

Case Report

Acute human lethal poisoning with hexaflumuron: A case report

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Abstract

Background: Hexaflumuron is a benzoyl urea pesticide widely used in agriculture. This is the first case of severe toxicity of hexaflumuron.

Case presentation: A 51-year-old man was admitted to the poisoning ward of the Emam-Reza Hospital for loss of consciousness and hypotension secondary to pesticide toxicity. He had metabolic acidosis, bradycardia, and diffuse erythematous skin color change in the abdomen and legs. The results of toxicology tests were negative except positive test result for tricyclic antidepressants in immunochromatographic assay of urine. He was treated with normal saline, norepinephrine infusion and bicarbonate. His intoxication finally resulted to cardiac arrest and death on the 4th day of hospitalization, secondary to septic shock.

Conclusion: Acute poisoning with hexaflumuron can be life-threatening, though its LD₅₀ is greater than 5000 mg/kg. It may change the patient's skin color to cherry and cause hypotension, loss of consciousness and metabolic acidosis, however, conclusive evidence to support these assumptions are required.

Keywords: Acute poisoning, Hexaflumuron, pesticide

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Poisoning is identified as an important health problem, counts for 30% of overall admissions via the emergency department (1, 2). In the recent years, the poisoning rate has increased in Asian countries, especially amongst agricultural workers, due to availability of poisons, cultural and religious influences (3, 4). As insecticides are widely used, particularly in agriculture, poisoning with them are much more common in countries where agriculture and animal husbandry thrive (3). Hexaflumuron is a systemic and penetrating pesticide belonging to the benzoylureas group (insect growth regulator (IGR)) that prevents insect growth by inhibiting chitin synthesis in the insect's body. This pesticide can be absorbed by human skin as well as respiratory and digestive tracts and causes toxic effects (5, 6). Some toxic effects of hexaflumuron include headache, dizziness, and nausea that are seen in farmers at occupational exposure (6). Hexaflumuron has an LD₅₀ of more than 5000 mg/kg for rat and classified as low-toxic substance (7). There is no report of human poisoning with this pesticide. The current paper reported the clinical findings of acute human lethal toxicity after ingestion of hexaflumuron 10% with a possible suicide attempt.

Case Presentation

The case of 51-year old man who had a history of asthma, found unconscious at home. He was taken to a local clinic and then to a regional hospital at about 8 A.M. It was suggested that he had swallowed some agricultural pesticide, organophosphate and therefore he underwent Atropine Challenge test which was negative.

He was intubated due to loss of consciousness (GCS: 8), and then he was sent to the poison centers. The patient's blood pressure (BP) was 65/40 mmHg and laboratory testing in the secondary hospital demonstrated metabolic acidosis. According to the consultation with subspecialized center; department of clinical toxicology, and possibility of poisoning by aluminum phosphide, he was treated with normal saline and norepinephrine infusion as well as bicarbonate and hydrocortisone and also the loading dose of N-acetylcysteine

(NAC). Before he referred to a higher-level hospital, his family brought the box of pesticide and it was a clarified ingestion of only one liter of hexaflumuron 10%. There was no evidence that he had taken any pills or other poisons. The patient was transferred to the third level hospital, Imam Reza Toxicology Center, at 12 P.M. He had a Glasgow Coma Scale (GCS) score of 5 on admission, and the following vital signs: BP=78/36 mmHg, Pulse Rate=80 beats /min, Axillary temperature = 37.2°C and Respiratory Rate=22 cycles/ min (fig. 1).

