INTRAVENOUS LIPID EMULSION INFUSION IN ACUTE INTOXICATION WITH FENITROTHION

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ABSTRACT

Acute intoxications with organophosphorus pesticides (OPs) are a challenge for the clinical toxicology, because they are common, severe and with high lethality. Most OPs are lipophilic. In recent years, intravenous lipid emulsion (ILE) has been successfully used to treat acute poisoning with lipophilic xenobiotics. A clinical case of a 64-year-old male hospitalized after oral intake of 50 ml of fenitrothion is reported. He had been hospitalized with tachypnea and depressed consciousness – 8 by Glasgow Coma Scale (GCS). Treatment standardized for this type of intoxication was initiated. On the 3rd hour treatment with Intralipid 20% was started, with a bolus dose of 1.5 ml/kg followed by infusion at a rate of 0.25 ml/kg/min to a total dose of 1000 ml. At the 16th hour consciousness was restored to GCS-15. In severe OPs intoxications ILE can be used as an additional method of controlling cardiotoxic and neurotoxic effects.

Keywords: *fenitrothion, organophosphorus pesticides, intravenous lipid emulsion, acute intoxication*

INTRODUCTION

Organophosphorus pesticides (OPs) are widely used in agriculture as insecticides, fungicides and rodenticides. They have a specific unpleasant odor. Due to their widespread use and high lethality, intoxications with them are a global problem (1,2). More than 200,000 people die each year after poisoning with OPs (3). Patients with acute organophosphorus intoxications require immediate treatment to prevent complications and lethal outcome. Despite the con-

temporary treatment approaches, lethality after poisoning with OPs is 20-30% (4). Most OPs have very high solubility in lipids. After identifying the antidote properties of intravenous lipid emulsion (ILE) and adopting regulations about its use for the treatment of local anesthetics causing systemic toxicity (5,6), it has also been adopted in the treatment of acute intoxications with other lipophilic xenobiotics. Its healing effect had been mainly demonstrated in acute poisonings with antidepressants, neuroleptics, calcium antagonists and beta blockers (7,8).

CASE REPORT

A 64-year-old man was admitted for treatment to the Clinic of Toxicology at the Military Medical Academy Hospital - Varna on 16 June, 2017, 24 hours after swallowing of 50 ml of fenitrothion. Shortly after hospitalization, he started vomiting. A tachycardia with a heart rate of 110 beats/min and high blood

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pressure values of 220/120 mmHg were detected by the doctor in the ambulatory.

The patient refused hospitalization. After gastric lavage and overcoming the hypertonic crisis, he was released from the hospital. Ten hours after the ingestion of the pesticide, a pronounced asthenia-adynamia occurred to an extent that the patient could not stand up alone from the bed without assistance, he got dyspnea and myofibrillations. On the 23rd hour he was examined again by a doctor at home. Hypersalivation, abundant sweating, 100/60 mmHg arterial pressure, and increased breathing rate were established. After administration of atropine the patient was directed to a stationary treatment.

Upon admission to the hospital, depressed consciousness according to Glasgow Coma Scale (GCS) - 8, tachypnea 30 breaths/min, heart rate 65 beats/min and blood pressure 140/80 mmHg were recorded. The pupils of the eyes were myotic with faint (slowed down) response to light, decreased muscle tonus and typical pungent smell of OPs were detected. Another gastric lavage was performed, atrophy was registered, a treatment with atropine, toxogonin, intravenous infusions of saline, 5% glucose, ringer-lactate, diazepam, and ceftriaxone was initiated. In the following days, the dose of atropine was titrated according to the clinical response and symptoms of atropinization.

Tracked in dynamics laboratory indices demonstrated mild renal and hepatic impairment, also indicated by the low pseudocholinesterase (PChE) levels (Table 1).

Upon admission to the hospital, the patient was with acute respiratory failure (Table 2).

