Therapeutic efficacy of charcoal hemoperfusion in patients with acute severe dichlorvos poisoning

Ai PENG[1], Fan-qing MENG, Lan-fang SUN[2], Zhan-sheng JI[2], Yu-hui LI[2]

Department of Medicine, Affiliated Drum Tower Hospital, School of Medicine, Nanjing University, Nanjing 210008;
[2]Department of Emergency, Coal Mining Central Hospital of North China Coal-mining Medical College, Zibo 255120, China

KEY WORDS dichlorvos; poisoning; hemoperfusion; therapeutics; adsorption

ABSTRACT

AIM: To assess the efficacy of hemoperfusion (HP) in the treatment of the patients with acute severe dichlorvos (DDVP) poisoning. **METHODS:** One hundred and eight patients with acute severe DDVP poisoning in the two teaching hospitals were enrolled. Sixty-seven patients were treated with HP (HP group) and forty-one patients accepted traditional treatment only as the control. Serum concentration of DDVP was determined by gas chromatography. **RESULTS:** The duration of coma, impaired consciousness, ICU stay, and mechanical ventilation was significantly shorter in the HP group than that in the control. The cumulative dosages (mg) of atropine required either in the first 24 h on admission (442±436 *vs* 899±485 in the control, $P<0.01$) or within the hospital (568±574 *vs* 1228±982 in the control, $P<0.01$) were markedly reduced in the HP patients. The lower incidence of mechanical ventilation required (13.4 % *vs* 36.6 % $P<0.01$), respiratory muscular paralysis (4.5 % *vs* 17.1 %, $P<0.05$) and the lower mortality of death (7.5 % *vs* 34.1 %, $P<0.01$) were observed in the HP group. HP could accelerate the recovery of suppressed cholinesterase activity. After the procedure, the DDVP level was decreased from (11±4) to (7±3) mg/L in parallel with a decline in APACHE II Score or dopamine dose and a rise in Glasgow Coma Scale ($P<0.05$). In addition, the mean values of peak clearance and reduction rate were (87±17) mL/min and 44 %±11 %, respectively. **CONCLUSION:** The rapid fall in blood DDVP level and the dramatic clinical response suggest that HP is effective in the treatment of acute severe DDVP poisoning.

INTRODUCTION

Inadvertent or suicidal organophosphate poisoning (OPP) represents a serious problem in the developing countries[1,2]. Every year pesticides cause about 3 million poisonings and 200 000 deaths in the world and it is estimated that there were 100 000 cases of acute OPP in China[3,4]. The reported mortality following OPP varies between 4 % and 30 %[5].

Dichlorvos (DDVP), an organic phosphate ester, is highly toxic for man because of its direct and powerful inhibitory effect on the cholinesterase (ChE) activity in the nervous system and other tissues[6]. Traditional treatment of OPP consists of 1) maintaining respiration; 2) administration of atropine, pralidoxime and forced diuresis; 3) removal of organophosphates by gastric lavage; and 4) other supportive measures including intravenous fluid to prevent the hypopotassemia or shock and antibiotics to handle pulmonary infection[7]. Oral organophosphorus insecticides cannot be completely removed by routine gastric lavage, the residues in the gastrointestinal tract are continuously transported

[1] Correspondence to Dr Ai PENG.
Phn 86-25-481-3516. E-mail pengai@hotmail.com
Received 2002-12-06 Accepted 2003-05-23

to the tissues through the blood circulation. Atropine is effectively antagonistic to the muscarinic effects, but not to the nicotinic effects[1,7,8]. The use of oximes in OPP may lead to neurologic damages, such as confusion, dizziness, and muscle weakness[7,9]. For these reasons, traditional treatment is only effective for the mild or even moderate OPP, but not for the severe patients. Thus, acute severe DDVP poisoning often results in a high mortality in China[4]. These make it tempting to speculate that, in the case of severe DDVP poisoning, removing DDVP from the body is more important than drug therapy to achieve successful treatment.

