CASE REPORT

G6PD deficiency might offer protection against fatal poisoning caused by Aluminum phosphide: A Case Series in North Iran

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Abstract

Introduction: Aluminum phosphide (AlP) is a highly toxic pesticide with a high mortality rate due to the lack of a specific antidote. Its toxicity is primarily mediated through the generation of phosphine gas, leading to severe oxidative stress, mitochondrial dysfunction, and multi-organ failure. Recent studies suggest that glucose-6-phosphate dehydrogenase (G6PD) deficiency may offer a protective effect by modulating oxidative stress pathways.
Case Reports: We report three cases of patients with confirmed AlP poisoning who were also diagnosed with G6PD deficiency. All patients presented to Razi hospital in Qaem Shahr, Mazandaran, Iran in February, July and December 2023 respectively with severe metabolic acidosis, hemolysis, hematuria, and systemic toxicity. They received intensive supportive care, including antioxidant therapy (N-acetylcysteine, vitamin C), magnesium sulfate, methylprednisolone, and aggressive hemodynamic support. Despite the usual high fatality rate associated with AlP poisoning, all three patients survived without major complications, suggesting a potential protective role of G6PD deficiency.
Discussion: G6PD deficiency impairs the pentose phosphate pathway, reducing NADPH availability, which may limit oxidative damage induced by phosphine gas. This paradoxical effect could contribute to improved outcomes in AlP poisoning. Early recognition and aggressive supportive management were crucial in achieving positive clinical outcomes.
Conclusion: These cases suggest that G6PD deficiency may confer a protective advantage in AlP poisoning by altering oxidative stress responses. Further research is warranted to explore the underlying mechanisms and potential therapeutic implications for AlP toxicity management.

Keywords: Aluminum phosphide poisoning, G6PD deficiency, Oxidative stress

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INTRODUCTION

Aluminum phosphide (AlP) poisoning is a major public health concern, where it is widely used as a pesticide [1]. Upon exposure to moisture, AlP rapidly releases phosphine gas, that leads to severe metabolic acidosis, multi-organ failure, and high mortality rates. The absence of a specific antidote further complicates treatment, making early intervention and supportive care crucial for improving patient outcomes [2-4].

The toxic effects of AlP primarily stem from its ability to inhibit cytochrome c oxidase, leading to mitochondrial dysfunction and excessive oxidative stress [5,6]. Despite these interventions, mortality rates remain high, necessitating further exploration of alternative protective mechanisms.

Several studies have explored the impact of glucose-6-phosphate dehydrogenase (G6PD) deficiency on oxidative stress and toxicological outcomes. G6PD plays a crucial role in cellular defense by maintaining the redox balance through the production of nicotinamide adenine dinucleotide phosphate (NADPH) [7,8]. While G6PD deficiency is typically associated with hemolytic anemia and increased oxidative susceptibility, some evidence suggests a paradoxical protective effect in specific toxicological conditions, including AlP poisoning [9,10]. Reports indicate that individuals with G6PD deficiency exhibit modified oxidative responses, potentially reducing phosphine-induced cellular damage [11,12]. Recent case studies have described improved survival outcomes in G6PD-deficient patients following AlP poisoning, further reinforcing this hypothesis [13,14].

Given the substantial morbidity and mortality associated with AlP poisoning, further investigation into the role of G6PD deficiency in modulating oxidative stress responses is

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warranted [15]. Understanding the molecular mechanisms underlying this potential protective effect may provide novel therapeutic insights for AlP poisoning management [16,17]. This study presents a case series of three patients with confirmed G6PD deficiency who survived AlP poisoning, with a focus on clinical manifestations, treatment approaches, and possible underlying protective mechanisms [18-21].

