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Case report

Endosulfan induced cardiac arrest treated with intravenous lipid emulsion

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Summary. *Objective:* Endosulfan is an organochlorine pesticide with high lipophilic features that makes it a well-absorbed agent and penetrates easily to the site of action. Endosulfan toxicities may result in disastrous complications and have high rates of mortality. Several case reports and some researchs discuss the evidence supporting intravenous lipid emulsion (ILE) therapy as a rescue therapy in lipophilic agents' toxicity. *Case report:* A 33-years-old healthy woman with a history of endosulfan ingestion of uncertain quantity in a suicide attempt six hours ago was admitted to our emergency department. Cardiac arrest ensued after one hour of admission. Cardiopulmonary resuscitation was initiated in accordance with advanced cardiac life support (ACLS) algorithm for asystole. During resuscitation, 2 mL/kg bolus of 20% intravenous lipid emulsion (ILE) was administered for three times at five-minute intervals in addition to ACLS guidance. Spontaneous circulation returned after twenty minutes of resuscitation. No additional antidotal or vasopressor therapies were required during the hospital course of the patient. To our knowledge, this is the first reported case with responded use of ILE treatment for endosulfan toxicity. *Conclusion:* This case report indicates that ILE treatment should be considered for life-threatening endosulfan intoxications. (www.actabiomedica.it)

Key words: endosulfan toxicity, intravenous lipid emulsion, cardiac arrest, emergency medicine

Introduction

Endosulfan is a kind of organochlorine pesticide (OCP) that contains chlorinated hydrocarbons (1). All organic chlorines are lipophilic so they are well-absorbed orally and by inhalation and they penetrate easily to their sites of action. Although its use is restricted in all European countries and in the USA, the use of endosulfan in unrestricted countries including ours may cause unintended toxicities that may lead to failure in various organs such as brain, heart, kidney and liver, and even to death (2). The use of intravenous lipid emulsion (ILE) therapy as a rescue therapy in lipophilic agents' toxicity is an ongoing discussion for two decades. Herein, we presented a case of cardiac arrest arising from endosulfan intoxication who was treated with intravenous lipid emulsion therapy and responded to the treatment successfully.

Case report

A 33-years-old healthy woman with a history of endosulfan ingestion of uncertain quantity in a suicide attempt six hours ago was admitted to our emergency department by local ambulance service. On arrival to the emergency department, the patient presented with generalized tonic-clonic seizure. The seizure was ceased by intravenous diazepam of 8 mg. Her blood pressure was 105/69 mmHg, heart rate was 100 bpm and body temperature was 36.7^{0}C. Then the patient underwent rapid sequence intubation by means of 10 mg midazolam and 70 mg rocuronium in order to pro-

vide secure airway and support ventilation. The intubation was confirmed by using capnometer, auscultation of positive breath sounds bilaterally and the absence of any sound over epigastrium during ventilation of the patient. The patient's laboratory findings were as follows: blood glucose 524 mg/dL, pH: 7.12, pCO2: 26 mmHg, saO2: 96.9%, lactate: 9.4 mmol/L, serum bicarbonate: 8.1 mmol/L, base deficit: -19.89 mmol/L. Electrolytes, complete blood count, liver and renal function tests were within normal limits. Electrocardiography displayed normal sinus rhythm. There was no significant finding on head computed tomography. Normal saline and insulin infusion was administered to control blood glucose levels. 40 minutes after intubation, the patient went in to cardiac arrest. Cardiopulmonary resuscitation was initiated according to advanced cardiac life support (ACLS) algorithm for asystole. During resuscitation, 1.5 mL/kg bolus of 20% intravenous lipid emulsion was administered for three times at five-minute intervals in addition to ACLS guidance. Spontaneous circulation returned after twenty minutes of resuscitation. After resuscitation her blood pressure and heart rate were ameliorated to normal limits within a few minutes. However; when the patient was reevaluated after achieving spontaneous circulation, it was realized that the patient's weight was thought to be much more than she was; so the real dose of given ILE was 2 ml/kg for each time to a total dose of 480 ml. The patient was admitted to intensive care unit for 28 days. No other antidotal or vasopressor therapies were required during hospital course of the patient. However; the patient's spontaneous respiration did not resume and she was discharged from the hospital with home ventilator and some neurologic sequel attributed to hypoxemic brain injury.