Direct removal of organophosphorus compounds in the blood using hemoperfusion (HP) with activated charcoal in the treatment of organophosphorus insecticide poisoning has been previously reported[10-14]. However, because of very few cases of OPP treated with HP and a lack of controlled clinical study, therapeutic efficacy of HP is still a matter of controversy[13, 15]. The objective of the present investigation is to determine whether HP is an effective measurement in reducing the mortality of acute severe DDVP poisoning.

MATERIALS AND METHODS

Patients selection The study was carried out from July 1995 to June 2001. During this period, all patients with acute DDVP poisoning who met all the following selection entry criteria were included: (1) age between 13 and 65 a; (2) oral intoxication due to suicidal attempts; (3) admitted directly to the Intensive Care Unit (ICU) in two teaching hospitals; (4) Glasgow Coma Scale (GCS) ≤7 with pulmonary edema, respiratory insufficiency or shock to a great or less extent; (5) Serum ChE activity <350 IU/L (normal values were 3500 to 6500 IU/L). Patients were excluded from enrollment if they had history and/or clinical evidence of lung disease, myopathy and any other pre-existing severe diseases which might influence the clinical course. A total of 108 patients (34 male, 74 female; mean age, 29±12 a; range, 14-65 a) were enrolled. Sixty-seven patients were treated with HP (HP group) and forty-one patients accepted traditional treatment only as the control (non-HP group). If the patient's coma was still persisting after traditional treatment, HP should be performed as soon as possible. The severity of DDVP poisoning was evaluated by Acute Physiology and Chronic Health Evaluation (APACHE II)[16] and the depth of impaired consciousness and coma by Glasgow Coma Scale (GCS)[17]. The classification of the degree of DDVP was based on the criteria described by Namba *et al*[7]. The investigators were responsible for making clinical decisions, evaluating patients for intubation or extubation and scoring for APACHE II or GCS. Ethics committee approval was obtained for the study from the two hospitals involved, and informed written consent obtained from the patient's family member before the HP could be performed. The clinical features of the two groups are shown in Tab 1.

Diagnosis The diagnosis of acute DDVP poisoning depended on the criteria described by Namba *et al*[7]. Respiratory failure (RF)[18] was diagnosed as respiratory distress, hypoventilation, and arterial blood gas with a P_{aO2} of less than 60 mmHg and /or a P_{aCO2} of greater than 45 mmHg accompanied by acidemia (pH<7.30). Respiratory muscular weakness was defined as RF with all three of following: 1) unable to be explained by any other poisonous complications including cerebral edema, brain stem damage, lung disease and shock; 2) mechanical ventilator support was required; 3) RF disappeared rapidly when mechanic ventilator support was established and the patient became conscious and rational. Respiratory muscular paralysis (RMP) was diagnosed when the patients had both respiratory muscular weakness and breathlessness. Mechanical ventilation was immediately and promptly given to all patients with respiratory muscle weakness or paralysis. Rebound phe-

Tab 1. General clinical features in the patients with acute severe dichlorvos poisoning on admission. HP: hemoperfusion. ChE: cholinesterase. BW: body weight. Mean±SD. [a]*P*>0.05 *vs* Non-HP.

Group	Age /a	Ingested dose /g·kg^{-1}	Lavage time /min	Lavage water /L	ChE activity /IU·L^{-1}	Respiratory failure/%	Shock /%	Glasgcow Score
HP (*n*=67)	29±13	1.3±0.7[a] (*n*=58)	52±39[a]	21±8[a]	301±134[a]	27 (40.3)[a]	27 (40.3)[a]	4.2±1.5[a]
Non-HP (*n*=41)	32±16	1.2±0.7 (*n*=35)	46±22	24±7	337±161	15 (36.6)	11 (26.8)	5.3±1.7

nomenon was described as symptoms and signs of OPP recurred that required further atropine treatment. The intermediate syndrome (IMS) was diagnosed as clinical signs and symptoms which the patient's muscular weakness affecting predominantly the proximal limb muscles, the cranial-nerve palsies and neckfexors were detected after the acute cholinergic crisis but before the expected onset of delayed neuropathy[19].

