APPLICATION OF HEMOPERFUSION COMBINED WITH PYRALOXIME IODIDE IN EMERGENCY TREATMENT OF PATIENTS WITH ACUTE ORGANOPHOSPHORUS POISONING AND ITS EFFECT ON HEPATIC AND KIDNEY FUNCTION

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ABSTRACT

Objective: *To explore the application of hemoperfusion (HP) combined with pyraloxime iodide (PI) in emergency treatment of patients with acute organophosphorus poisoning and its effect on hepatic and kidney function.*

Methods: *According to the object screening criteria in this study, 88 patients with acute organophosphorus poisoning treated in the emergency department of our hospital (January 2019 - January 2021) were selected and divided into the PI group and PI+HP group according to the treatment methods, with 44 cases each, so as to compare their clinical efficacy.*

Results: *No statistical between-group differences in patients' general information were observed (P>0.05); the marked effective rate and total effective rate of the PI+HP group were significantly higher than those of the PI group (P<0.05); 6 h, 12 h and 24 h after treatment, the PI+HP group obtained significantly higher serum cholinesterase (CHE) levels than the PI group (P<0.05); after one week of treatment, the PI+HP group obtained significantly lower levels of alanine aminotransferase (ALT), aspartate transaminase (AST) and total bilirubin (Tbil) indicators than the PI group (P<0.05); after treatment, renal function indicators such as serum creatinine (Scr) and blood urea nitrogen (BUN) in patients of the PI+HP group were obviously lower than those of the PI group (P<0.05); during treatment, the patients in both groups suffered from damage to important organs, intermediate syndrome, and rebound, but the incidence rates were significantly lower in the PI+HP group than in the PI group (P<0.05).*

Conclusion: *In the emergency treatment of patients with acute organophosphorus poisoning, applying HP combined with PI can obviously enhance the clinical efficacy and effectively promote the recovery of hepatic and renal function in patients.*

Keywords: *Hemoperfusion (HP), pyraloxime iodide (PI), acute organophosphorus poisoning, liver and kidney function.*

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Introduction

According to statistics, about 5 million people suffer from organophosphorus pesticide poisoning every year in China, with a mortality rate up to 40%[(1-2)]. The disease has an urgent onset and rapid progression, especially the acute one has always been a difficult point in clinical rescue. The treatment methods for acute organophosphorus poisoning mainly include general therapy, drug therapy, and blood purification therapy, and at present, the combination therapy with drugs such as cholinesterase reactivators (pyraloxime iodide, etc.), choline receptor blocker (atropine) and compound preparations is mainly adopted[(3-6)]. Among them, pyraloxime iodide (PI), a cholinesterase reactivator commonly used in the clinic, can dissociate organic phosphorus and cholinesterase and restore cholinesterase activity, which is more effective against nicotinic like toxic reactions, but has an unclear effect on the alleviation of poisonous mushroom like reactions and central respiratory depression, and usually exerts a better

treatment effect with choline receptor. However, larger drug doses in traditional regimens produce hepatic and renal burdens in patients. Reports have indicated that acute organophosphorus poisoning can be treated by blood purification using detoxicant combined with hemoperfusion (HP) at the same time, which can effectively remove the toxicant from the blood[7-9]. Hence, the clinical treatment of organophosphate poisoning is mostly based on the combination regimen, but there are few reports related to the treatment of organophosphate poisoning by HP combined with PI at present, and strong data support is lacking. Based on this, the application of combining HP with PI in emergency treatment of patients with acute organophosphorus poisoning was explored herein, so as to provide data support for clinically optimizing treatment regimen.

Data and methods

Inclusion criteria

• The patients met the diagnosis criteria of acute organophosphorus poisoning in Diagnostic Criteria and Treatment Principles of Acute Organophosphorus Pesticide Poisoning[10];

• At the time of admission, the patients' serum cholinesterase (CHE) was less than 500 U/L;

• The patients were poisoned by oral organophosphorus pesticides via the digestive tract;

• The time from poisoning to visiting the clinic was less than 4 h;

• The study was a retrospectively analysis study, which only analyzed the clinical data of patients and not intervened with the treatment scheme, and patients and their family members agreed to join the study and signed the informed consent.

