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Case Report

A case of glyphosate poisoning

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ABSTRACT

Glyphosate is a commercially available herbicide which also acts as a human toxin. It produces a wide range of clinical manifestations ranging from throat irritation, GI tract erosion and bleeding, surfactant elated liver and kidney injury, metabolic acidosis and even death. We are reporting a case of a 36 year old female who consumed around 400ml of the pesticide and presented to our tertiary care hospitals after 12 hours of ingestion, in a state of renal shutdown, Severe acidosis and hyperkalemia and shock. We started on hemoperfusion and CRRT apart from the initial resuscitation. She was successfully treated and discharged home. This case report emphasise on the use of hemoperfusion toxin removing cartridge for sever glyphosate poisoning as there is no known antidote of this toxin and also the mechanism of toxicity is still not well-established?

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1. Introduction

Glyphosate herbicides are among the world's most widely used herbicides. Round-up, containing the active ingredient glyphosate, developed in the late 20th century, is a broad-spectrum systemic herbicide and crop desiccant that inhibits plant enzymes. The lethal dose has been seen to be more than 150 ml in cases reported earlier. We report a case of alleged self-harm by ingesting about 400 ml of the herbicide "Roundup" which was bought to our tertiary care center about 12 hours after ingestion. The primary effects following ingestion include irritation of mucous membranes, abdominal pain, vomiting and diarrhea, and esophageal and gastric erosions. Severe cases develop hypotension and renal shutdown and in fatal cases, cardiac arrhythmias, metabolic acidosis, pulmonary edema, and shock have been terminal events. Treating such cases with Hemadsorption with toxin removal cartridges instead of the traditional protocol of organophosphate poisoning has

shown better outcomes as seen in this reported case also.

2. Case Report

2.1. Presentation

2.1.1. Course in emergency department

A 36-year-old lady presented to our ER with alleged ingestion of Round-up (41% glyphosate) about 12 hours ago. The ingestion was not witnessed and she was found by her brother with a bottle of ROUNDUP pesticide next to her. She was initially treated in a local hospital (Minimal documents available about the treatment course). She was possibly treated as a case of organophosphorus poisoning. In the ER of our hospital, she was extremely anxious, confused and restless. On examination, she had bilaterally dilated pupils, tachycardia(144/min), and tachypnea (35/min) with and low blood pressure. Arterial blood gas was done immediately and it showed High Anion Gap Metabolic Acidosis with high lactate (4.3 mMol/L), and potassium was 6.8 mMo/L. Resuscitation with intravenous crystalloid was initiated immediately and all anti-hyperkalemic measures

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(dextrose insulin, calcium gluconate, nebulization with beta agonist) were started. She soon developed a wide complex tachycardia for which appropriate measures were taken as per ACLS protocol. She was started on vasopressor support and was urgently shifted to ICU.

3. Course in ICU

On arrival at ICU, she was drowsy but arousable, pupils were 4mm with absent light reaction, normothermic, having sinus tachycardia with blood pressure 90/60 mmHg. Her chest was clear on auscultation and her abdomen was soft. Intravenous fluid resuscitation was continued with proper monitoring of volume status. In the next hour, she got intubated and ventilated with volume control ventilation as her sensorium worsened further and she remained hypotensive requiring multiple vasopressor supports. Central venous line, and arterial lines were also established in the ICU. She remained anuric since her arrival at the hospital. Laboratory investigations were sent and the following results were noted.