Treatment In addition to the gastric lavage and other supportive measures, repeated doses of atropine were given intravenously until clinical signs of atropinization appeared (mydriasis, heart rate >100 beats/min, flushing, xerostomia, anhydrosis, slight agitation). A maintenance dose was administrated to keep the patients atropinized until the onset of HP. After HP atropine was continuously used to keep the patients atropinized for 24-48 h and then atropine should be tapered off. The pralidoxime (1-2 g every 6 h in the doses) was administrated intravenously within the first day on admission.

Hemoperfusion HP consists of a blood pump (XG-2, Zhongli Electrical Equipment Company, China) and a cellulose-coated activated charcoal (200 g) cartridge (BS-1, Zibo Pharmaceutical Factory, China). Access to blood stream was achieved via the femoral artery and cephalic or basilic vein using 14-gauge catheters. The initial dose of heparin (0.6-1.0 mg/kg) was administrated intravenously and additional 5-10 mg of heparin was given every 30 min during the procedure. Blood flow was held constantly at approximately 160-180 mL/min. The patient accepted one to three HP. Each procedure lasted for 2 h. The time interval from the onset of DDVP intoxication to HP was (6.0±6) h. The patients were not given atropine during HP.

Chemical analysis of DDVP residues Blood samples for determination of DDVP concentration were obtained directly from the vein of five patients at the start of HP and at half-hour intervals thereafter, and the samples for determination of blood clearance of DDVP were from the inlet and outlet of activated charcoal cartridge. Blood 1.5 mL was placed into a 5 mL tube containing 1.5 mL of phosphoric acid (0.74 mol/L). A 0.5 mL of acidified whole blood was mixed with 25 mL of the internal standard and extracted for 15 min with 250 mL of toluene. The tubes were centrifuged for 5 min at 3000×*g* and 2 μL of the organic phase were injected. The serum concentration of DDVP was measured by gas chromatograph (Hewlett-Packard 5890II) equipped with a flame ionization detector[20]. A fused-silica capillary column (HP-5, 30 m×0.32 mm ID×0.25 mm film thickness) was used. The column temperature was maintained at 50 ºC for 1 min, and programmed to 120 ºC at 10 ºC/min and then to 180 ºC at 10 ºC/min. The injection port and the detector temperature were 240 ºC and 260 ºC, respectively. Reduction rate was calculated from the changes of the blood DDVP level at the start and end of the procedure and the blood clearance was from the formula described by the Okonek[10].

Statistical analysis Data were expressed as mean and standard deviation for quantitative variables and as percentages for categorical data. Student's *t*-test was applied for quantitative variables, Kruskal-Wallis (K-W) test for non-parametric variables and Chi-square test for the occurrence of categorical variables. All reported *P* values are two sides, and *P* values of less than 0.05 were considered to indicate statistical significance.

RESULTS

There was no significant difference in the clinical characteristics on admission between HP and non-HP patients ($P>0.05$), indicating that the patients between the two groups were comparable (Tab 1).

The duration of coma, impaired consciousness, ICU stay, and mechanical ventilation were significantly shorter in the HP group than that in non-HP group (K-W test, $P<0.01$). The cumulative doses of atropine required either in the first 24 h on admission or within the hospital were markedly reduced in patients treated with HP (K-W test, $P<0.01$). But no significant different doses between two groups were observed. The frequency of mechanical ventilation required or RMP and the number of death in the HP group were significantly reduced as compared with the control (K-W test, $P<0.01$). However, no significant differences of the frequency in respiratory muscular weakness, rebound phenomenon, IMS, and pulmonary infection were observed ($P>0.05$, Tab 2).

After HP, the reduction of APACHE II Score and dopamine dose and the elevated GCS were observed ($P<0.05$). The counts of white blood cell (WBC) and platelet were only slightly reduced. No changes of serum ChE activity level and blood hemoglobin level were found ($P>0.05$, Tab 3).

At the time of admission following on d 1,3,5, and 7 the values of ChE activity in the patients with and without HP were 326±140, 339±151, 746±376, 1955±1065, 3505±1179, and 334±163, 317±147, 613±299, 1349±644, 2755±963 (IU/L), respectively.

