



Case report

Utilization of plasmapheresis for organophosphate intoxication: A case report

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ABSTRACT

Organophosphate (OP) compounds are extremely toxic chemicals that may be absorbed via skin, conjunctiva, gastrointestinal and respiratory systems. Treatment of OP poisoning is a critical and aggressive process which includes decontamination, antidote administration (atropin and oximes), mechanical ventilation support and extracorporeal elimination procedures if needed. Here we present a young female patient who was unintentionally poisoned by an OP (trichlorfon) after using it to moisture her skin. The importance of this patient is the dermal disease that makes her unprotective to dermal exposure of chemicals and application of plasmapheresis to treat her poisoning.

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1. Introduction

Organophosphate (OP) compounds are frequently used insecticides in agriculture, animal care and pest control in living areas. These chemicals are toxic because they inhibit the enzyme acetylcholinesterase in erythrocyte membranes, skeletal muscle and nerve tissue that result in cholinergic crisis. These insecticides can be absorbed from mucous membranes, skin, conjunctiva, gastrointestinal and respiratory tracts. Poisonings may result from accidental exposures or intentionally in homicides and suicides.¹ Here we present a 19-year old woman who admitted to emergency department of our university hospital with the complaints of nausea, vomiting and fatigue after using a solution containing trichlorfon to moisture her skin with the advice of a veterinary.

2. Case presentation

A 19-year-old female was referred from an urban hospital to the emergency department (ED) of our university hospital after using a

solution containing trichlorfon to moisture her skin with the advice of a veterinary the day before. She had ichthyoses and could not benefit from any other topical medicine to hydrate and soften her skin. She was complaining about nausea, vomiting and fatigue. Her vital signs were as follows: blood pressure, 140/80 mmHg; pulse, 95 beats/min; respiratory rate, 40 breaths/min; and axillary temperature, 36.7 °C. She had salivation, myosis, tachypnea and increased bowel sounds on admission. A total of 130 mg atropin bolus was administered to dry secretions and 1200 mg pralidoxime (2-PAM) was ordered. Her clothes were removed, her skin was gently rinsed and washed. Supplemental oxygen was administered at a rate of 4 L/min. Cardiac and pulse oxymetric monitoring were also initiated. Fluid replacement was initiated (3000 mL/m²/day). Her plasma pseudocholinesterase level was remarkably low on admission. The laboratory findings including serum pseudocholinesterase levels are listed in Table 1. Atropin infusion at a dose of 15 mg/day was started because recurrent atropin doses were needed to resolve salivation. Tachypnea, respiratory depression and fatigue became obvious with decreased pulse oximetric saturation. Diarrhea was added as a cholinergic sign on the second day of hospitalization. Endotracheal intubation, mechanical ventilatory support and repeated atropin boluses were needed to manage secretions. Atropine sulfate infusion rate was increased from 15 mg/day to 100 mg/day after drying the secretions with a total dose of 50 mg given in a few minutes. Her hairs were shaved and plasmapheresis was performed on the 3rd day of hospitalization,

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Table 1
Laboratory findings of the patient.

Parameter (normal range)	On admission	4st day	7th day	10th day	Follow-up visit 15th day
WBC (4.3–10.3 u/L)	15,600	–	–	8400	–
Hb (12–16 g/L)	12.1	–	–	13.0	–
Hct (39.53–50.33%)	34.6	–	–	38.2	–
Plt (156–373.3 u/L)	277	–	–	336	–
AST (5–40 U/L)	35	–	100	74	24
ALT (<41 U/L)	24	–	151	148	60
BUN (5–20 mg/dL)	10	7	9	14	7
Cr (0.8–1.2 mg/dL)	0.59	0.37	0.39	0.47	0.45
Na (135–145 mmol/L)	138	137	135	137	140
K (3.5–5.1 mmol/L)	4.0	3.9	4.0	4.3	4.5
PcHe (4.9–11.9 KU/L)	1.9	2.3	3.5	4.9	6.2

WBC: White blood cell, **Hb:** Hemoglobin, **Hct:** Hematocrite, **Plt:** Platelet, **AST:** Aspartate aminotransferase, **ALT:** Alanine aminotransferase, **BUN:** Blood urea nitrogen, **Cr:** Creatinine, **Na:** Sodium, **K:** Potassium, **PcHe:** Pseudocholinesterase.

because of clinical worsening despite the 2nd dose of 2-PAM given on the second day. Plasmapheresis was performed in the ED by a trained nurse from Therapeutic Apheresis Unit with an automatic device (Fresenius-AS-TEC 204, Fresenius Hemocare, Redmon, WA). Eight bags of fresh frozen plasma (1600 mL), a total of 500 mL of human albumin 20% and 1500 mL 0.9% NaCl were used as replacement.

Her cholinergic findings were resolved the next day and she was extubated on the 4th day when atropin infusion was decreased to 60 mg/day. She was started total parenteral nutrition (TPN) on the 6th day. TPN was stopped because of elevation of hepatic enzymes next day when her atropin infusion was decreased to 30 mg/day. Atropin infusion was tapered to zero in the next 2 days. She was fed orally after 9th and discharged without any sequela on the 10th day.

