CASE REPORTS

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Intravenous lipid emulsion in treatment of cardiocirculatory disturbances caused by glyphosate-surfactant herbicide poisoning

Primena intravenske emulzije masti u lečenju kardiocirkulatornih poremećaja prouzrokovanih trovanjem glifosat-surfaktant herbicidom

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Abstract

Introduction. Glyphosate is the first widely used herbicide against weed in genetically modified crops. Though glyphosate itself has a low toxicity, commercial products are more dangerous because of increased toxicity due to surfactants addition. There is no specific antidote for the poisoning with glyphosate-surfactant (Gly-SH). In recent times, the efficacy of intravenous lipid emulsion (ILE) administration for the treatment of acute poisoning caused by Gly-SH has been investigated. **Case Report.** A 50-year-old man was admitted 3 h after self-poisoning with herbicide containing glyphosate and polyoxyethyleneamine, as a surfactant. On admission, the patient was in a coma, hypotensive (80/50 mmHg) and without spontaneous breathing. Electrocardiogram showed wide-complex tachycardia, and arterial blood gas (ABG) revealed acidosis (pH 7.07). Conventional treatment included mechanical ventilation, intravenous fluids, bicarbonate and dopamine. As there was no improvement, ILE was started. The patient received 100 mL of 20% Intralipid® bolus followed by infusion of 400 mL over 20 minutes. Prior to expiration of infusion, a gradual rise in blood pressure was noted, and within 2 hours sinus rhythm was restored. **Conclusion.** This case report suggests that the use of ILE may be an additional option for the treatment of cardiocirculatory disturbances caused by commercial products of glyphosate herbicide.

Key words:
herbicides; poisoning; fat emulsions, intravenous; cardiovascular system; treatment outcome.

Apstrakt

Uvod. Glifosat je prvi herbicid namenjen za uništavanje korova na genetski modifikovanim usevima. Sam glifosat je malo toksičan, ali komercijalni proizvodi sadrže i surfaktante koji povećavaju njegovu otrovnost. Za lečenje trovanja ovim preparatima ne postoji specifičan antidot, a u novije vreme se ispituje mogućnost primene intravenskih lipidnih emulzija (ILE). **Prikaz bolesnika.** Bolesnik, star 50 godina, primljen je 3 časa nakon samotrovanja preparatom koji sadrži glifosat i surfaktant polioksietilenamin. Na prijemu je bio u stanju kome, bez spontanog disanja, hipotenzivan 80/50 mmHg, sa tahikardijom širokih kompleksa na elektrokardiogramu. Analize arterijske krvi pokazale su postojanje acidoze (pH 7.07). Primenjena je konvencionalna terapija koja je uključivala mehaničku ventilaciju, intravensku primenu tečnosti, bikarbonata i dopaminsku stimulaciju. Kako nije dovela do popravljanja hemodinamskih poremećaja, primenjen je Intralipid® 20%, 100 mL u bolusu, a zatim 400 mL u infuziji tokom 20 minuta. Pre isteka infuzije došlo je do postepenog porasta krvnog pritiska, a u roku od 2 sata i uspostavljanja sinusnog ritma. **Zaključak.** Prikaz ovog bolesnika potvrđuje da bi primena intravenskih emulzija masti mogla biti dodatna terapijska opcija u lečenju kardiocirkulatornih poremećaja prouzrokovanih trovanjem komercijalnim preparatima herbicida glifosata.

Ključne reči:
herbicidi; trovanje; masne emulzije, intravenske; kardiovaskularni sistem; lečenje, ishod.

Introduction

Glyphosate is in focus of not only professionals, but also the general population, because it is the first herbicide against which crops have been genetically modified to increase their tolerance. It is the one of the most widely used general-purpose herbicide in the world. Animal experiments have shown that glyphosate is a relatively low toxic herbicide [1], but it turned out that commercial preparations containing it could cause severe poisoning with fatal outcome in humans [2, 3]. These products are commonly available as glyphosate-surfactant (Gly-SH) mixture, made of glyphosate in the form of isopropylamine salt dissolved

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in surfactants which seem to significantly contribute to the acute toxicity of formulations [4].

