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Application of hemoperfusion in severe acute organophosphorus pesticide poisoning

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Background/aim: The aim of this research is to investigate the clinical efficacy of hemoperfusion in the treatment of severe acute organophosphorus pesticide poisoning (AOPP).

Materials and methods: Patients meeting the inclusion criteria were divided into Groups 1 and 2 according to whether hemoperfusion was applied or not. Group 2 was observed as the control group. Conventional therapy for AOPP was given to Groups 1 and 2. Besides conventional treatment, patients in Group 1 were also treated with hemoperfusion therapy. Cholinesterase activity and blood glucose concentration were tested before hemoperfusion and for the first 3 days afterwards. The recovery time of 50% cholinesterase was recorded. At the same time, the incidence and mortality of intermediate syndrome was observed and compared.

Results: The incidence and mortality of intermediate syndrome in Group 1 was obviously decreased, and the recovery time of cholinesterase activity was significantly shortened compared with Group 2.

Conclusion: Hemoperfusion, used for treating severe AOPP, contributes to the improvement of cholinesterase activity, low incidence and mortality of intermediate syndrome, and increase in curative rate.

Key words: Hemoperfusion, severe acute organophosphorus pesticide poisoning, cholinesterase activity

1. Introduction

Acute organophosphorus pesticide poisoning (AOPP) is a harmful condition that causes death (1). Data from the World Health Organization indicate that approximately three million people each year are at risk of organophosphorus pesticide poisoning (2). Research has shown that the major mechanism of organophosphorus pesticide poisoning is the inhibition of organic phosphorus acting on cholinesterase. This inhibition leads to a large accumulation of acetylcholine in the tissue space, which further results in a series of dysfunctions in the nervous system, myocardial cells, and respiration (3,4). Severe AOPP can cause acute cholinergic crisis, including the stimulation of nicotinic receptors and muscarinic receptors, which leads to the main cause of death, namely respiration failure (5). Muscarine can induce sympathetic excitement, stimulate the secretion of glucagon, and elevate the level of blood glucose (6). Therefore, cholinesterase activity and blood glucose concentration can be the detection index of severe AOPP.

At present, the traditional treatment for severe AOPP is intravenous injection of the anticholinergic drugs atropine and cholinesterase reactivators. Due to the short half-life, large dose, high risk of side effects, and tedious implementation, patients lack confidence in atropine therapy (7). Since the 1970s, hemoperfusion has been applied in the treatment of severe AOPP. With the help of a solid adsorbent, hemoperfusion can effectively remove toxic substances and purify blood with obvious clinical effects, which contributes to patient recovery (8). However, the clinical efficacy of hemoperfusion has received mixed reviews. This study was carried out to evaluate the clinical efficacy of hemoperfusion on severe AOPP by observing the clinical data of cholinesterase activity and toxic substance concentrations in the blood in order to provide a theoretical basis for the clinical application of hemoperfusion.

2. Materials and methods

2.1. Participants

Patients with severe AOPP admitted to our hospital from January 2011 to December 2015 were selected as participants. All patients were orally ingesting organophosphorus pesticides such as dichlorvos, dimethoate, parathion, and omethoate. Simultaneously, patients were suffering from

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dottiness or stupor, accompanied by sweating, extreme narrowing of the pupils, systemic muscle fasciculation, rales in the lungs, dyspnea, slow heartbeat, arrhythmia, decrease of blood pressure, irregular gait, and reduction of whole blood cholinesterase activity below 30%. The symptoms were in line with the criteria of severe AOPP established in the seventh edition of the guidelines of the Department of Internal Medicine. The exclusion criteria were hypertension or diabetes; allergy to equipment; and thrombocytopenia, leukopenia, other coagulopathies, or coma caused by other causes.

2.2. Grouping

Patients treated with hemoperfusion in the clinic were in the experimental group (Group 1), and an equal number of patients without hemoperfusion were in the control group (Group 2). Patients in Groups 1 and 2 were matched according to complications, admission time, age, and sex.