Discussion

Endosulfan is a widely used insecticide made of chlorinated hydrocarbon chemically and have high lipid soluble features. Endosulfan is termed a non-competitive gamma-amino butyric acid (GABA) antagonist, since it does not directly involve the GABA binding site. It attaches to and blocks the chloride channel coupled with the GABA receptor, inhibiting the binding of GABA to its receptor.

Physiologically, GABA receptors are the primary inhibitory neuro-receptors in humans, and antagonism of GABAergic neurons leads to generalized brain stimulation. The binding of GABA to its receptors leads to an inflow of Cl ions into neurons across an electrochemical gradient, causing hyperpolarization of cell membranes, and decreasing neuron excitability (3). By blocking the GABA receptor and preventing Cl influx, endosulfan inhibits the inhibitory postsynaptic effect of GABA binding to its receptor, thereby causing uninhibited nerve stimulation (4).

Another potential mechanism of CNS excitation is thought to be the inhibition of Ca- and Mg ATPases, causing build-up of calcium ions and eliciting an uncontrolled release of excitatory neurotransmitters, with predominantly CNS effects, and little or no effect on the peripheral component of the nervous system (5, 6). Furthermore, the central nervous system symptoms, particularly seizure, are the major clinical signs of acute endosulfan toxicity as seen in our patient. In addition to central nervous system effects, acute pulmonary edema, gastrointestinal irritation, disseminated intravascular coagulation, hepatic and renal failure are the other clinical manifestations of endosulfan toxicity (5). Besides, Eyer and colleagues reported the cardiotoxic effects of endosulfan detected by echocardiography (7). As in the most institutions, the measurement of endosulfan levels were not immediately available in our hospital so that endosulfan toxicity was diagnosed based on the history obtained from patient's family and clinical signs of the patient.

The mainstay of treatment of endosulfan intoxication is supportive management (8). However; when cardiac arrest ensued in our patient and given the high lipid soluble feature of endosulfan; we administered intravenous lipid emulsion (ILE) to our patient during resuscitation according to the theory that the lipid soluble agents respond to lipid infusion that results in an expanded plasma lipid phase called "lipid sink" furthermore decreasing tissue drug levels (9). Historically ILE therapy was first used in local anesthetic toxicity in rats and subsequent case reports demonstrated the reversal of toxicity in patients suffering from intoxications other than local anesthetics (10-14). Thereafter, Fettiplace and colleagues notified the cardiotonic effect of lipid emulsion besides sequestration effect (15).

Although there is no certainty, the recommended protocols are a bolus dose of 1.5 mL/kg 20% lipid emulsion followed by 0.25 mL/kg/minute infusion and if the patient does not respond to the first dose or if circulatory stability is not attained, rebolus dose of the agent or increasing the infusion rate should be considered. Rothschild et al. recommended upper limit as 10 mL/kg for 30 minutes but the upper limit of the dose of ILE was not reported by American College of Medical Toxicologoy (9,16).

Moon and colleagues notified 31% of mortality in endosulfan toxicity and reported a case of endosulfan-induced cardiovascular collapse resuscitated with 1.5 ml/kg 20% ILE whom responded first but collapsed again and died (5, 17). In our case, the patient responded three boluses of 2 ml/kg ILE treatment during resuscitation and sustained hemodynamic stability until being discharged from the hospital. The main difference between previous report and ours was the total dose of given ILE. So we may speculate that the higher dose of ILE creates a more intense lipid sink that should sequestrate more drug from the target tissue and more cardiotonic effect resultant with successful resuscitation and sustained hemodynamic stability. To our knowledge, this is the first reported case with responded use of ILE treatment in endosulfan toxicity.

Conclusion

We consider that this case report indicates the significant importance of ILE therapy for acute life-threatening endosulfan toxicity. Earlier use of ILE therapy should be considered for patients with severe endosulfan toxicity in order to prevent any hemodynamic compromise thereafter hypoxemic brain injury. In addition, emergency physicians might be aware of ILE therapy in the management of poison induced cardiac arrest.

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