Glyphosate - Surfactant Herbicide Poisoning : A Case Report

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ABSTRACT

Glyphosate-surfactant herbicide is a non-selective herbicide widely used across domestic and commercial settings. Ingestion of large volumes of concentrates can be rapidly fatal. We describe here a patient who had consumed 50ml of the compound, was comatosed, developed acute kidney injury, hyperkalemia and metabolic acidosis. He was managed in an intensive care unit with mechanical ventilation and IV Intralipid. He regained consciousness after 2 days, his renal function recovered completely without requiring any renal replacement therapy. He was discharged after 10 days of admission without any neurological deficit. This case report emphasizes on timely systemic supportive measure as the sole method of treatment since this poison has no known speci?c antidote and on the use of IV lipid emulsion for a successful outcome.

Introduction :

Glyphosate (N-(phosphonomethyl) glycine) surfactant herbicide (GlySH) is the most commonly used general-purpose herbicide in the world. Glyphosate kills plants by suppressing the shikimic metabolic pathway.[1] It has no anticholinesterase effect and no organophosphate-like CNS effects. GlySH intoxication has a case fatality rate of between 3.2% and 29.3%. Proposed mechanisms of GlySH toxicity to mammals include uncoupling of oxidative phosphorylation and glyphosate-or polyethoxethyleneamine (POEA)-mediated direct cardiotoxicity.[2] Surfactants, the inert ingredients that are added to herbicides to increase the absorption of the active component also contribute to the toxicity.[1] A study found that hypotension is primarily caused by myocardial depression with surfactant.[3] The ingestion of small amounts of glyphosate-surfactant herbicide usually causes only mild symptoms however large volumes are potentially fatal. With no antidote available, the mainstay of treatment is decontamination and aggressive supportive therapy[4] with early continuous veno-venous hemodiafiltration (CVVHDF) contributing to increased survival.[5,6]

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Case Report :

A 52-year-old male, presented to the Emergency Medical Services with history of consumption of 50 ml of Glycel ***(Fig. 1 A & B),*** a glyphosate herbicide 5 hour prior to presentation, followed by 3 episodes of vomiting. The patient was initially taken to a PHC where Gastric Lavage was given and then referred to our institute for further management. At presentation, patient was conscious, oriented, responding to verbal commands, pulse rate : 90/min, BP : 110/70, Sp02 : 98 on room air, RR : 16/min, GCS Score : 15/15, Pupils: normal sized reacting to light, RBS : 116. Rest of his systemic examination was unremarkable. The patient was shifted to intensive care unit for monitoring and further management.

Routine blood investigations were as follows : Hb:14.8 g/dl, total leucocyte count:10,200 and platelet count : 1.65 lakh cells/ cu mm. Serum creatinine:1 mg/dl, blood urea:31 mg/dl, serum sodium:143 meq/L, potassium:5.8 meq/L, total bilirubin:0.7 mg/dl, SGOT: 29U/L, SGPT:23U/L, serum albumin:3.8 gm/dl. Arterial Blood Gas Analysis revealed pH:7.31, PC02:37.7, P02:96, HCO3:18.4. He received calcium gluconate IV and dextrose-insulin infusion for hyperkalemia.

On day 2 of admission, his consciousness deteriorated to coma and he went into respiratory distress. He a pulse rate of 120/min, BP of 100/70mmHg, RR of 28/min, SpO2 of 90 on room air, pupils: constricted, sluggish reaction to light,

Fig. 1 : Glycel compound ingested by the patient

GCS Score of 3/15 and bilateral extensor plantar response. Auscultation revealed bilateral basal crepitations. The patient was intubated and put on mechanical ventilation.

His laboratory parameters on day 2 were, Hb : 14 g/dl, total leucocyte count : 11,700 and platelet count : 2.65 lakh cells / cu mm. Serum creatinine : 1.3 mg/dl, blood urea : 43 mg/dl, serum sodium : 139 meq/L, potassium : 3.7 meq/L, total bilirubin : 1 mg/dl, SGOT : 48 U/L, SGPT : 23 U/L, serum albumin : 3.8 gm/dl, serum procalcitonin : 0.7 ng/ml (<0.5), serum lactate : 2.4 mg/dl (0.5-1.39). IV lipid emulsion ***(Fig. 2)*** (20% intralipid 100 ml) was given once daily for 3 days.