Exclusion criteria

• The patients had severe liver and kidney dysfunction or disorders;

• The patients were poisoned by multiple kinds of pesticides;

• The patients had other severe internal and surgical diseases;

• The patients gave up treatment or transferred to another hospital during treatment;

• The patients were allergic to iodide.

Patients screening and grouping

According to the inclusion and exclusion criteria, the clinical data of 88 patients with acute organophosphorus poisoning treated in the emergency department of our hospital (January 2019 to January 2021) were screened for retrospective analysis, and the patients were divided into the PI group and the PI+HP group according to the treatment methods, with 44 cases each. The study was approved by the Hospital Ethics Committee.

Methods

PI group:

• Help patients to escape from the poisoning environment, thoroughly clean their skin and hair, and conduct inducing vomiting, gastric lavage or adsorption with activated carbon[11-13];

• Use catharsis agent to remove the toxic substances in the intestinal tract;

• Intravenously inject sufficient amount of atropine in the early stage, and administer PI injection (specification: 2 ml/0.5 g; manufactured: Shanghai Xudong Haipu Pharmaceutical Co., Ltd.; NMPA approval no. H31020803) via intravenous drip, for those with mild poisoning, mix 0.5-1.0 g of PI with 250 ml of normal saline evenly for intravenous drip, and for those with moderate to severe poisoning, mix 1.0-1.5 g of PI with 250 ml of normal saline, and repeat the administration for 1-3 times within 2 h according to the patients' condition. In addition, perform fluid replacement, infection prevention, diuresis, prevention of damage to important organs such as the heart, kidney and liver and other symptomatic treatments(14);

• In case that the patients had intermediate syndrome during emergency treatment, perform tracheal intubation immediately and connect ventilator for assisted ventilation.

PI+HP group:

On the basis of PI group, select the femoral vein for puncture catheterization, and perform HP treatment with the HP machine (model: SwS-2000A) and perfusion apparatus (model: YIS-150) under the rate of 140-200 ml/min for 2-3 h, choose the heparin as anticoagulant and use 0.8-1.2 mg/kg at first and then add 5-10 mg in every half an hour, meanwhile, perform electrocardiogram monitoring, and give proper amount of protamine after perfusion to neutralize the heparin inside the patients' body.

Observation indicators

The patients' information including their age, gender, CHE level at admission, dose of poison taken, time from poisoning to visiting the

clinic, poisoning degree (mild, moderate, severe), and the type of poisoning pesticides (paraquat, rogor, dichlorvos, mathamidophos, parathion, or phosphoramidothionate) were recorded in detailed. The diagnosis criteria were proposed according to the Diagnosis Criteria and Principles of Management of Occupational Organophosphorus Poisoning[15]: it was considered as marked effective if the patients' serum CHE levels basically returned to normal and their clinical signs and symptoms disappeared after one week of treatment; effective if the patients' serum CHE levels basically returned to normal and their clinical signs and symptoms disappeared after two weeks of treatment; and ineffective if the patients' clinical signs and symptoms were not ameliorated after two weeks of treatment, or the patients were dead. The total effective rate = (marked effective + effective) / total number × 100%.

The patients' CHE levels were measured according to the semiqualilative method with the blood gas analyzer (model: Rapidpoint405); the patients' alanine aminotransferase (ALT), aspartate transaminase (AST), total bilirubin (TBil), serum creatinine (Scr) and blood urine nitrogen (BUN) were measured with the automatic biochemical detector. Occurrence of complications during treatment was recorded, mainly including damage to important organs such as heart, liver, kidney and lung, intermediate syndrome, and rebound.

Statistical processing

In this study, the between-group differences in data were calculated with SPSS21.0, the picture drawing software was GraphPad Prism 7, items included were enumeration data and measurement data, which were examined by X^2 test and t-test, respectively, and differences were considered statistically significant at $P<0.05$.

