Case Report

Glyphosate surfactant herbicide poisoning and management

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Abstract

Glyphosate is a widely used herbicide in agriculture, forestry, industrial weed control and aquatic environments. Glyphosate potential as herbicide was first reported in 1971. It is a non-selective herbicide. It can cause a wide range of clinical manifestations in human beings like skin and throat irritation to hypotension, oliguria and death. We are reporting a case of a 35-year-old male patient who was admitted to our tertiary care hospital following intentional ingestion of around 200 ml of herbicide containing glyphosate. Initially, gastric lavage done and the patient was managed with intubation and mechanical ventilation, noradrenaline and vasopressin infusion, continuous veno-venous hemodiafiltration and intravenous (IV) lipid emulsion (20% intralipid 100 ml), patient was successfully treated and discharged home. This case report emphasizes on timely systemic supportive measure as a sole method of treatment since this poison has no known specific antidote and the use of IV lipid emulsion for a successful outcome.

Keywords: Gastric lavage, glyphosate, intravenous fat emulsion, poisoning, surfactant herbicide

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Introduction

Glyphosate is a non-selective herbicide, widely used in agriculture, forestry, industrial weed control and aquatic environments. Proposed mechanisms of glyphosate surfactant herbicide (GlySH) toxicity to mammals include uncoupling of oxidative phosphorylation and glyphosate-or polyethoxethyleneamine (POEA)-mediated direct cardiotoxicity. It can cause a wide range of clinical manifestations in human beings from skin and throat irritation to hypotension and death.

Case Report

This was a case report of a 35-year-old male patient who brought to our hospital with intentional ingestion of approximately 200 ml of glyphosate (herbicide) at around 10:15 AM at home. Later (after 15 m) when the family members recognized the consumption, he was taken immediately to a local hospital where gastric lavage was done and subsequently shifted to our multispecialty hospital. In the casualty the patient was conscious and obeying commands. On examination the patient was afebrile, pulse rate: 110/m, blood pressure (BP): 94/60 mm Hg, SpO_2-97%, Glasgow coma scale 15/15, cardiovascular, respiratory and gastrointestinal systems were normal. The patient was initially stabilized with intravenous (IV) fluids in casualty and later shifted to the intensive care unit for further management.

Routine blood investigations were as follows: Hb%: 14.9 g/dl, total leucocyte count (TLC) 18,600 and platelet count: 2.9 lakh cells/cu mm. Serum creatinine: 2.1 mg/dl, blood urea: 44 mg/dl, serum sodium: 148 meq/l, potassium: 6.5 meq/l, chloride: 101 meq/l. Total bilirubin: 0.6 mg/dl, SGOT-11 U/l, SGPT-67 U/l, serum albumin: 5.3 g/l. Arterial blood gas analysis:

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P^H: 7.2, PCO_2: 31, PO_2: 171, HCO_3: 12.2. Sequential organ failure assessment score: 4 and acute physiology and chronic health evaluation score: 16.

He received calcium gluconate 1 g (10 ml) IV, dextrose-insulin infusion along with salbutamol nebulization for hyperkalemia. After 6 h of admission continuous veno-venous hemodiafiltration started in view of severe acidosis, hyperkalemia and raised creatinine levels.

After 10 h of ingestion patient had sudden respiratory distress along with hypotension and was hence intubated and ventilated. For hypotension after adequate fluid resuscitation with central venous pressure of 9-10 mm Hg (also using ultrasound guided-inferior venacaval collapsibility/distensibility), noradrenalin infusion started at 0.05 mcg/kg/min.

After 24 h, the patient was febrile, heart rate (HR): 160 beats/min, BP: 90/60 mm Hg (with high noradrenalin: 3 mcg/kg/min and vasopressin: 0.04 U/min) anuric, procalcitonin: >10 and serum lactate: 37.5 mg/dl (reference value 4-20 mg/dl), serum creatinine 6.1 mg/dl and TLC-13,000 cells/cumm. Patient was started on empirical antibiotic meropenem. IV lipid emulsion (20% intralipid 100 ml) once daily for three consecutive days (which started from 2nd day). On 4th day patient improved hemodynamically with HR: 90 beats/min, BP: 120/78 mm Hg with minimal inotropic support. TLC: 7800, serum potassium: 3.5 meq/l, serum creatinine: 3.5 mg/dl, P^H: 7.42, PCO_2 35.6 and PO_2 145. The hemodynamic parameters from admission to first 5 days has been shown in Table 1.