Table 1. Laboratory findings in the course of the treatment of a patient with OPs poisoning (PChE, pseudo cholinesterase; ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase; GGT, gamma glutamyl transferase; -, not measured)

Laboratory indices	1 st day	2 nd day	3 rd day	7 th day	10 th day
PChE (U/l)	1500	1300	1100	1400	2200
Urea (mmol/l)	10.7	13.7	-	8.3	7.4
Creatinine (mkmol/l)	170.8	191.9	75.1	69	-
Creatine phosphokinase (U/l)	378.2	341.3	-	54.7	-
ASAT (U/l)	19	-	-	30.1	-
ALAT (U/l)	22.8	-	-	78	-
GGT (U/l)	43.9	-	-	106	-

Table 2. Blood gas analysis findings in the course of the treatment of a patient with OPs poisoning

Laboratory indices	1 st day	3 rd day
pH	7.31	7.44
pO ₂ (kPa)	3.6	8.1
pCO ₂ (kPa)	6.5	4,6
HCO ₃ (mmol/l)	24	28
Oxygen saturation (percentages)	44	92

Chest roentgenography indicated pulmonary arrest. On the electrocardiogram a sinus rhythm with a frequency of 68 beats/min and an indifferent electric position were recorded.

On the following days normal values from the blood and gas analyses were established, the only exception being PChE laboratory tests and the slightly elevated aspartate aminotransferase (ASAT) and gamma-glutamyl transferase (GGT) values. The other vital indicators were also stabilized - blood pressure, heart rate, and respiration. The patient was discharged from the hospital on the 10th day of his stay in a good overall state.

DISCUSSION

Organophosphorus intoxication develops in three phases (9,10): acute cholinergic phase, intermediate syndrome, and late polyneuropathy.

The clinical picture includes symptoms of a number of body organs and systems that develop after a short latency period - from a few minutes to 1-2 hours:

- ◆ Gastrointestinal tract - nausea, vomiting, abdominal pain, diarrhea;

- ◆ Nervous system - myosis, sweating, intoxication psychoses, quantifiable changes in consciousness up to coma, myofibrillations, convulsions;
- ◆ Respiratory system - obturation-aspiration disorders due to bronchorrhea and bronchospasm, pulmonary edema, pneumonia, respiratory muscles paralysis;
- ◆ Cardiovascular system - early hypertonic syndrome, rhythm and conduction disorders, exotoxic shock;
- ◆ Liver and kidney manifestations - manifestations of toxic hepatitis with prevalence of non-icterus forms and renal impairment to acute renal failure (ARF). More often, non-oliguric forms of ARF develop.
- ◆ Multiple organ syndrome failure - develops very often in acute intoxications with OPs.

The available anamnestic data and the observed clinical symptoms have made it easier to diagnose our patient. The diagnosis was confirmed by the low PChE values. Tachycardia detected at first examination and high blood pressure resulted from the predominance of nicotine over muscarinic effects at the onset of intoxication. After the hospitalization of the patient, therapy standard for organophosphorus intoxication was undertaken. Due to the late arrival at the hospital and the developed clinical picture with dominating neurological symptoms, ILE was administered 3 hours after admission to the hospital. Fenitrothion is practically insoluble in water but it is well soluble in organic solvents. In recent years, ILE has been successfully applied to poisoning with various lipophilic xenobiotics, and not only to control local anesthetics-caused systemic toxicity (LAST). It removes not only cardiotoxic but also neurological manifestations (11). The therapeutic effect of ILE in organophosphorus poisonings has been described for the first time for acute parathion intoxication (12). A number of authors recommend ILE as a new potential method for the treatment of severe organophosphorus intoxications (13,14,15). The main mechanism of action of ILE is the so-called "lipid sink" phenomenon. The rapid administration of a lipid emulsion as a bolus dose creates a new, extended lipid phase that absorbs lipophilic xenobiotics (16) and prevents their binding to the corresponding receptors. Decreased serum concentration of the xeno-

biotic leads to its extraction from tissues and reduced toxicity (17). ILE increases intracellular fatty acids and restores the synthesis of adenosine triphosphate in myocardial cells, improving myocardial contractility. The lipid emulsion increases the concentration of intracellular calcium, resulting in a direct positive inotropic effect. ILE was administered as a bolus dose of 1.5 ml/kg Intralipid 20% followed by intravenous infusion at a rate of 0.25 ml/kg/min. The total dose of lipid emulsion administered was 1000 ml. On the 16th hour of the hospitalization, the patient recovered clear consciousness - GCS - 15. No side effects related to the administration of the lipid emulsion were observed.

CONCLUSION

Most OPs are liposoluble. In the case of severe organophosphorus intoxication, ILE could contribute to their successful treatment and reduction of lethality rate. This method is recommended in addition to the established in clinical practice treatment.

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