Results

General information

No statistical between-group differences in patients' general information were observed ($P>0.05$), see Table 1 for specific data.

Clinical efficacy

The marked effective rate and total effective rate of treatment were significantly higher in the PI+HP group than in the PI group ($P<0.05$), with statistically significant between-group differences. See Figure 1.

Observation indicator	PI group	PI+ HP group	X^2/t	P
Age (years)	39.85±4.96	40.11±5.20	0.240	0.811
Gender (male/female)	15/29	13/31	0.210	0.647
CHE (U/L)	454.35±76.27	461.96±73.32	0.477	0.645
Dose of poison (ml)	135.00±95.00	130.00±90.00	0.253	0.801
Time from poisoning to visiting the clinic (h)	1.75±0.36	1.79±0.34	0.536	0.594
Poisoning degree				
Mild	6 (13.64)	9 (20.45)	0.723	0.395
Moderate	17 (38.64)	16 (36.36)	0.049	0.826
Severe	21 (47.73)	19 (43.18)	0.183	0.669
Poisoning pesticides				
Paraquat	12 (27.27)	10 (22.73)	0.242	0.622
Rogor	11 (25)	8 (18.18)	0.604	0.427
Dichlorvos	8 (18.18)	9 (20.45)	0.073	0.787
Mathamidophos	5 (11.36)	7 (15.91)	0.386	0.534
Parathion	4 (9.09)	6 (13.63)	0.451	0.502
Phosphoramidothionate	4 (9.09)	4 (9.09)	0.000	1.000

Table 1: Between-group comparison of general information (n=44).

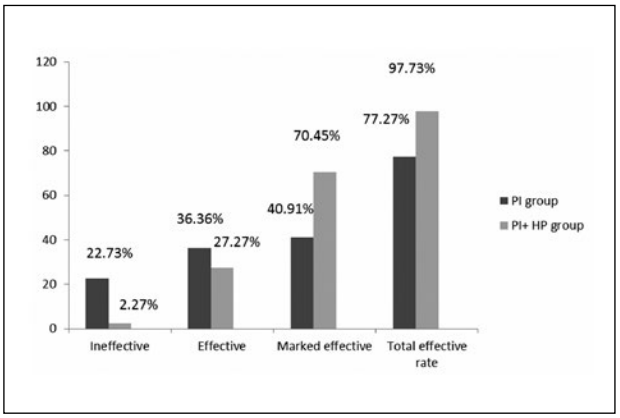

Figure 1: Between-group comparison of clinical efficacy (n=44, %).

Note: There were 10 ineffective cases, 16 effective cases and 18 marked effective cases in the PI group after treatment, and the total number of effective cases was 34; There were 1 ineffective cases, 12 effective cases and 31 marked effective cases in the PI+HP group after treatment, and the total number of effective cases was 43; The between-group difference in the marked effective rate of treatment was significant (t=7.782, P=0.005); and The between-group difference in the total effective rate of treatment was significant (t=8.416, P=0.004).

CHE level

After 6 h, 12 h and 24 h of treatment, the PI+HP group obtained significantly higher CHE levels than the PI group (P<0.05). See Figure 2.