On day 3, the patient had an improved sensorium and was given a successful spontaneous breathing trial. 24 hours later, the patient had a complete neurological recovery, was successfully extubated and put on oxygen mask for 1 day. The patient throughout the course of admission was stable haemodynamically. His renal function returned to the baseline levels on day 5. A repeat ABG was well within the normal limits. The patient had an uneventful recovery and was discharged on day 10 of admission.

Discussion :

Glyphosate-surfactant herbicide is the most commonly used general-purpose herbicide in the world and is found frequently in both commercial and domestic settings. 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 culminating in the death of the plant. In humans the toxicity is less due to the absence of shikimic acid pathway. The formulations available for domestic use are weaker than those intended for commercial application (1% vs 41%). It contains carbon and phosphorous moiety but has no anticholinesterase effect and does not demonstrate organophosphate-like effects. The formulation, Glycel, consumed by our patient and the one most commonly available, contains water, 41% glyphosate and 15% polyoxyethyleneamine (POEA). Some studies have suggested that the POEA surfactant may contribute the greater part of the product's toxicity in humans.[7-9] Uncoupling of oxidative phosphorylation and glyphosate-or POEA-mediated direct cardiotoxicity are the proposed mechanisms of toxicity in humans.[2,9]

An abnormal chest x-ray, respiratory distress necessitating intubation, shock (systolic blood pressure less than 90 mmHg), altered consciousness, renal failure necessitating haemodialysis. Larger amount of ingestion (>200mL), hyperkalemia and metabolic acidosis are predictors of poor outcomes and mortality.[4,10] There is a significant correlation between the amount of glyphosate-surfactant herbicide ingested and the adverse consequences. Tominack and colleagues examined 97 cases of glyphosate-surfactant herbicide ingestion and showed that the average amount ingested by survivors was 120 $\pm$ 112 mL and by nonsurvivors was 263 $\pm$ 100 mL.[11] Our patient consumed around 50 ml of the poison, which was associated with a good outcome.

After oral ingestion of glyphosate 30-36% is absorbed and peak concentration occurs in tissues after 6 hours. It undergoes little metabolism and is excreted mostly unchanged in the faeces and

secondarily in the urine. Gastrointestinal symptoms are the most common manifestations after oral ingestion. 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.[7] Our patient had severe CNS manifestations in the form of deep coma besides non-oliguric AKI, hyperkalemia and metabolic acidosis.

Glyphosate exposure can be measured in blood or urine by gas chromatography and high-performance liquid chromatography. There is no antidote for GlySH and treatment is supportive. Gastric lavage or activated charcoal can be administered in patients who present within 1 h of ingestion.

Our patient did not require renal replacement therapy (RRT). However, RRT can be used to improve acidosis, hyperkalaemia and renal failure. Haemodialysis is considered to be superior to haemofiltration for the removal of smaller molecules from the circulation, and it can remove the glyphosate, but not the surfactant that may be mainly responsible for the toxic effects. In patients with severe lactic acidosis, lactate-free replacement fluid/dialysate should be used in order to avoid worsening the metabolic acidosis.[12] Some authors[5,13,14] suggest that early renal replacement therapy may improve prognosis, but there is no significant body of evidence to support this at present. Sampogna & Cunard[15] advise early initiation of renal replacement therapy when a large quantity of poison is ingested (>200 mL).

Early upper alimentary endoscopy should be performed in patients who present with features suggesting significant corrosive effects. A study suggested that those who have ingested >100 mL of GlySH should have upper GI endoscopy performed.[16] This same study revealed some degree of upper GI tract injury in 94% of patients following GlySH ingestion.

A study by *Han et al.*[17] showed the effectiveness of IV fat emulsion (IFE) in a severe poisoning patient with cardiovascular collapse who was refractory to inotropic support but showed immediate improvement with fat emulsion. 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 toxicity. IFE has also a role in the management of toxicity caused by local anaesthetics, calcium channel blockers, tricyclic antidepressants and beta blockers.[18] Although our patient did not have hemodynamic instability but instead had severe CNS toxicity and was therefore administered IFE, following which he had considerable neurological improvement within 24 hours.

Conclusion :

Most cases of glyphosate ingestion are asymptomatic or have minimal manifestations but life-threatening complications have also been identified and reported thus mandating close observation of the patient. Early recognition of the complications is of paramount importance for early institution of supportive therapy, in the absence of a specific antidote. Administration of IV fat emulsion should be considered in severe systemic toxicity.

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