2.3. Methods

Patients in both Groups 1 and 2 were treated with conventional AOPP therapy. Patients removed contaminated clothes, were repeatedly given gastric lavage and indwelling gastric tubes, and took active carbon and cathartics. At the early stage of AOPP, patients were given anticholinergic drugs, cholinesterase reactivators, and comprehensive treatment including correction of acid-base imbalance, control of infection, and mechanical ventilation. On the basis of conventional treatment, patients in Group 1 were treated with hemoperfusion within 3 h of poisoning. Vascular access was established via a double-cavity central venous catheter and subclavian vein catheter. Hemoperfusion machine JF-800A and hemoperfusion apparatus HA330 (Lizhu Medical Biomaterial Co. Ltd., Zhuhai, China) were applied in the treatment of AOPP at 150–200 mL/min for 2 h. Heparin was routinely used for anticoagulation, and air was used for returning treated blood after the process. Hemoperfusion was performed once a day for 3 days.

Cholinesterase activity was detected by spectrophotometer before hemoperfusion and in the first 3 days afterwards. The recovery time of 50% cholinesterase (T50) was recorded. Blood glucose concentration was detected simultaneously. We observed the incidence and mortality of intermediate syndrome in the two groups and compared them during the treatment.

2.4. Statistical analysis

SPSS 21.0 was used to analyze the clinical data. Two-way and multilevel analyses of variance for repeated measurement data were used to analyze the measurement data (cholinesterase activity, toxic substance concentrations, and blood glucose concentration). Numerical data, such as intermediate syndrome and cases of death, were analyzed by chi-square test. There was statistical significance at $P < 0.05$. Statistical figures were drawn according to the clinical data.

3. Results

In this research, there were 130 patients in Group 1 and 130 in Group 2. There was no statistical difference in age or sex among patients in Groups 1 and 2 ($P > 0.05$), which excludes the effect of age and sex on the results of the study.

3.1. Intermediate syndrome

Intermediate syndrome is a group of syndromes with respiratory paralysis and muscle paralysis in extremities of proximal muscle and innervated muscle by cranial nerves III, IV, and X, caused by postsynaptic nerve–muscle junction dysfunction (8). In this research, there were only 5 (3.8%) cases with intermediate syndrome after hemoperfusion in Group 1. Compared to Group 2 (14, 10.7%), the incidence of intermediate syndrome in Group 1 was significantly reduced and mortality was remarkably decreased, which had a notable statistical difference ($P < 0.05$).

3.2. Cholinesterase activity

Cholinesterase activity in the two groups was restored after treatment. The detected data on cholinesterase activity showed that it had decreased on the first day but was restored quickly in the following 2 days. In the same period, the recovery of cholinesterase activity in Group 1 was much higher than that of Group 2 ($P = 0.037 < 0.05$), and the resurrection time of 50% cholinesterase in Group 1 was shorter than in Group 2, with significant differences ($P = 0.023 < 0.05$). It demonstrated that the recovery time of cholinesterase activity in Group 1 was remarkably shorter compared to Group 2. See Tables 1 and 2 and Figure 1A for detail.

3.3. Decrease of blood glucose

In the two groups, blood glucose concentration was significantly decreased after treatment compared to before treatment. Blood glucose level in the second and third days after treatment was obviously lower than that before treatment ($P < 0.05$). There was no obvious difference in the comparison between the two groups ($P > 0.05$). See Table 3 and Figure 1B for detail.

4. Discussion

It was demonstrated in the research that AOPP could immediately cause cholinergic crisis and respiratory muscle paralysis, leading to intermediate syndrome, central respiratory failure, and acute encephaledema and finally causing death. Currently, the mortality of drug treatment for AOPP is 26.2%. Especially for severe AOPP, drug treatment could result in multiple organ dysfunction syndromes, which further increase mortality (9,10).

The phosphate radical of organophosphorus compounds binds irreversibly with cholinesterase in

Table 1. Clinical data on severe AOPP.

	Group 1 (n = 130)	Group 2 (n = 130)	P
Age, years#, mean ± SD	38.5 ± 12.93	39.3 ± 11.67	0.600
Sex*, female (%)	76 (58.5)	71 (54.2)	0.488
Recovery time of 50% cholinesterase, days	5.0 ± 3.2	5.8 ± 2.4	0.023
Intermediate syndrome*, n (%)	5 (3.8)	14 (10.7)	0.033
Mortality*, n (%)	12 (9.2)	25 (19.1)	0.023

#: t-test; *: chi-square test.

Table 2. Comparison of cholinesterase activity in the two groups before and after treatment.