Sustained low efficacy dialysis was done daily for first 4 days and later on alternate days for next four dialysis and stopped in view of adequate urine output from 14th day. Patient weaned from the ventilator on 4th day, later bi-level positive airway pressure support for few hours and oxygen mask for next 24 h. The inotrope and vasopressor tapered and stopped over next 24 h from day 4. Patient was successfully treated and discharged home on 18th day of admission.

Table 1: Hemodynamic parameters for first 4 days after admission

Days after admission	Heart rate (bpm)	Blood pressure (mm Hg)	Vasopressor	Dialysis	Lipid (20%) (ml)	Serum creatinine (mg/dl)
1st	110	94/60	Noradrenalin	Done		2.1
2nd	160	90/60	Noradrenalin + vasopressin	Done	100	6.1
3rd	124	104/70	Noradrenalin	Done	100	4.8
4th	90	120/78	Noradrenalin	Done	100	3.6
5th	85	132/84	-	-	-	2.7

Discussion

Glyphosate surfactant is a widely used herbicide in agriculture, forestry, industrial weed control, lawn, garden and aquatic environments. Glyphosate potential as herbicide was first reported in 1971. It is a non-selective herbicide.

In plants, glyphosate disrupts the shikimic acid pathway resulting in a deficiency of 5-enolpyruvylshikimate-3-phosphate production which leads to reductions in protein synthesis and plant growth, death of the plant occurs in 4-20 days. The median half-life of glyphosate in soil is between 2 and 197 days.[1]

In humans the toxicity is less due to the absence of shikimic acid pathway. The mechanism of toxicity of glyphosate in mammals is thought to be uncoupling of oxidative phosphorylation.[2] The acute oral lethal dose (LD_{50}) in rats is > 4320 mg/kg, dermal LD_{50} is > 2 g/kg and inhalation lethal concentration 50 is > 4.43 mg/l. Data from Taiwan, Korea and Japan reported a combined case fatality of 7.7%.[3]

After oral ingestion of glyphosate 30-36% is absorbed, peak concentrations occurs in tissues 6 h following dosing, undergoes little metabolism and is excreted mostly unchanged in the feces and secondarily in the urine. Gastrointestinal symptoms are the most common manifestations after oral ingestion. It causes erosion of the gastrointestinal tract, difficulty in swallowing and gastrointestinal hemorrhage. Eye and skin irritation have occasionally been reported from dermal exposure. Inhalation of spray mist may cause oral/nasal discomfort, tingling and throat irritation. Severe poisoning causes dehydration, hypotension, pneumonitis, oliguria, altered level of consciousness, hepatic dysfunction, acidosis, hyperkalemia and dysrhythmias.[4] It has not been determined whether these clinical features reflect primary (direct) or secondary (indirect) toxic effects of these herbicide formulations. Patients developing acute kidney injury, hyperkalemia, pulmonary edema and metabolic acidosis are more likely to die.[5] Early renal replacement therapy may improve prognosis but there is no evidence to support this and requires identification of those at risk.[6]

There is no antidote for GlySH and treatment is supportive. The mainstay of treatment for systemic toxicity is decontamination and aggressive supportive

therapy. Gastric lavage or activated charcoal can be administered in patients who present <1 h after ingestion and who have no evidence of buccal irritation or burns. There is no evidence, however, that either of these reduce the systemic absorption of GlySH.

Intravenous fat emulsion (IFE) has been used in the management of severe local anesthetic toxicity, calcium channel blockers, tricyclic antidepressants and beta blockers. Proposed mechanisms of GlySH toxicity to mammals include uncoupling of oxidative phosphorylation and glyphosate-or POEA-mediated direct cardiotoxicity. A study by Han *et al*.[7] demonstrated the effectiveness of IFE in severe poisoning patient who was refractory to inotropic support later showed recovery after administration of IFE, surviving to hospital discharge without further sequelae. The mechanism of action of IFE may be due to the lowering of serum concentration of the free surfactant POEA component of GlySH (which are more lipophilic) by dragging into the lipid sink formed by the IFE, thereby blunting its cardiovascular toxicity. Glyphosate exposure can be measurement in blood or urine by gas chromatography and high-performance liquid chromatography.

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