UREA	CREATININE	Na	K	Cl	BICARBONATE
42	2.3	147	4.7	102	16
TOTAL BIL.	DIRECT BIL.	SGOT	SGPT	ALKALINE PHOS.	
0.4	0.2	106	61	45	

In view of the potential surfactant-related injury to the liver and kidney by the herbicide ingested, N acetylcysteine infusion along with thiamine were initiated. The patient remained hemodynamically unstable, anuric, and no improvement in acidosis was noted. A nephrology consult was taken to initiate RRT. Continuous Renal Replacement Therapy (CRRT) was initiated along with utilization of the toxin removal HA 230 haemadsorbition cartridge. About 2 hours after starting CRRT her vasopressor requirement started to taper down, her sensorium improved, urine output picked up and subsequent ABGs showed resolving acidosis (Figure 2). The next day we were able to completely stop the vasopressors and the patient had a urine output of more than 0.5 ml/kg/hour. She was awake, comfortable and communicating and after a pressure support trial of two hours she was extubated. She was under close observation in the ICU for next 48 hours and showed no signs of any new nephrotoxicity, neurotoxicity or gastro toxicity. Her renal functions and transaminitis also got resolved. She was also reviewed by a psychiatrist and was shifted to the ward with family members. She got discharged after 6 days of hospitalization.

Gradual change in blood gas analysis through the time of treatment

ABG	pH	pO2	pCO2	HCO3	AnGap	Lac	K.
Presentation in ER	7.224	89	20	8	17.2	4.35	6.88
Initial correction Of electrolytes and Acidosis	7.199	52	37	14	24.5	7.71	5.30
CRRT on going	7.200	266.7	45.2	16.7	16.8	6.68	4.78
Extubation and on PSV	7.386	77	46	27	3.6	1.36	3.36

NOTE: After extubation she was kept on alternating nasal cannula and NIV support and Ryle's tube feeding started from evening with clear liquids. Serial APTT monitoring for coagulation profile and electrolyte supplementation with IV fluids were continued. Total toxin removal cartridge used was 4 in number throughout the CRRT.

4. Discussion

Glyphosate {N-(phosphonomethyl) glycine}, commercially available as Roundup, is a broad spectrum systemic herbicide. It acts by inhibiting the plant enzyme 5-enolpyruvylshikimate-3-phosphate synthase. The commercial preparation consists of around 5 salts of glyphosate, a surfactant (polyoxyethylene amine) and other minor agents like coloring agents and anti-foaming agents.^{1,2} It is difficult to pinpoint the exact agent responsible for the acute toxicity but most experimental studies concluded that the toxicity due to the surfactant is more than the glyphosate.² Accidental ingestion of the commercial preparation usually produces mild transient and GI features. Most reported cases are of deliberate ingestion, and ingestion of more than 85 ml of the agent leads to significant toxicity.¹ There are GI corrosive effects, hepatic and renal impairment (often caused by reduced organ perfusion), impaired consciousness, respiratory distress, chest infiltrates, pulmonary edema, severe metabolic acidosis, and worsening renal functions. severe hyperkalemia, and broad complex tachycardias, bradycardias are common pre terminally.³

Despite the C and PO₄ moiety, glyphosate lacks antiChE effect, and hence no organophosphorous-like action. Studies point towards the direct cardiotoxic and uncoupling of oxidative phosphorylation as the main mechanism of toxicity.^{4,5} Renal Replacement therapy has been used to

counter the metabolic effects of acidosis and hyperkalemia and improve hemodynamics.^{6,7} Apart from conventional renal replacement therapies, use of toxin removal cartridges to directly adsorb and remove the toxin is an area of great potential. There have been multiple studies on the use of these cartridges in various toxicities. HA-230 has been used for intoxication, it has a resin pore size of 200 Da -10,000 Da, and can easily remove hydrophobic or protein-bound toxins of size 500 Da to 10,000 Da.⁸ HA 230 has been used in 85 patients of paraquat poisoning and was found to be effective in decreasing its level,⁹ the study showed that toxin removal got slower with time as the cartridges got saturated. HA 230 has been successfully used in series of organophosphorus poisoning.¹⁰

Though glyphosate is easily removed in dialysis, the surfactant is not. Studies regarding the removal of surfactants are lacking. There have been case reports of using intralipid in glyphosate poisoning¹¹ but since our patient was anuric since admission with worsening metabolic parameters, and would have required RRT we decided to go ahead with CRRT along with the use of HA 230 cartridge.

5. Source of Funding

None.

6. Conflict of Interest

None.

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