Original Article

Management of 2, 4- Dichlorophenoxyacetic Acid Intoxication by Hemodialysis: A Case Report

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ABSTRACT

Background: The herbicide 2, 4-dichlorophenoxyacetic acid (2, 4-D) can cause moderate to lethal poisoning. Although urine alkalization has been recommended as the main treatment, hemodialysis (HD) may be more effective in severe cases.

Case: On 24th June 2014, a 53- year-old man ingested a high amount of 40% 2, 4-D. He suffered from mouth and epigastric burning sensation, vomiting and nausea. He was treated, in Emam Reza's Hospital of Mashhad University Of Medical Sciences, Mashhad , Iran, with maintenance daily fluid infusion plus 10 meq/L NaHCO3. Up to 9 hours after exposure, he became progressively stuporous. He developed diarrhea and hypotension, BP=100/60, unresponsive to volume replacement therapy. He received regular hemodialysis (HD) with bicarbonate for three hours. At the end of HD, his blood pressure rose to 110/70 and the level of consciousness began to improve. Four hours later, he was fully conscious with stable blood pressure (130/80 mmHg).

Conclusion: HD may be an effective, safe and fast method for 2, 4-D high dose intoxication induced coma.

Keywords: 2, 4- dichlorophenoxyacetic acid, Alkaline diuresis, Hemodialysis, Herbicide intoxication, Iran.

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INTRODUCTION

2, 4- dichlorophenoxyacetic acid (2,4-D) is a one of the most widely used herbicides in the world [1]. 2, 4-D also is one of the Agent Orange ingredients which has wildly used in Vietnam war. Clinical manifestation of herbicide 2, 4-D poisoning are varied from vomiting, gastrointestinal hemorrhage to coma and death [2-3]. Although urine alkalization (UAlk) has been recommended as the main treatment of 2, 4-D intoxication, there are some evidences about effectiveness of hemodialysis (HD) in severe cases [2, 4]. Here we report a case of 2, 4-D intoxication with coma who has been treated by HD.

CASE

On 24th June 2014, A 53- year-old farmer man ingested unknown amount of 40% 2,4-D, seven hours before admission. Four hours later, the local physician administrated activated charcoal and referred him. When we visited him in Emam Reza's Hospital of Mashhad University Of Medical Sciences, Mashhad, Iran, he was confused and suffered from severe nausea, vomiting, mouth, and epigastric burning sensation with a mild pharyngeal congestion without ulcer. His physical finding at the time of admission included: blood pressure (BP) =110/70 mmHg and heart rate=115 beats/min. He had a penetrating odor of the breath due to herbicide ingestion. Other physical exam findings especially neurological exams were normal.

He was treated with maintenance daily fluid infusion plus10 meq/L NaHCO3. During the first 2 hours of admission, the level of consciousness (LOC) reduced progressively and he had unresponsive to stimulation. One hours later, the patient developed diarrhea and hypotension (BP=90/60) unresponsive to volume replacement therapy. He become candidates for

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urgent HD and received regular HD with bicarbonate for three hours. His BP rose to 110/70 at the end of dialysis and the LOC began to improve. Four hours later, he was fully conscious with stable BP (130/80 mmHg). He remained in hospital another day to reduce the risk of rebound.

The laboratory tests results and electrocardiogram findings were in normal range. He was discharged in good condition. Unfortunately, our patient was lost to follow-up.

The authors committed to the Helsinki Convention at all stages of the investigation. An informed consent form was taken from the patient.

DISCUSSION

Some of the most important mechanisms associated with the toxicities of 2, 4-D include interaction with the plasma membrane, interference with cellular metabolic pathways involving acetyl coenzyme-A and uncoupling of oxidative phosphorylation. The dose dependent 2, 4-D central nervous system toxicity may be due to the dose dependent integrity distraction of blood brain barrier that accumulates the herbicide in brain. Severe toxicity of 2, 4-D presents with coma, rhabdomyolysis, renal failure and death [5-6].