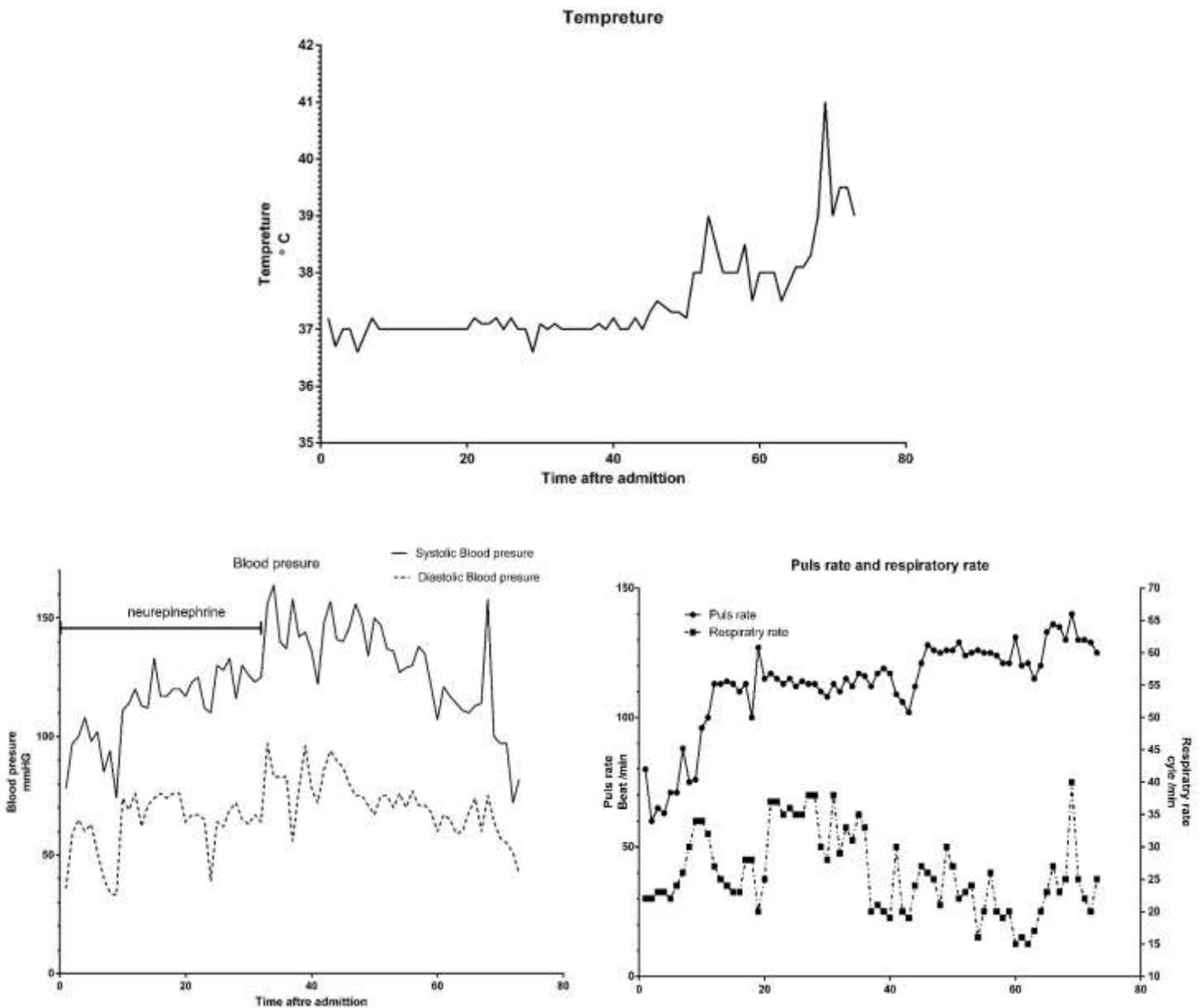


Figure 1: The changes in vital signs of Hexaflumuron intoxicated case.