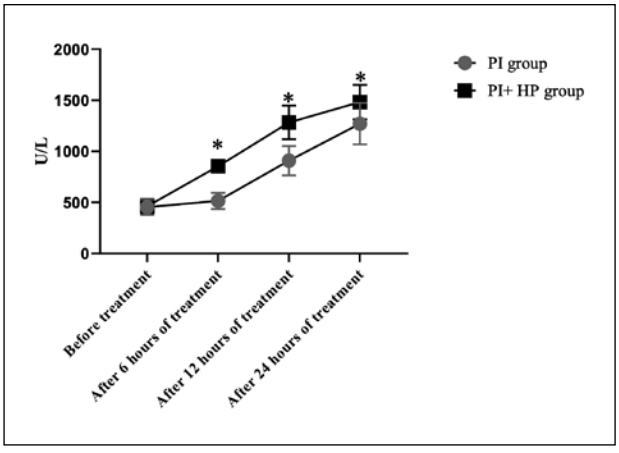

Figure 2: Between-group comparison of CHE level ($\bar{x}\pm s$). *Note: The horizontal axis indicated the test time points, and the vertical axis indicated the CHE level in U/L; Before treatment and after 6 h, 12 h and 24 h of treatment, the CHE levels of the PI group were (454.35±76.27), (515.27±78.64), (908.76±143.98) and (1,271.33±202.41), respectively; Before treatment and after 6 h, 12 h and 24 h of treatment, the CHE levels of the PI+HP group were (461.96±73.32), (854.27±65.91), (1,283.16±163.74) and (1,482.56±168.37), respectively; and *from left to right indicated that the differences in CHE levels after 6 h, 12 h and 24 h of treatment were significant (t=21.915, 11.390, 5.322, P all<0.001).*

Liver function indicators

After one week of treatment, the measured levels of ALT, AST and Tbil indicators were significantly lower in the PI+HP group than in the PI group (P<0.05), with significant between-group differences. See Table 2.

Indicator		PI group	PI+HP group	t	P
ALT (U/L)	Before treatment	25.48±10.06	26.12±12.39		
	After one week of treatment	74.68±15.72	49.30±14.13	7.965	<0.001
AST (U/L)	Before treatment	35.61±13.29	35.82±13.71		
	After one week of treatment	52.94±15.66	30.65±15.72	6.663	<0.001
TBil (μmol/L)	Before treatment	12.86±7.41	13.16±6.40		
	After one week of treatment	25.58±9.72	11.43±7.85	7.512	<0.001

Table 2: Between-group comparison of ALT, AST and Tbil levels ($\bar{x}\pm s$).

Kidney function indicators

After treatment, the kidney function indicators such as Scr and BUN were obviously lower in the PI+HP group than in the PI group (P<0.05). See Table 3.

Indicator		PI group	PI+HP group	t	P
Scr (mmol/L)	Before treatment	68.85±8.46	69.13±7.62		
	After one week of treatment	65.04±7.11	60.16±7.01	3.242	0.002
BUN (mmol/L)	Before treatment	5.57±1.05	5.68±1.14		
	After one week of treatment	4.71±1.13	4.23±1.08	2.037	0.045

Table 3: Between-group comparison of Scr, BUN and uric acid ($\bar{x}\pm s$).

Incidence rates of complications

During treatment, patients in both groups had damage to importance organs, intermediate syndrome and rebound, but the incidence rates were significantly lower in the PI+HP group than in the PI group (P<0.05). See Figure 3.

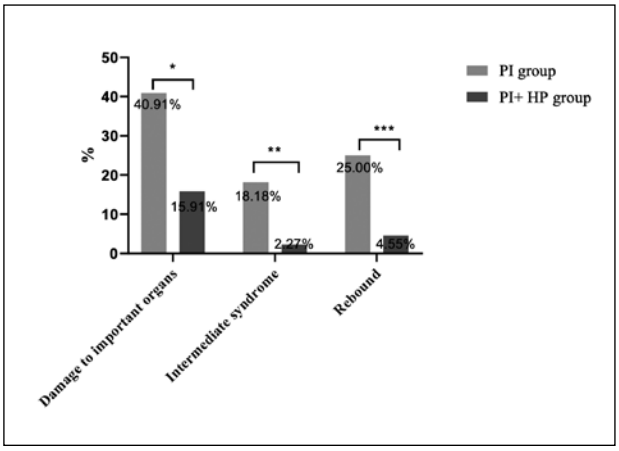

Figure 3: Between-group comparison of complication incidence rates (%).