3. Discussion

Organophosphates cause serious human toxicity which depends on the type, amount and concentration of the agent as well as the route of exposure. The clinical effects may become apparent in 5 min–24 h after exposure. Time to onset of symptoms by inhalation is the most rapid while by dermal exposure is the least.¹ But dermal integrity is a barrier, that means dermatitis or excoriations may hasten the process.² Cholinergic crisis is the sum of symptoms of nicotinic and muscarinic effects of poisoning. The mnemonics DUMBELLS, SLUDGE and the “Killer Bees” are all used to describe the clinical manifestations (**D**efecation, **U**rination, **M**yosis, **M**uscle Weakness, **B**radycardia, **B**ronchorrhoea, **B**ronchospasm, **E**mesis, **L**acrimation, **S**alivation and **G**astrointestinal Pain). Unintentional dermal exposure is not a rare way of poisoning by presenting accidentally in sprayed or fogged areas in farms or houses. The liposolubility and dermal absorption of these agents make them potent and continuous toxic if dermal exposure is not realized or sufficient decontamination is not achieved.¹

Decontamination is one of the major steps in the management of intoxicated patients. Especially in dermal contamination, removal of clothes, cleaning the skin by wiping out or washing with soap and warm water, shaving contaminated hairs are essential for both patient and medical staff to reduce ongoing absorption and recontamination. Skin integrity is also a barrier for chemical absorption.^{2,3} Absorption of poison can be easier and excessive for the patients with dry, thickened and scaly skin like ichthyoses. It is a dilemma to wash-wipe-shave such a patient or not because these may let the poison permeate easier. As performed in our patient, cleaning the skin may not be enough to reduce absorption, or even may increase it.

Seek for other treatment modalities like blood transfusions, hemodialysis, peritoneal dialysis, hemoperfusion for poisoning cases took place in medical literature for the last 50 years. In the

management of intoxicated patients, extracorporeal elimination techniques are used and still being studied on since new benefits are being identified. Which method for extracorporeal elimination is going to be preferred depends on water solubility, volume of distribution, protein binding capacities, and elimination pathways of toxic substances. Hemodialysis and hemoperfusion one by one or in combination were used to eliminate OP compounds from blood. There are many cases reporting the effectiveness of these methods.^{4,5} Plasmapheresis (actually therapeutic plasma exchange) as another elimination process has been used to remove immune complexes. Plasmapheresis has some advantages over hemodialysis and hemoperfusion. First of all, patients do not have to have central catheters because this procedure can be performed via two large peripheral veins. Plasmapheresis, different from hemodialysis and hemoperfusion, is independent from the size of molecule to be cleared. Plasmapheresis is effective in elimination of substances with high plasma protein binding capacity (>80%) and low distribution volume (<0.2 L/kg bw).^{1,6,7} There are several reports indicating effectiveness of plasmapheresis in different poisonings like amitriptyline, phalloid mushroom, propranolol, amlodipine, diltiazem, verapamil, carbamazepine, theophylline, l-thyroxine, and heavy metals like mercury.⁷ It is the protein binding capacity of those drugs/substances which make sense to use plasmapheresis for reducing plasma levels, and poisoning symptoms as well. There are opposite opinions on the effectiveness of plasmapheresis in the management of OP poisoning. Nenov et al. reported that they had tried to eliminate dimethoate (an OP) but they could not detect any decrease in plasma concentrations of the toxic after plasmapheresis.⁸ On the other hand, Guven et al reported clinical improvement in patients with OP poisoning who were performed plasmapheresis for sepsis.^{9,10} It may not be only the elimination of OP but replacement of cholinesterase by fresh frozen plasma by plasma exchange which helps in clinical improvement in patients poisoned with OP. Plasmapheresis and therapeutic plasma exchange (TPE) are terms that identify different procedures but cause confusion and are frequently misused.¹¹ Plasmapheresis is the procedure in which less than 15% of total plasma is removed and is not replaced. TPE is another procedure in which separated plasma is replaced with albumin and/or fresh frozen plasma and crystalloids. Similar as in other articles in the toxicology field, we misuse plasmapheresis since the procedure we performed was TPE to eliminate toxic substances.

There are several reports supporting effectiveness of plasmapheresis in OP poisoning and intermediate syndrome.^{11–13} Our patient had mild symptoms in the beginning but experienced cholinergic crisis on the second day, when her skin was dried with atropine. We conclude that her cracked and scaly skin has let an easier penetration and absorption of OP. Despite aggressive atropine and repeated oxime administration, she had confusion, was

hypoxic due to dysfunction of respiratory muscles and excessive secretions. After plasmapheresis was performed, she became alert, oxygen saturation was elevated, and plasma cholinesterase levels were increased.

Plasmapheresis was performed in our patient once, and clinical improvement was achieved. We suggest the widespread usage and availability of plasmapheresis in toxicology clinics to manage extraordinary and serious cases of OP intoxication, especially when clinical worsening occurs despite atropine and oxime treatment. Since this is an anecdotal case, further studies are needed to support use of plasmapheresis.

Author contributions

Concept – N.R.D.; Design – N.R.D. and A.A.; Supervision: Z.K. and A.S.; Data Collection and Processing – N.R.D., A.A., A.S.; Literature Review - N.R.D., A.A., A.S. and Z.K.; Writer – N.R.D.; Critical Review – A.S. Z.K. and A.A.

Conflicts of interest statement

The authors declared no conflict of interest.

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Patient consent

A written consent was obtained from the patient in this case report.

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