Clinical picture of severe Gly-SH poisoning usually includes irritant, or even corrosive lesions on the gastrointestinal tract, hypotension refractory to fluid resuscitation, inotropes or vasopressors, cardiac arrhythmias, respiratory distress, impaired consciousness, hepatic injury, renal failure, metabolic acidosis and hyperkaliemia [5, 6].

Treatment of glyphosate-surfactant toxicity is mainly supportive. In recent years, potential therapeutic effects of intravenous lipid emulsion (ILE) in the patients with acute Gly-SH poisoning has been examined [7]. We report the unique case of acute Gly-SH poisoning with refractory wide complex tachycardia and hypotension successfully treated with ILE.

Case report

A 50-year-old man ingested 250 mL of herbicide which contained 48% glyphosate as an isopropylamine salt dissolved in polyoxyethyleneamine surfactant and water. He phoned the ambulance shortly after, so he was brought to local hospital. The patient was alert and agitated at presentation one hour post-ingestion. However, his condition rapidly deteriorated. He became drowsy, dyspnoeic and hypotensive with blood pressure of 80/40 mmHg. Despite the supportive treatment with intravenous fluids, his blood pressure decreased to undetectable level. The patient was intubated, infusion of dopamine was initiated and after consultation with the National Poison Control Centre in the Military Medical Academy in Belgrade, he was transferred to the toxicology ward of the Centre.

On admission, 3 hours after herbicide ingestion, the patient was in a coma, with a Glasgow coma scale score of 3. His pupils were dilated and unresponsive. He had no spontaneous breathing, and blood pressure was 80/50 mmHg. Electrocardiogram revealed wide complex rhythm (Figure 1). The results of the arterial blood gas analysis were as follows: pH 7.07; PaO2 53 mmHg, $PaCO_2$ 27 mmHg, lactates 7.2 mol/L and bicarbonates 7.8 mmol/L. Complete blood count, serum electrolyte concentrations and other chemistry tests results were within the normal range. A chest radiograph showed normal findings.

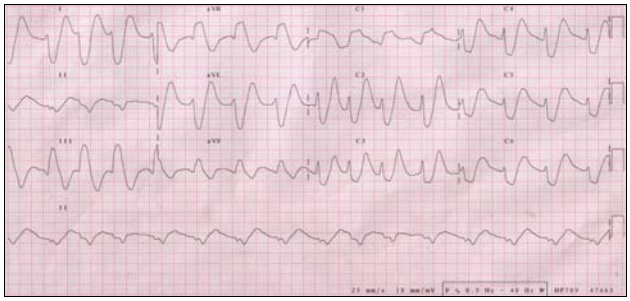

Fig. 1 – Electrocardiogram (ECG) on admission at 11.50 h.

The patient was admitted into intensive care unit and placed on mechanical ventilation. Despite fluid resuscitation, sodium bicarbonate administration and continuous infusion of dopamine (10 μg/kg/min), the patient remained comatose and hypotensive.

Because the patient responded poorly to conventional therapy, about 2.5 h after admission ILE was started. He received 100 mL of 20% Intralipid® (ILE) bolus followed by an infusion of 400 mL over 20 minutes. At a moment when ILE was initiated, the patient's blood pressure was 70/40 mmHg, and there was no improvement of ECG (Figure 2). Elevation of blood pressure was noticed about 15 min after the start of infusion. Within following 2 h sinus rhythm was re-established (Figure 3), blood pressure reached the value of 120/75 mmHg and the patient started to response to stimuli. He remained stable, so dopamine infusion was ceased. Seven hours post-admission the patient was alert, with normal clinical findings except for sore throat and incipient mild left lung pneumonia. After 2 days the patient was transferred to the psychiatric ward for further psychiatric treatment.

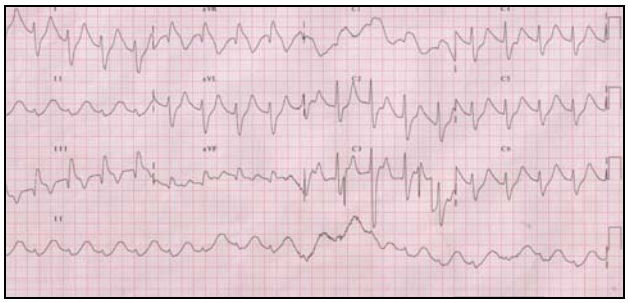

Fig. 2 – Electrocardiogram (ECG) after bicarbonate and before intravenous lipid emulsion (ILE) at 14.15 h.