Tab 2. Comparison of clinical characteristics in the patients with and without hemoperfusion. Mean±SD. $^{b}P<0.05$, $^{c}P<0.01$ *vs* non-hemoperfusion.

Item	Hemoperfusion (*n*=67)	Non-hemoperfusion (*n*=41)
Duration of ICU stay/d	4.0±1.5[b]	6.0±2.0
Clinical manifestations		
Convulsion	4 (6.0 %)	1 (2.4 %)
Muscular fasciculations	15 (22.4 %)	5 (12.2 %)
Duration of coma/h	9±6[c]	15±8
Duration of impaired consciousness/h	16±10[c]	23±14
Medication		
Atropine requirement/mg		
In the first 24 h on admission	442±436[c]	899±785
Within the hospital	568±574[c]	1228±982
Pralidoxime/g	4.6±1.1	4.8±1.6
Mechanical ventilation required	9 (13.4 %)[c]	15 (36.6%)
Length of mechanical ventilation/d	5±3[b]	8±3
Complications		
Rebound phenomenon	16 (23.9 %)	8 (19.5.%)
Respiratory muscular paralysis	3 (4.5 %)[b]	7 (17.1 %)
Respiratory muscular weakness	7 (10.4 %)	10 (24.3 %)
Intermediate syndrome	20 (29.9 %)	15 (36.6 %)
Pulmonary infection	7 (10.4 %)	9 (22.0 %)
Death	5 (7.5 %)[c]	14 (34.1 %)

Tab 3. Changes of clinical and laboratory data after hemoperfusion. HP: hemoperfusion. WBC: white blood cell. ChE: cholinesterase activity. Mean±SD. $^{b}P<0.05$ *vs* pre-HP group.

Group	APACHE II score	Glasgow score	Dopamine dose/ $mg\cdot kg^{-1}\cdot min^{-1}$	ChE activity/ $IU\cdot L^{-1}$	Hb/$g\cdot L^{-1}$	$10^{-9}\times$WBC/L^{-1}	$10^{-9}\times$Platelet count/L^{-1}
Pre-HP (*n*=67)	19±4	5.4±1.4	12±4 (*n*=26)	329±134	131±27	14±5	191±60
Post-HP (*n*=67)	15±4[b]	6.9±2.1[b]	6±3[b] (*n*=26)	338±151	127±19	12.1±2.9[b]	160±41[b]

On d 5 and d 7 the patients in the HP group had a higher ChE activity than the control ($P<0.05$).

The serum DDVP concentration was determined in five patients with DDVP poisoning. Serum DDVP concentration was markedly decreased after the HP ($P<0.05$). The reduction rate and mean value of peak clearance were 44 %±11 % and (87±17) mL/min, respectively (Tab 4).

Five patients in HP group died of RMP in 2 cases and severe depression of respiratory center in 3 cases. Fourteen patients without HP died of RMP in 2 cases, cardiac arrest in 2 cases, gastrointestinal tract haemorrhage in 1 case, severe depression of respiratory center in 9 cases. A higher mortality rate resulted from severe brain damage was observed in the HP group ($P<0.05$).

DISCUSSION

HP with activated charcoal was able to shorten the duration of coma, impaired consciousness, ICU stay and mechanical ventilation and reduce the cumulative doses of atropine and dopamine, the frequency of endotracheal intubation required, APACHE II Score in parallel with elevation of GCS. In addition, charcoal HP could improve the depression of ChE activity and reduce mortality rate of severe DDVP poisoning. These clinical evidences strongly suggest the efficacy of HP with activated charcoal in the treatment of the patients

Tab 4. Dichlorvos removed by hemoperfusion with activated charcoal. $^{b}P<0.05$ compared between before and after hemoperfusion. BW: body weight.