*Note: The horizontal axis indicated the types of complications, and the vertical axis indicated the incidence rate (%); There were 18 cases with damage to important organs, 8 cases with intermediate syndrome, and 11 cases with rebound in the PI group; There were 7 cases with damage to important organs, 1 cases with intermediate syndrome, and 2 cases with rebound in the PI+HP group; *indicated significant between-group difference in the incidence of damage to important organs (X^2=6.761, P=0.009); **indicated significant between-group difference in the incidence of intermediate syndrome (X2=0.065, P=0.014); and ***indicated significant between-group difference in the incidence of rebound (X^2=7.311, P=0.007).*

Discussion

In general, organophosphorus pesticides can enter human body through digestive tract, respiratory tract, and skin, and combines with CHE to form phosphine CHE, which can lead to a large amount of acetylcholine accumulation in patients and then trigger a series of poisoning symptoms[16]. At present, the main clinical treatment of acute organophosphate poisoning is drug combination, which, although

has a certain effect, presents larger bottleneck in the emergency treatment of the disease. The main problems include the facts that organophosphorus pesticides can be rapidly absorbed in the body and accumulate in the liver, kidney, and adipose tissue, the condition of patients is changing so rapidly that the absorbed toxic substances cannot be immediately cleared even with fast administration, and the dosage of drugs used is not easy to control[17-19].

In recent years, the intensive development of blood purification treatment techniques has brought hopes to the clinical treatment of organophosphate poisoning. Currently, the commonly used blood purification technique in the clinic is HP, which introduces the patients' blood into a perfusion apparatus with solid adsorbent, adsorbs out exogenous or endogenous toxins that are difficult to clear by dialysis, and finally, transports the purified blood back into the patients. It was reported in the study by Getnet[20] that HP exerts no effect on CHE that has been combined with organophosphorus, but can be applied jointly with cholinesterase reactivators, and at the same time, effectively reduces the dose of cholinesterase reactivators and improves the survival rate of patients. PI is currently one of the most commonly used cholinesterase reactivators in the clinic. The author fully recognizes the value and significance of HP combined with PI in rescuing patients with acute organophosphate poisoning, but currently relevant studies are very few and there is a lack of relevant data analysis. Hence, the clinical data of 88 patients with acute organophosphorus poisoning treated in the emergency department of our hospital were retrospectively analyzed herein, with the results as follows.

The marked effective rate and total effective rate of treatment were significantly higher in the PI+HP group than in the PI group ($P<0.05$), demonstrating that the combined therapy was preferred in the emergency treatment of patients with acute organophosphorus poisoning and clearly had better overall efficacy than single drug treatment regimen. In addition, after 6 h, 12 h and 24 h of treatment, the CHE levels were obviously higher in the PI+HP group than in the PI group ($P<0.05$); after one week of treatment, the levels of ALT, AST and Tbil indicators were significantly lower in the PI+HP group than in the PI group ($P<0.05$); and the renal function indicators such as Scr and BUN were obviously lower in the PI+HP group than in the PI group ($P<0.05$). The onset in patients with acute organophosphate poisoning mostly involves acute cholinergic crisis phase, intermediate syndrome phase and multiple neuropathy phase[21-24], and these phases will proceed gradually along with the degree of poisoning, so the key point of clinical treatment is to clear the absorbed toxic substances in a timely manner. HP is an effective way to clear the absorbed toxins, and the combined use of PI is more conducive to the activation of cholinesterase. Therefore, the CHE level in patients of the PI+HP group returned to normal faster; also, the changes in the levels of ALT, AST, Tbil, Scr and BUN indicators showed that applying HP based on PI could effectively promote the recovery of various liver and kidney function indicators. Finally, it was found after analyzing patients' adverse reactions that all patients had damage to important organs, intermediate syndrome and rebound during treatment, but the incidence rates were significantly lower in the PI+HP group ($P<0.05$), further proving that the combined therapy could greatly reduce the incidence rate of prognostic complications, which was consistent with the study by Masson[25].