Case 1

A 40-year-old male, was admitted to Razi hospital in Qaem Shahr, Mazandaran, Iran in February 2023 after alleged 6 ALP tablets for Suicide purposes. he experienced multiple episodes of vomiting and sign of, icteric and cold extremities related to poor blood circulation. He was conscious but hemodynamically unstable. His vital signs were as follows: heart rate (HR) of 95 bpm, respiration rate (RR) of 17 bpm, blood pressure (BP) of 100/60 mm Hg, His body temperature was normal and oxygen saturation of 85% on room air. The possible history of favism and jaundice is mentioned in the past medical history. Subsequent testing confirmed persistent G6PD deficiency. The patient was intubated in 48 h after hospitalization. Table. 1 depicts a laboratory test following the ingestion of ALP. On his first day, he developed mildly metabolic acidosis [pH: 7.32, pCO2: 32.8 mmHg, HCO3:16.6mmol/L]. This was aided with antioxidants like N-Acetyl cysteine (NAC), thiamine, vitamin C and hydrocortisones. Intravenous magnesium sulfate, Amp Vit E, Amp ca gluconate and drip NAC. After 48 hours of ICU stay, He had shortness of breath and decreased oxygen saturation without respiratory distress. CXR revealed mild bilateral pleural effusion and a small amount of pericardial effusion and the appearance of linear atelectasis. on the fourth day of hospitalization, he developed hemolysis and hematuria and his main complaint is Right Upper Quadrant abdomen. Pulse Methylprednisolone 500 mg for 3 days were initiated. He necessitating the use of invasive ventilation for one day. After three cycles of Methylprednisolone infusion, a slight decrease in the hepatic enzymes. 5 units of packed red cell were transfused during hospitalization.

Case 2

A 64-year-old male presented to the Razi hospital in Qaem Shahr, Mazandaran, Iran in July 2023 with an alleged history of consumption of 3 tablet of Aluminum Phosphide. The patient experienced Nausea, vomiting, abdomen tenderness. His medical history was G6PD deficiency and Hypertension. On arrival, his examination revealed hypotension (105/75 mmHg), and oxygen saturation 88% was on room air. The patient had Normal acid- base balance [pH 7.44, Hco3 20.9, Pco2 31]. On first day, antioxidants like thiamine, vitamin C, and other intervention like Amp hydrocortisone, Intravenous magnesium sulfate, Amp selenium stat, Amp Vit E, Amp Calcium gluconate and drip NAC. On day 4, the patient had hematuria and his Blood tests is given in detail in Table 2. fluid therapy and pulse methyl prednisolone 500mg daily for 3 days obviate his hematuria and hemolysis. 5 units of packed red cell were transfused during hospitalization.

Case 3

A 32-year-old female presented to Razi hospital in Qaem Shahr, Mazandaran, Iran in December 2023 with alleged history of consumption of 1/2 tablet of Aluminum Phosphide followed by nausea, vomiting, weakness. The patient's examination revealed cold extremities, hypotension (80/50 mmHg) and pulse rate of 82 bpm, and oxygen saturation of 93% on room air. She had mildly metabolic acidosis [pH 7.31, Hco3 16.1, Pco2 33] and her Blood tests showed on table 3. On first day, drip magnesium sulfate, Amp Calcium gluconate, Amp Vit C, pearl Vit E, and tablet vit B1 300 mg, drip Amp NAC, Amp Hydrocortisone 100mg IV initiated. On day 3, she had dark urine and raise liver function test. Fluid

Table 1. Lab investigations during hospital stay (case 1)

Lab data	Day 1	Day 2	Day 3	Day 4	Day 5
Hemoglobin (g/dL)	10.8	8.7	5.4	3.3	6.6
Aspartate transferase	26		111	114	35
Alanine transferase	14		22	25	19
Alkaline phosphatase (IU/L)	125		104	119	120
Bilirubin total (mg/dl)	7.2	10.3	8	11	5.5
Bilirubin indirect (mg/dl)	0.9	0.7	0.6	1.5	1.5
Prothrombin time (seconds)	15	12	14.7	14.9	16
Activated partial thromboplastin time (seconds)	38	30	36	32	31
Lactate dehydrogenase (IU/L)				1240	
Creatinine (mg/dl)	0.7	0.7	0.4	0.7	0.7
Na (mEq/L)	141	145	145	145	145
K (mEq/L)	3.6	3.2	2.8	2.9	3.5
Ca (mg/dl)	9.6	9.1	11.5	10.1	9.1
Coombs direct	Negative			Negative	
Mg (mg/dL)	2.1	2	2.2	2.3	2.3

Table 2. Lab investigations during hospital stay (case 2)