Patient	Ingested dose /g·kg^{-1}	Serum level on admission /mg·L^{-1}	Serum dichlorvos level /mg·L^{-1}		Reduction rate /%	Peak clearance /mL·min^{-1}	Time to HP /h	Number of HP	Outcome
			Before HP	After HP					
1	1.19	13.3	11.3	6.73	40.4	83.9	5.5	2	Survival
2	0.91	20.1	16.4	8.6	47.6	96.1	3.7	1	Survival
3	1.15	9.4	11.5	5.21	54.7	109.4	3.9	2	Survival
4	1.79	7.6	5.71	2.91	49.0	78.0	5.8	1	Survival
5	1.17	6.9	10.3	7.62	26.1	66.0	6.6	3	Death
Mean±SD	1.24±0.33	12±5	11±4	7±3^{b}	44±11	87±17	5.1±1.3	1.8±0.8	

with acute severe DDVP poisoning.

In the present study, the blood DDVP level was rapidly reduced using the HP with activated charcoal (Tab 4). Activated charcoal had a high adsorption capacity of DDVP. These experimental evidences also supported the efficacy of charcoal HP. In addition, the rapid fall in blood DDVP level and the dramatic clinical response noted during the procedure suggested that direct removal of DDVP from the blood was the main mechanism of HP in the treatment of DDVP poisoning.

The ingested high dosages of xylene, benzene and any other compounds in the DDVP-solvent mixtures often exceeded the toxic level, which aggravated the depression of central nervous system[21]. Charcoal HP can eliminate these chemical compounds in the blood[22]. Thus the rapid recovery of coma in acute severe DDVP poisoning may also ascribe to the removal of these mixed compounds by HP.

In vitro trials and clinico-toxicological investigations have been performed in order to test whether HP with coated activated charcoal could be used in the treatment of organophosphate intoxications. *In vitro* investigation into the elimination of dimethoate from the blood had revealed HP technique achieved a good clearance at 88 mL/min at a blood flow rate of 100 mL/min[10]. Nagler *et al*[23] described a severe case of dimethoate poisoning. Two hours after suicidal ingestion of 10 g dimethoate (plasma level 2.34 mg/L 30 min after ingestion), HP with activated charcoal was performed. A HP clearance of 95 mL/min at blood flow rate of 200 mL was observed, which was in agreement with the *in vitro* finds. With treatment the patient's clinical condition improved rapidly and she was discharged fully recovered. In our present study the DDVP concentration before the HP from the five patients was (11±4) mg/L, but converted to (7±4) mg/L after HP (Tab 4). Moreover the peak of blood clearance rate was (87±17) mL/min at the blood flow of (171±35) mL/min. Most people's state of consciousness was improved rapidly after HP. These evidences not only showed that HP with activated charcoal was able to remove the organophosphate compounds from the blood but also supported the effectiveness of HP technique. By contrast, Martinez-Chuecos *et al*[13] retrospectively analyzed the ten patients with OPP in whom one to three HPs was underwent. A small amount of organophosphoates was removed by HP and no changes in symptoms were observed after HP procedure. There was distinctively different between DDVP and other organophosphorus compounds in many aspects such as clinical manifestation, intoxicated mechanism and their metabolites[11]. Furthermore, it should be noted that the toxic action of organophosphorus compounds was located in the tissue compartments where it bound reversibly and after some time irreversibly to the nerve endings. Only the reversibly bound organophosphorus compounds in the tissues were in equilibrium with them in the blood[14]. Therefore HP should be more effective during the very early stage of the intoxication when the distribution of organophosphorus compounds in tissue was not complete. In our patients the time interval from the onset of intoxication to HP was markedly shortened in our study as compred with Martinez-Chuecos's report (5.6±4.8 *vs* 27±32 h)[13]. These might be responsible for the difference of clinical observation.

Although the correlation between serum ChE activity and the severity of OPP has not been well established[24]. The evaluation of the degrees of severity

in acute OPP poisoning is still based on serum ChE activity in clinical practices[1]. As we expected, no changes of serum ChE level were observed during the HP in our study. However, HP technique was able to accelerate the recovery of suppressed ChE activity in the DDVP poisoning after HP. The possible explanation for this is that DDVP acts as irreversible ChE inhibitor[25]. The recovery of ChE activity may depend on its regeneration.