He was intubated and mechanically ventilated with Synchronized intermittent mandatory ventilation (SIMV) Mode. His pupils were normal. Cherry-colored skin was observed on his lower limbs and abdomen (fig. 2). The bedside blood glucose level at admission was 204 mg/dL. The patient underwent fluid therapy and cardiac monitoring just after admission and was ventilated as well. Due to reduced blood pressure and no obvious manifestations of organophosphate poisoning, and high incidence of aluminum phosphide poisoning in Iran, aluminum phosphide poisoning treatment was performed. The patient was administered norepinephrine (under a systolic blood pressure condition of lower than 100 mmHg at a dose of 5-10µg/min), 200-mg hydrocortisone intravenously, and NAC (140 mg/kg IV). In addition, paraclinical evaluations such as level of carboxyhemoglobin, qualitative urine paraquat test, and serum and red blood cell cholinesterase levels were performed. The urine immunoassay was positive for tricyclic antidepressant (table 1). There was no evidence of blocking cardiac sodium channel on the electrocardiogram, however, regarding corrected QT (QTc) = 0.56, the patient received 2 g magnesium sulfate over 20 minutes. The administration of magnesium sulfate was repeated every 8 hours on the first day and continued one dose a day. The echocardiographic finding revealed normal wall motion with ejection fraction of 55%.

The patient was transferred to the intensive care unit three hours after admission. His blood pressure was 80/50 at 4:15

Table 1: Results of toxicological tests in Hexaflumuron intoxicated case

Test	Result
Serum salicylate	Not Detected
Serum Acetaminophen	Not Detected
Serum Ethanol	Not Detected
Serum Methanol	Not Detected
Serum Butyrylcholinesterase (U/L)	8540
Erythrocyte Acetylcholinesterase (IU/mL)	5.1
Urine Immunochromatography tests	Tricyclic Antidepressants
Carboxyhemoglobin (%)	<10
Urine Paraquat	Not Detected
Urine Diquat	Not Detected
Thallium in urine	Not Detected
Arsenic in urine	Not Detected

P.M., and he was re-administered one liter of normal saline. Considering venous blood gas (VBG) values (table 2), positive urinary test and suspicion of aluminum phosphide poisoning, 100 mEq bicarbonate was administered and continued to receive 5% dextrose serum containing 150 mEq bicarbonate and 20 mEq potassium every 8 hours.

Table2: Results of biochemical and hematological tests of Hexafluoromoren intoxicated case

Day → Time after admission (hours) → tests (unite)↓	2nd level hospital	1st	1st	1st	2nd	2nd	3rd	3rd	3rd	4 th
		2	3	9	12	28	37	47	55	60
White Blood Cell (*1000/ µL)	21.81	23.2			13.5		10.4			4.8
Hemoglobin (g/dl)	15.1	15			15.1		12			11.9
Hematocrit (%)	44.5	44			42.3		34.8			36.2
Platelet (*1000/ µL)	434	396			295		150			105
Neutrophil (%)	53	66.9			89.2		80			97.5
Lymphocyte (%)	44	30.5			5.7		10			4.8
PT(sec)		15.4			15		21			17
INR		1.49			1.34		2.31			1.64
PTT(sec)		30			30		59			32
PH	Not available		7.039	7.18	7.292		7.327		7.368	7.273
PCO2 (mm Hg)	Not available		43.8	44.5	30.9		54.3		56.2	59.6
HCO3 (mEq/L)	Not available		11.8	16.6	14.9		28.4		32.3	27.5
Base excess (Mmol/L)	Not available		-19.0	-11.8	-10.1		1.4		6.0	0.4
PO2 (mm Hg)	Not available		115.5	53.3	167		114.4		57.2	65.8
O2sat (%)	Not available		95.5	76.4	98%		97.7		88.5	89.3

Sodium (mg/dL)	138	139	140	140	141
Potassium (mg/dL)	3.3	3.8	4	3.9	3.9
Chloride (mg/dL)			114		
Calcium (mg/dL)		8.7	8.2	8.2	7.3
Phosphorus (mg/dL)		2.2	3.1	5.1	7.1
Magnesium (mg/dL)			2.7	3.3	3
Urea (mg/dL)	28	33	48	91	123
Creatinine (mg/dL)	2.1	1.8	2.6	3	3.7
Blood sugar (mg/dL)	247	237	178	160	174
Lactate dehydrogenase (U/L)		622		1060	
Creatine Phosphokinase (U/L)		444		910	
Aspartate Aminotransferase (U/L)	40	43		90	
Alanine Aminotransferase (U/L)	23	37		30	
Alkaline phosphatase (U/L)	181	194			
Total Bilirubin (mg/dL)	0.88	0.5		0.7	
Direct Bilirubin (mg/dL)	0.24	0.3		0.2	
Tropinin I		8.5			
NT pro BNP (Pg/ML)				1142	
Procalcitonine (ng/ml)				0.92	