The deficiencies of the study are as follows. For drug poisoning with large molecular weight, high lipid solubility and high protein binding rate, especially in acute severe patients, HP should be the first choice, but it is less effective in removing toxicants containing substances such as kanamycin, penicillin C, methanol, ethanol, oxalic acid, boric acid, camphor and bromuret, and plasma exchange can be chosen in such case; moreover, clinical analysis found that HP has the risk of triggering thrombocytopenia, coagulation disorders, hypotension and cardiac dysfunction, but due to the small sample size and the short follow-up period in this study, none of the above complications were observed, so further studies with larger sample size on the long-term mechanism and safety are still needed. In conclusion, in the emergency treatment of patients with acute organophosphorus poisoning, applying HP combined with PI can obviously promote the clinical efficacy, and compared with traditional drug therapy, HP can effectively clear the organophosphorus substances that affect the liver and kidney function in patients and promote the recovery of such function.

References

1) Jackson,C. J., Carville, A., Ward, J., et al. Use of OpdA, an organophosphorus (OP) hydrolase, prevents lethality in an African green monkey model of acute OP poisoning[J]. Toxicology: An International Journal Concerned with the Effects of Chemicals on Living Systems, 2014, 3171-5.
2) Eddleston, Michael, Chowdhury, Fazle Rabbi. Pharmacological treatment of organophosphorus insecticide poisoning: the old and the (possible) new[J]. British Journal of Clinical Pharmacology, 2016, 81(3): 462-470.
3) Hulse, Elspeth J., Davies, James O. J., Simpson, A. John, et al. Respiratory Complications of Organophosphorus Nerve Agent and Insecticide Poisoning Implications for Respiratory and Critical Care[J]. American journal of respiratory and critical care medicine, 2014, 190(12): 1342-1354.
4) Steven B. Bird, Predrag Krajacic, Keigo Sawamoto, et al. Pharmacotherapy to protect the neuromuscular junction after acute organophosphorus pesticide poisoning[J]. Annals of the New York Academy of Sciences, 2016, 137486-93.
5) Chowdhury, Fazle Rabbi, Rahman, Md. Mustafezur, Ullah, Parash, et al. Salbutamol in acute organophosphorus insecticide poisoning - a pilotdose-response phase II study[J]. Clinical toxicology: the official journal of the American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists, 2018, 56(9): 820-827.
6) Alahakoon, Chanika, Dassanayake, Tharaka, Gawarammana, Indika, et al. Revisiting respiratory failure in acute organophosphorus insecticide self-poisoning in Sri Lanka[J]. Clinical toxicology: the official journal of the American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists, 2018, 56(7): 683-684.
7) Shaimaa. el-Gendy, Inas. el-Mehallawi, Abdelhamid. elwy. A randomized clinical trial to evaluate the efficacy of single versus multiple gastric lavage in the management of patients with acute organophosphorus poisoning[J]. Tanta Medical Journal, 2017, 45(4): 181-191.
8) L. A. Konickx, K. Bingham, M. Eddleston. Is oxygen required before atropine administration in organophosphorus or carbamate pesticide poisoning?-A cohort study[J]. Clinical Toxicology, 2014, 52(5): 531-537.
9) Michael Eddleston, Fazle Rabbi Chowdhury. Pharmacological treatment of organophosphorus insecticide poisoning: the old and the (possible) new[J]. British Journal of Clinical Pharmacology, 2016, 81(3): 462-470.
10) Worek, F., Thiermann, H. The value of novel oximes for treatment of poisoning by organophosphorus compounds[J]. Pharmacology and Therapeutics: The Journal of the International Encyclopedia of Pharmacology and Therapeutics, 2013, 139(2): 249-259.
11) Banerjee, I., Tripathi, S.k., Roy, A. Efficacy of pralidoxime in organophosphorus poisoning: Revisiting the controversy in Indian setting[J]. Journal of postgraduate medicine, 2014, 60(1): 27-30.
