoning: a clinical, electrocardiographical and histopathological correlation. Indian J Crit Care Med 13: 41-43.
7. Chugh SN, Chugh K, Ram S, Malhotra KC (1991) Electrocardiographic abnormalities in aluminium phosphide poisoning with special reference to its incidence, pathogenesis, mortality and histopathology. J Indian Med Assoc 89: 32-35.
8. Bailey B (2003) Glucagon in beta-blocker and calcium channel blocker overdoses: a systematic review. J Toxicol Clin Toxicol 41: 595-602.
9. Boyd R, Ghosh A (2003) Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Glucagon for the treatment of symptomatic beta blocker overdose. Emerg Med J 20: 266-267.
10. Lee J (2004) Glucagon use in symptomatic beta blocker overdose. Emerg Med J 21: 755.
11. Peterson CD, Leeder JS, Sterner S (1984) Glucagon therapy for beta-blocker overdose. Drug Intell Clin Pharm 18: 394-398.
12. Papadopoulos J, O'Neil MG (2000) Utilization of a glucagon infusion in the management of a massive nifedipine overdose. J Emerg Med 18: 453-455.
13. Love JN, Howell JM (1997) Glucagon therapy in the treatment of symptomatic bradycardia. Ann Emerg Med 29: 181-183.
14. Holger JS, Engebretsen KM, Obetz CL, Kleven TL, Harris CR (2006) A comparison of vasopressin and glucagon in beta-blocker induced toxicity. Clin Toxicol (Phila) 44: 45-51.
15. Mayo KE, Miller LJ, Bataille D, Dalle S, Göke B, et al. (2003) International Union of Pharmacology. XXXV. The glucagon receptor family. Pharmacol Rev 55: 167-194.