Twenty (29.9 %) patients with apparent IMS in HP group and fifteen (36.6 %) in non-HP group suggest IMS is not rare. Ten out of one hundred and eight patients had RMP induced by DDVP and 4 patients died of it. Unlike previously described by de Bleecker *et al*[26], this evidence showed that the outcome of IMS was not favorable. Up to date the relationship between HP and IMS has not been documented. According to our data, HP did not affect the incidence of IMS (Tab 2). However, HP could dramatically reduce the frequency of RMP suggesting its potential beneficial role in amelioration of muscle paralysis induced by DDVP. That might resulted from the local DDVP elimination by the HP.

Patient 5 had a relatively lower blood DDVP concentration (Tab 4). However, this patient had a poor response to HP and other support treatment and died after consecutive 3 HPs. In contrast, patient 2 had the highest blood DDVP concentration in the five patients and regained consciousness rapidly through only one HP. This evidence showed no direct relationship between blood DDVP level and the poisonous severity of clinical course of the patients with acute severe DDVP poisoning.

In the non-HP patients, the leading cause of death in the severe DDVP poisoning was severe depression of central nervous system, often resulting in the RF and multiple organ failure (MOF). In contrast, the rapid improvements of coma and impaired consciousness were observed during or after the HP, suggesting the reduced mortality rate in the severe DDVP poisoning might mainly ascribe to alleviate the cerebral damage.

Since limited data are available on the effect of HP on the toxicokinetic characteristics of DDVP in the poisonous dosage setting, it is uncertain whether the DDVP in the tissues could also be removed through HP. In fact, DDVP distributed uniformally throughout the available body compartment[27]. Thus lacking of monitoring the toxicokinetic characteristics of blood DDVP metabolism, we cannot evaluate when the poisoned patients are safe and the HP could be stopped. What the close relationship between HP and the toxicokinetics of DDVP in the body needed to be further explored.

HP requires careful monitoring to prevent its potential complications. The main complications of HP were a temporary reduction of the total platelet or WBC counts and a slight decline in blood pressure caused by charcoal adsorption (Tab 3). Because of the microencapsulated charcoal used, the platelet and WBC counts usually fell by less than 10 % (Tab 3), which was improved to normal level after 1 to 2 d, indicating the HP was a safe measure in the treatment of DDVP poisoning. With other support measures HP should be applied as early as possible so that the patients with shock could be saved.

The incidence of clinical manifestations such as convulsion and muscular fasciculation did not differ between the two groups (Tab 2). All the DDVP in the body compartment cannot be completely eliminated by HP. In addition, 5 cases did not recover after consecutive 1 to 3 HPs (Tab 2). These evidences indicated that HP technique could not solve all of the problems induced by DDVP poisoning. Traditional treatment combined with HP should be stressed in the treatment of severe DDVP poisoning.

CONCLUSION

We have presented evidences in support of our speculation that HP technique with activated charcoal are able to help the comatose patients regain consciousness rapidly, prevent toxic encephalopathy formation and deterioration, alleviate the muscular paralysis, and markedly reduce the mortality rate of severe DDVP poisoning.

REFERENCES

1 Tafuri J, Roberts J. Organophosphate poisoning. Ann Emerg Med 1987; 16: 193-202.
2 Karalliedde L. Organophosphorus poisoning and anaesthesia. Anaesthesia 1999; 54: 1073-88.
3 Jeyaratnam J. Acute pesticide poisoning: a major global health problem. World Health Stat Q 1990; 43: 139-44.
4 He F, Xu H, Qin F, Xu L, Huang J, He X. Intermediate myasthenia syndrome following acute organophosphates poisoning-an analysis of 21 cases. Hum Exp Toxicol 1998; 17: 40-5.
5 Yamashita M, Yamashita M, Tanaka J, Ando Y. Human mortality in organophosphate poisonings. Vet Hum Toxicol 1997; 39: 84-5.
6 Desi I, Nagymajtenyi L. Neurotoxicologyic investigations of