Figure 2: Disseminated erythema in the abdomen and leg of hexaflumuron intoxicated case.

Thirty hours after admission (the second day), the patient's norepinephrine infusion was discontinued (figure 2) and decreased QTc intervals led to discontinuation of magnesium sulfate. The patient had serum creatinine level of 2.6 mg/dl, and low urinary volume, therefore furosemide was administered. As his urine output reached an appropriate volume, fluid therapy was continued. The bicarbonate administration was also continued because of metabolic acidosis.

Regarding following VBGs values, he improved on the third day, the bicarbonate infusion was discontinued. He was not ready for withdrawal of ventilator support. With regard to the clinical evidence of pulmonary edema, he received

treatment including morphine and furosemide. He responded appropriately, and his echocardiogram indicators were also normal by that time. On the third day, the patient showed evidence of pneumonia in the pulmonary x-ray and lung examination, and antibiotic treatment was started. The pulmonary x-ray showed an increase in the broncho-vascular markings and para-cardiac opacity. A few hours later, patchy opacity in both lungs and uniform opacity in the inferior and right inferior zones of right lung were observed clearly. Blood and urine cultures were performed and urine culture was positive for Ecoli, however, no germ grew in blood culture. The patient developed a fever on the third day of hospitalization and underwent treatment which did not respond appropriately. In the morning of the fourth day, he suffered bradycardia and hypotension, and finally a cardiac arrest and underwent cardiopulmonary resuscitation for 45 minutes, which eventually led to his death.

Discussion

According to the studies on the effects of pesticide in the developing and the less developed countries, it is worth pointing out that pesticide poisoning can be extremely dangerous due to easy availability and failure to observe safety tips (8). Poisoning epidemiology in different regions is significantly affected by cultural and economic conditions and

partly by environmental conditions of the region. Therefore similar areas have equal prevalence rate of poisoning that occurred more deliberately and with suicide attempts (2). Hexaflumuron had a high LD₅₀ (> 5000 mg/kg rat body weight) (5) and the intoxicated person likely had used it in excessive amount of 200 ml intentionally, with a suicide attempt. Ingestion of large amount of hexaflumuron can cause metabolic acidosis associated with bradycardia.

Although, there was no conclusive evidence in the use of antidepressant, his positive TCA test result as well as the increased QTc interval, impaired consciousness and hypotension were justified by TCA poisoning. However, TCA poisoning could not justify all the patient's problems such as cherry-red skin, and long-lasting metabolic acidosis. The changes in the patient's skin color, which were similar to those in cyanide and carbon monoxide intoxicated patients, were also unjustified. The hypotension, impaired consciousness and metabolic acidosis as well as skin color changes were consistent with cyanide and carbon monoxide poisonings, while his carboxyhemoglobin level was normal, and the test identified negative for cyanide according to medical forensic reports. Hexaflumuron is a non-toxic compound and clinical process and the patient's death also suggested an indication of death from sepsis. This was the first case reporting severe toxicity of hexaflumuron. Acute poisoning with hexaflumuron can be life-threatening, though its LD₅₀ is greater than 5000 mg/kg. It may change the patient's skin color into cherry and cause hypotension, loss of consciousness and metabolic acidosis, however, conclusive evidence to support these assumptions are required.

It should be mentioned that this pesticide has no specific antidotes and the treatments are supportive, also despite the higher prevalence of organophosphates poisoning, poisoning by hexaflumuron should be considered as a differential diagnosis.

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