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SHORT REPORT

Use of a lipid emulsion in a patient with refractory hypotension caused by glyphosate-surfactant herbicide

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Context. Circulatory shock is a major cause of mortality in glyphosate-surfactant herbicide (GlySH) poisoning, and this condition responds poorly to conventional therapies. We report a case of GlySH poisoning with shock that was refractory to vasopressors but responsive to intravenous fat emulsion (IFE). *Case details*. A 52-year-old man was brought to the emergency department by ambulance. He was found unconscious in his living room along with an empty bottle of GlySH herbicide, which contained glyphosate, polyoxyethyleneamine (POEA) surfactant, and water. He was drowsy at presentation. His heart rate was 44 beats/min, his blood pressure could not be measured with an arm cuff, but he had a palpable femoral pulse. After about 2.5 h of supportive care after admission, he remained hypotensive, and his systolic blood pressure was 80 mmHg. A 500 mL bottle of 20% IFE product was prepared. As a bolus, 100 mL of IFE was injected, and the remaining 400 mL was then infused. His blood pressure was 100/60 mmHg 1 h after the bolus injection. At 5 h after IFE injection, his blood pressure reached 160/100 mmHg and vasopressors were tapered. *Conclusion*. IFE should be considered in cases of refractory hemodynamic instability caused by GlySH after aggressive fluid and vasopressor support.

Keywords Acute poisoning; Antidote; Glyphosate; Surfactant; Fat emulsion

Glyphosate is a nonselective herbicide commonly used in agriculture worldwide.[1] Although glyphosate has a low toxicity in mammals, mortality following the ingestion of the glyphosate-surfactant herbicide (GlySH) product is significant.[1–3] Circulatory shock is a major cause of mortality in GlySH poisoning,[1] and this condition responds poorly to conventional therapies, such as fluid resuscitation or vasopressors.[4,5] No specific antidote exists that is effective against shock caused by GlySH poisoning.

Emerging evidence suggests that intravenous fat emulsion (IFE) can reverse hemodynamically significant poisonings, particularly when the toxin is lipophilic, and IFE can be used as an adjunct therapy in hemodynamically compromised patients.[6] We report a case of GlySH poisoning with shock that was refractory to vasopressors but responsive to IFE.

Case report

A 52-year-old man was brought to the emergency department by ambulance. He was found unconscious in his living room along with an empty 300 mL bottle of GlySH herbicide, which contained 41% glyphosate as an isopropylamine salt, 15% polyoxyethyleneamine (POEA) surfactant, and water. He was drowsy at presentation, with a Glasgow coma scale score of 11 (E3, V4, M4). His heart rate was 44 beats/min, his blood pressure could not be measured with an arm cuff, but he had a palpable femoral pulse, and his respiratory rate was 15 breaths/min. He was intubated and a mechanical ventilator was used. A central venous catheter was inserted and vasopressor support was initiated with the infusion of dopamine. Atropine was administered to treat bradycardia. Gastric lavage was performed and 50 g of activated charcoal was given through a gastric tube. A chest radiograph showed normal findings and an electrocardiogram revealed atrial rhythm with junctional premature complexes. The results of the arterial blood gas analysis were as follows: pH 7.298; $PaCO_2$, 26.9 mmHg; PaO_2, 240.2 mmHg; and HCO_3, 13.3 mEq/L. Serum electrolyte concentrations were as follows: Na, 134.4 mEq/L; K, 3.79 mEq/L; and Cl, 94.6 mEq/L. The serum ethanol concentration was 152.8 mg/dL. Other chemistry tests and complete blood count results were within normal limits. After about 2.5 h of supportive care after admission, he remained hypotensive, and his systolic blood pressure was 80 mmHg. The central venous pressure was 30 mmHg and fluid resuscitation was sufficient. Because he was refractory to conventional medical therapies including infusion of dopamine

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and dobutamine, and remained in critical condition, an intravenous lipid emulsion was initiated. A 500 mL bottle of 20% fat emulsion product (Smoflipid; Fresenius Kabi, Bad Homburg, Germany) was prepared. As a bolus, 100 mL of IFE was injected, and the remaining 400 mL was then infused at a rate of 1.5 mL/min. His radial pulse strengthened immediately after the bolus injection. His blood pressure was 100/60 mmHg 1-h after the bolus injection and he extubated himself. At 5 h after IFE injection, his blood pressure reached 160/100 mmHg and vasopressors were tapered. He remained stable for 6 days after hospital admission and was discharged. Other than a sore throat, he experienced no complication or complaint.

Discussion

The usual formulation of glyphosate herbicide products used in Asian countries is 41% glyphosate as an isopropylamine salt, water, and a variable amount of surfactant, most commonly POEA.[5] A recent prospective observational study reported that mortality after ingestion of GlySH was 3.2%, and 5.5% of cases had symptoms requiring intervention, such as hypotension, respiratory failure, dysrhythmia, cardiac arrest, marked sedation, seizures, or oliguria.[4] Although the mechanism of GlySH toxicity is not yet completely understood, POEA is primarily or partially responsible for the cardiovascular toxicity, possibly through mitochondrial dysfunction.[5,7] Cardiovascular collapse is a major cause of death after GlySH exposure,[1–3] and patients respond poorly to conventional fluid and vasopressor therapy.[4,5] Moon et al. suggested that removal of toxins by hemodialysis can reverse the hemodynamic suppression caused by GlySH,[8] but reported cases have demonstrated other indications for hemodialysis, such as acidosis or hyperkalemia. The decision to use hemodialysis in patients with hemodynamic instability and without the typical indications is very challenging.

IFE is gaining attention as an antidote to lipophilic toxins that cause hemodynamically significant poisonings.[6] Promising experimental and anecdotal evidence exists suggesting that IFE can be effective in the treatment of toxicities caused by substances such as local anesthetics, calcium-channel blockers, and tricyclic antidepressants,[6,9–12] but no report regarding IFE and GlySH herbicide exists to our knowledge.

The lipid solubility of the offending toxin is an important factor in determining the efficacy of IFE.[6] Glyphosate is a water-soluble compound with an octanol/water partition coefficient (log *P*) of −3.40,[13] and it is unlikely that IFE acts on the toxicity of glyphosate itself. POEA is a nonionic surfactant, which is a mixture of polyethoxylated long-chain amines synthesized from animal-derived fatty acids, and is capable of solubilizing lipids.[14] Although the log *P* of the specific POEA product was not available, POEA can be considered lipid-soluble because, generally, log *P* of nonionic surfactants ranges between 1.39 and 6.40.[15] IFE has the potential to reduce symptoms of GlySH poisoning by lowering free POEA concentration, which blunts its cardiovascular toxicity.

IFE is not used as a first-line therapy for poisoned patients, except for cases of local anesthetic toxicity, but IFE could be used as an adjunct treatment for poisoning by lipid-soluble substances.[6] Our patient was in critical condition, and conventional therapy was not very effective; thus, IFE was used as a rescue therapy and was associated with hemodynamic improvement. More data are needed to establish the effects and potential side effects of IFE on GlySH poisoning, and plasma POEA concentrations before and after IFE administration would clarify any causal relationship. For the present, IFE should be considered in cases of refractory hemodynamic instability caused by GlySH after aggressive fluid and vasopressor support.

Declaration of interest

The authors report no declaration of interest. The authors alone are responsible for the content and writing of this paper.

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