the pesticide dichlorvos (DDVP). Effects on the central and peripheral nervous system. Toxicology 1988; 49:141-8.
7 Namba T, Nolte CT, Jackrel J, Grob D. Poisoning due to organophosphate insecticides. Am J Med 1971; 50: 475-92.
8 Milby TH. Prevention and management of organophosphate poisoning. JAMA 1971; 216: 2131-3.
9 de Silva HJ, Wijewickrema R, Senanayake N. Does pralidoxime affect outcome of management in acute organophosphate poisoning? Lancet 1992; 339: 1136-8.
10 Okonek S. Hemoperfusion with coated activated charcoal in the treatment of organophosphate poisoning. Acta Pharmacol Toxicol(copenh) 1977; 41 (Suppl 2): 85-90.
11 Guven H, Tuncok Y, Gidener S, Gelal A, Demetci M, Fowler J, *et al*. *In vitro* adsorption of dichlorvos and parathion by activated charcoal. J Toxicol Clin Toxicol 1994; 32: 157-63.
12 Luzhnikov EA, Yaroslavsky AA, Molodenkov MN, Shurkalin BK, Evseev NG, Barsukov UF. Plasma perfusion through charcoal in methylparathion poisoning. Lancet 1977; 1: 38-9.
13 Martinez-Chuecos J, del Carmen Jurado M, Paz Gimenez M, Martinez D, Menendez M. Experience with hemoperfusion for organophosphate poisoning. Crit Care Med 1992; 20: 1538-43.
14 Koppel C, Forycki Z, Ibe K. Hemoperfusion in severe dimethoate poisoning. Intensive Care Med 1986; 12: 110-2.
15 Garella S. Extracorporeal techniques in the treatment of exogenous intoxications. Kidney Int 1988; 33: 735-54.
16 Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: A severity of disease classification system. Crit Care Med 1985; 13: 818-29.
17 Teasdal G, Jennett B. Assessment of coma and impaired consciousness. A practical scale**.** Lancet 1974; 2: 81-4.
18 Goswamy R, Chaudhuri A, Mahashur AA. Study of respiratory failure in organophosphate and carbamate poisoning. Heart Lung 1994; 23: 466-72.
19 Senanayake N, Karalliedde L. Neurotoxic effects of organophosphate insecticides: an intermediate syndrome. N Engl J Med 1987; 316: 761-3.
20 Machin AF, Quick MP, Waddell DF. The rapid determination of the organophosphorus pesticides diazinon and dichlorvos in blood by gas chromatography. Analyst 1973; 98: 176-80.
21 Yang PY, Lin JL, Hall AH, Tsao TC, Chern MS. Acute ingestion poisoning with insecticide formulations containing the pyrethroid permethrin, xylene, and surfactant: a review of 48 cases. J Toxicol Clin Toxicol 2002; 40: 107-13.
22 Sevcik P, Hep A, Peslova M. Intravenous xylene poisoning. Intensive Care Med 1992; 18: 377-8.
23 Nagler J, Braeckman RA, Willems JL, Verpooten GA, De Broe ME. Combined hemoperfusion-hemodialysis in organophosphate poisoning J Appl Toxicol 1981; 1: 199-201.
24 Nouira S, Abroug F, Elatrous S, Boujdaria R, Bouchoucha S. Prognostic value of serum cholinesterase in organophosphate poisoning. Chest 1994; 106:1811-4.
25 Kobayashi H, Yuyama A, Imajo S, Matsusaka N. Effects of acute and chronic administration of DDVP (dichlorvos) on distribution of brain acetylcholine in rats. J Toxicol Sci 1980; 5: 311-9.
26 De Bleecker J, Van den Neucker, Colardyn F. Intermediate syndrome in organophosphorus poisoning: A prospective study. Crit Care Med 1993; 21: 1706-11.
27 Shimizu K, Shiono H, Fukushima T, Sasaki M, Akutsu H, Sakata M. Tissue distribution of DDVP after fatal ingestion. Forensic Sci Int 1996; 83:61-6.