Lab data	Day 1	Day 2	Day 3	Day 4	Day 5
Hemoglobin (g/dL)	15.7	11.4	8	7	7.1
Aspartate transferase	11				122
Alanine transferase	7				35
Alkaline phosphatase (IU/L)					112
Bilirubin total (mg/dl)					5
Bilirubin direct (mg/dl)					2.2
Prothrombin time (seconds)	31	30	30	36	36
Lactate dehydrogenase (IU/L)				3427	805
Creatinine (mg/dl)	0.9	0.7	0.9	0.7	0.8
Na (mEq/L)	145	136	135	137	135
K (mEq/L)	3.8	4.4	3.6	2.8	2.9
Ca (mg/dl)	9.8	9.2	8.8	9.4	8.9
Coombs direct				Negative	
Mg (mg/dL)	1.8	2.3	2.1	2.3	2

Table 3. Lab investigations during hospital stay (case 3)

lab data	Day 1	Day 2	Day 3	Day 4	Day 5	Day6
Hemoglobin (g/dL)	14.5	14.5	10	9.2	8.3	7.7
Aspartate transferase	1220	810	313	25	20	25
Alanine transferase	1070	540	415	163	133	101
Alkaline phosphatase (IU/L)	190	139	196	165	156	164
Bilirubin total (mg/dl)		5.3	2.95			0.6
Bilirubin direct (mg/dl)		1.6	0.8			0.4
Prothrombin time (seconds)	14.7		13.4	13.4	12.5	13.6
Lactate dehydrogenase (IU/L)						1773
Creatinine (mg/dl)	0.8	0.5	0.3	0.6	0.6	0.6
Na (mEq/L)	148	144	141	145	143	146
K (mEq/L)	3.9	3.8	3.45	3.1	3.1	3.1
Ca (mg/dl)	7.9	8.7	9.9	8.3	8.9	9.5
Coombs direct				negative		
Mg (mg/dL)	1.9	1.9	2.2	2	2.1	2

therapy and pulse Methylprednisolone 500mg daily for 3 days obviate her hematuria, hemolysis and normalized her liver enzymes.

DISCUSSION

Our findings support the hypothesis that G6PD deficiency may play a protective role in AlP poisoning, aligning with previous reports in the literature. It has been suggested that G6PD deficiency leads to a modified oxidative stress response, potentially reducing phosphine-induced cellular damage. The observed clinical outcomes in our patients, including the absence of profound metabolic acidosis and improved survival, reinforce this hypothesis. The mechanisms underlying this protective effect may include decreased production of reactive oxygen species (ROS), enhanced buffering capacity of hemoglobin, and preservation of lysosomal integrity, which collectively contribute to improved cellular resilience [5, 22,23].

Unlike previous reports where severe AlP poisoning was associated with a sharp decline in bicarbonate levels and rapid clinical deterioration, none of our patients exhibited such extreme metabolic disturbances. This suggests that G6PD deficiency may alter metabolic pathways that influence the progression of AlP toxicity, warranting further investigation [24,25].

Recent advancements in therapeutic approaches

complement our findings. Paraffin oil gastric lavage has demonstrated efficacy in reducing phosphine absorption, while antioxidant therapy, including NAC and vitamins C and E, remains a cornerstone of AlP poisoning management [6]. The spontaneous ignition of phosphine gas during gastric suction, as reported in previous cases, highlights potential risks to both patients and healthcare providers, emphasizing the need for strict safety protocols in emergency settings [26]. Whole blood exchange transfusion has also emerged as a potential intervention, particularly in cases of severe hemolysis, as it facilitates the removal of damaged red blood cells and alleviates oxidative stress [16,27].

Although our case series indicates a possible protective role of G6PD deficiency, further large-scale studies are necessary to confirm these findings and elucidate the underlying biochemical mechanisms.

CONCLUSION

This study provides preliminary evidence supporting the potential protective effect of G6PD deficiency in AlP poisoning. The observed clinical outcomes suggest that altered oxidative stress responses may play a role in reducing the severity of toxicity. Given the high mortality associated with AlP poisoning, further research is warranted to explore the therapeutic implications of G6PD modulation in clinical settings.

Ethical Considerations

This study was conducted in accordance with ethical guidelines for case report publications. Written informed consent was obtained from all patients or their legal guardians for participation and publication of anonymized data. Patient confidentiality was strictly maintained, and all identifying information was removed.

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