Bradberry et al. reviewed sixty-six cases of chlorophenoxy herbicide ingestion and reported that coma was a constant feature of fatal cases. However, coma also was seen in two third of nonfatal cases and lasted for several days. The patients who rapidly became comatose or shocked had poorer prognosis, recovered over weeks to months, and might have prolonged neuromuscular complication [4].

Management of acute 2, 4-D intoxication is mainly supportive and includes decontamination and rehydration [6]. The primary clinical controversy in treatment of 2,4-D intoxication is enhance elimination of the herbicide by alkaline diuresis or HD [4]. Animal studies [7], several case reports [8-11], standard clinical toxicology textbooks [12], and expert reviewers [3-4] recommend UAlk for severely 2, 4-D poisoned patients. Only one case series included four cases, that we could find, suggested application of extra corpuscular removing in 2, 4-D poisoned patients [2].

As 2, 4-D is a week acid, with Pka= 2.64 - 3.31, and its renal clearance is directly related to urinary pH. Thus, UAlk will be effective for enhancing the herbicide renal elimination through ion trapping [4, 6]. Prescott et al. reported a case of severe 2, 4-D poisoning (6.8g) treated by forced UAlk [8]. They administered 14 L fluid containing 69.3 g sodium bicarbonate (825 mmol) within 48 hours and induced the patient urine flow rate greater than 200 mL/h with pH> 7.5 [8].They could significantly reduce the herbicide plasma half-life from 219 to 3.7 hours. However, the patient remained at hospital for one week and was comatose for at least 4 days. The maximum renal clearance of 2, 4-D that achieved by them was 1.4 mL/min. The uncorrected renal clearance for 2, 4-D will reach to 63 mL/min if the urine pH is 8.3 with flow rate approximately 600 mL/h, that achievement to such level is too fast, easy and safe, especially in comatose patients [4]. However, this clearance could be easily achieved by HD. The total clearance of 2, 4-D after 3-5 hours hemodialysis was 56 to 96 ml/min [2].

The half-life of 2, 4-D in human was estimated 10-28 hours with first order kinetic. Therefore, about 99% of herbicide can be excreted after seven half-lives (70- 196 hours/ 2-8 days) [13]. Moreover, the half-life of 2, 4-D is prolonged in overdose due to its nonlinear pharmacokinetic resulting from saturable renal clearance [14].

Some criteria of 2,4-D that make it suitable for extra corpuscular removing by HD are low molecular weight, low volume of distribution, high water solubility and low renal clearance [2, 12]. However, some of the inappropriate criteria are three compartments kinetic and extensively bound to plasma proteins [4, 13, 15] (Table 1).

Durakovic et al. have recommended HD in early phase of high dose 2, 4-D ingestion. They treated poisoned patient who ingested high lethal dose of 2, 4-D, 20-160 g, by HD. The fatal outcome of 2, 4-D poisoning may occur after ingestion of at least 6.5 g [2].

Hypotension is a prominent feature, which presents in one third of the patients and may be due to gastrointestinal fluid loss and direct effect of the herbicide on vascular resistance [4]. Our case had also hypotension and his BP elevated after HD and toxin excretion.

Table 1. Comparison between the criteria of xenobiotics that could be removed by hemodialysis and characteristics of 2, 4- dichlorophenoxyacetic acid (2,4-D).

Criteria	Appropriated for hemodialysis	2,4-D
Volume of distribution	< 1 L/kg	0.02-0.3 L/kg
Compartment kinetic	Single compartment kinetic	Three compartment kinetic
Endogenous clearance	< 4 ml/min/kg	≈ 0.11 ml/kg/min It is saturable
molecular weight	<500 Dalton	221.0 Dalton
solubility	Water	Water soluble (900 mg/L)
Plasma protein binding	No – low binding	extensively bound to serum proteins at low plasma concentrations, and binding becomes saturated at higher concentrations

CONCLUSION

HD may be an effective, safe and, fast method for severe 2, 4-D intoxication with coma.

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