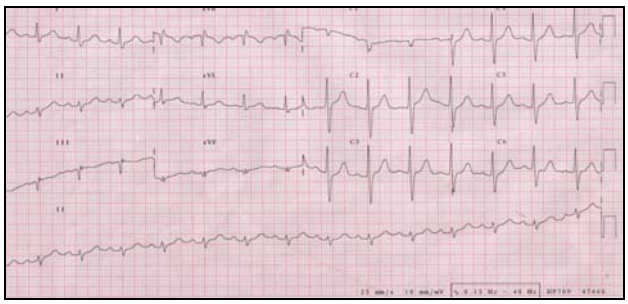

Fig. 3 – Electrocardiogram (ECG) after intravenous lipid emulsion (ILE) at 15.52 h.

Discussion

In massive ingestion of Gly-SH herbicide fatal outcome may occur despite early recognition of severity of the poisoning and intensive treatment. On the basis of published cases, it can be concluded that after large ingestion of Gly-SH, marked sedation, refractory hypotension, respiratory failure, metabolic acidosis, dysrhythmia, elevated creatinine, and hyperkalemia are important risk factors for fatal outcome [8]. In our patient, many of those factors were present, including coma, respiratory failure, metabolic acidosis, refractory hypotension and wide complex tachycardia.

The mainstay of treatment for Gly-SH toxicity is decontamination, supportive and symptomatic therapy. Our patient was admitted 3 hours after the herbicide ingestion, in critical condition, so gastric lavage was not indicated for decontamination. Haemodialysis may be effective as a method of decontamination in GlySH poisoning [9] and could be performed even before acute renal failure developed [10]. However, this type of treatment could add to hypotension and thus be very hazardous. In our case,

haemodialysis was not considered because the patient was haemodynamically instable and had life-threatening arrhythmia. Conventional treatment of hypotension with dopamine in our patient was not effective, as there was no elevation of blood pressure and urine output. Sodium bicarbonate was indicated for two reasons – correction of acidosis and treatment of arrhythmia. As there was no effect on cardiac rhythm, ILE was used as a rescue therapy. Before the second hour from ILE application expired, sinus rhythm was re-established and haemodynamic stability was achieved. As the result, the patient's condition improved and further complications, like renal failure, were thus prevented.

In recent years, ILE has been demonstrated to be effective in treatment of cardiocirculatory toxic effect caused by many liposoluble agents [11, 12]. Its beneficial effect is first and foremost explained by "lipid sink theory" suggesting that a lipophilic agent may be shifted from tissue and captured by an extended lipid compartment in the blood [13]. Except for that mechanism, ILE may recover cardiac contractility by increasing fatty acid content and calcium level in cardiomyocytes [14, 15]. Experimental and anecdotal evidence indicated the lipid solubility of toxic agent may be a crucial factor in determining the efficacy of ILE. Glyphosate is a water-soluble compound with low solubility in lipids, and it is unlikely that the "lipid sink" mechanism acts on the toxicity of glyphosate itself. On the other hand, the first well documented case of life saving effect of a lipid emulsion in a patient with refractory hypotension caused by Gly-SH herbicide was published in 2010 [16]. Authors explanation was that commercial product contained non-ionic surfactant polyoxyethylene amine (POEA) which contributed to the toxicity and was capable of solubilising fats, so the whole mixture was liposoluble.

ILE was for the first time introduced for the treatment of cardiotoxic effects caused by bupivacaine [17], local anaesthetic able to generate depression of cardiac conduction by blocking the fast inward sodium channels in myocardium [18]. Wide complex tachycardia is usually caused by the same mechanism. In the present case, like in the case of propranolol cardiotoxicity we had reported earlier, [19] ILE was effective in abolition of this type of arrhythmia.

Conclusion

This case suggests that intravenous lipid emulsion could be a new, additional option for treatment of acute poisoning by commercial products of glyphosate-surfactant herbicide, characterized by haemodynamic and heart rhythm disturbances.

Acknowledgements

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