12) Brvar, Miran, Chan, Ming Yin, Dawson, Andrew H., et al. Magnesium sulfate and calcium channel blocking drugs as antidotes for acute organophosphorus insecticide poisoning - a systematic review and meta-analysis[J]. Clinical toxicology: the official journal of the American Academy of Clinical Toxicology and European Association of Poisons Centres and Clinical Toxicologists, 2018, 56(8): 725-736.
13) Cristian Gómez-Canela, Daniel Tornero-Ca? Adas, Eva Prats, et al. Comprehensive characterization of neurochemicals in three zebrafish chemical models of human acute organophosphorus poisoning using liquid chromatography-tandem mass spectrometry[J]. Analytical and bioanalytical chemistry, 2018, 410(6):1735-1748.
14) Pang Li, Liu Junlan, Li Wei, et al. Serum ubiquitin C-terminal hydrolase L1 predicts cognitive impairment in patients with acute organophosphorus pesticide poisoning[J]. Journal of clinical laboratory analysis., 2019, 33(7).
15) N. E. Pore, K.n. Pujari, S. P. Jadkar. Oxidative Stress Markers in Patients with Organophosphorus Poisoning[J]. International Journal of Biotechnology and Biochemistry, 2018, 14(1): 59-64.
16) Hulse, Elspeth J., Haslam, James D., Emmett, Stevan R., et al. Organophosphorus nerve agent poisoning: managing the poisoned patient[J]. British journal of anaesthesia, 2019, 123(4): 457-463.
17) Dhakne, Rajesh, Mishra, Kshirod K., Kumar, Vinay, et al. Prolonged Apnea During Modified Electroconvulsive Therapy in a Patient of Suicidal Attempt by Organophosphorus Poisoning A Case Report[J]. The journal of ECT, 2016, 32(2): 136-138.
18) Masson, Patrick. Novel approaches in prophylaxis/pretreatment and treatment of organophosphorus poisoning[J]. Phosphorus, Sulfur, and Silicon and the Related Elements, 2016, 191(10/12): 1433-1443.
19) Liu, Lunzhi, Ding, Guohua. Effects of Different Blood Purification Methods on Serum Cytokine Levels and Prognosis in Patients With Acute Severe Organophosphorus Pesticide Poisoning[J]. Therapeutic apheresis and dialysis: official peer-reviewed journal of the International Society for Apheresis, the Japanese Society for Apheresis, the Japanese Society for Dialysis Therapy, 2015, 19(2): 185-190.
20) Getnet, Derese, Gautam, Aarti, Kumar, Raina, et al. Poisoning with Soman, an Organophosphorus Nerve Agent, Alters Fecal Bacterial Biota and Urine Metabolites: a Case for Novel Signatures for Asymptomatic Nerve Agent Exposure[J]. Applied and Environmental Microbiology, 2018, 84(21).
21) Wu, Xinkuan, Xie, Wei, Cheng, Yuelei, et al. Severity and prognosis of acute organophosphorus pesticide poisoning are indicated by C-reactive protein and copeptin levels and APACHE II score[J]. Experimental and therapeutic medicine, 2016, 11(3): 806-810.
22) Kranawetvogl, Andreas, Siegert, Markus, Eyer, Florian, et al. Verification of organophosphorus pesticide poisoning: Detection of phosphorylated tyrosines and a cysteine-proline disulfide-adduct from human serum albumin after intoxication with dimethoate/omethoate[J]. Toxicology Letters: An International Journal Providing a Forum for Original and Pertinent Contributions in Toxicology Research, 2018, 29911-20.

23) Scheffel, Corinna, Niessen, Karin V., Rappenglueck, Sebastian, et al. Counteracting desensitization of human alpha 7-nicotinic acetylcholine receptors with bispyridinium compounds as an approach against organophosphorus poisoning[J]. Toxicology Letters: An International Journal Providing a Forum for Original and Pertinent Contributions in Toxicology Research, 2018, 293149-156.
24) El-Ebiary, Ahmad A., Elsharkawy, Rasha E., Soliman, Nema A., et al. N-acetylcysteine in Acute Organophosphorus Pesticide Poisoning: A Randomized, Clinical Trial[J]. Basic & clinical pharmacology & toxicology., 2016, 119(2): 222-227.
25) Masson, Patrick, Nachon, Florian. Cholinesterase reactivators and bioscavengers for pre-and post-exposure treatments of organophosphorus poisoning[J]. Journal of neurochemistry., 2017, 142(S2): 26-40.

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