Groups	Before treatment	Frequency of hemoperfusion		
		First time (first day)	Second time (second day)	Third time (third day)
Group 1 (n = 130)	18.3 ± 1.9	15.5 ± 2.5	53.2 ± 5.1	76.9 ± 7.4
Group 2 (n = 130)	19.6 ± 2.0	16.6 ± 1.8	46.6 ± 5.9	71.2 ± 8.6

Variance analyses of repeated measurement data were adopted to analyze the data. Pairwise comparison between the two groups was performed by LSD method after treatment. Comparison between the two groups: $P = 0.037$; comparison in time: $P < 0.001$; interaction: $P > 0.05$. P-value among four points in time was less than 0.05 after treatment.

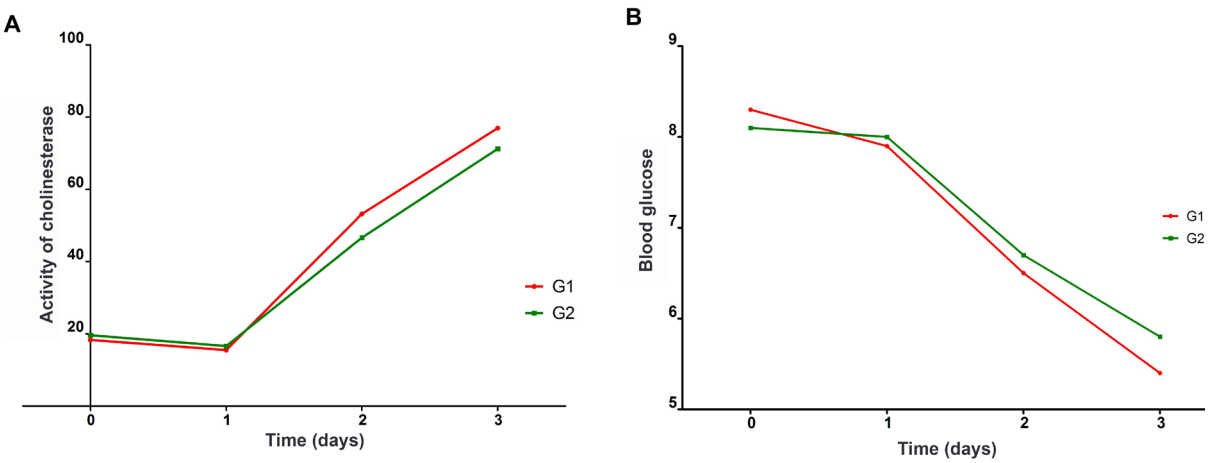

Figure 1. Blood glucose concentration and cholinesterase activity before and after hemoperfusion: A) cholinesterase activity before and after hemoperfusion; B) blood glucose concentration before and after hemoperfusion. In the figure, 0 on the horizontal axis means before hemoperfusion and 1, 2, and 3 are the first, second, and third days after hemoperfusion, respectively. The red line represents the results in Group 1. The green line represents the results in Group 2.

plasma, red blood cells, the central nervous system, and the peripheral nervous system. This decreases cholinesterase activity; results in the accumulation of a large amount of acetylcholine in the body; leads to overexpression of cholinesterase receptors in the autonomic nervous system, central nervous system, and synapses of the neuromuscular junction; and gives rise to a series of clinical symptoms. Furthermore, dyspnea can appear suddenly in patients, especially in cases of type II respiration failure, which is the main cause of death (11,12). Intermediate syndrome can appear during the recovery from cholinergic crisis for patients with moderate or severe AOPP (13). The

Table 3. Comparison of blood glucose concentration in the two groups before and after treatment.

Groups	Before treatment	Frequency of hemoperfusion		
		First time (first day)	Second time (second day)	Third time (third day)
Group 1 (n = 130)	8.3 ± 1.84	7.9 ± 2.15	6.5 ± 1.77	5.4 ± 1.76
Group 2 (n = 130)	8.1 ± 2.15	8.0 ± 1.93	6.7 ± 1.91	5.8 ± 1.67

Variance analyses of repeated measurement data were adopted to analyze data. Pairwise comparison between the two groups was performed by LSD method after treatment. Comparison between the two groups: $P = 0.621$; comparison in time: $P < 0.001$; interaction: $P > 0.05$. Comparison among four points in time adopted pairwise comparison after treatment. Comparison between pretreatment and the first day after treatment gave $P \geq 0.05$. When the data before treatment were compared to those of the second and of the third day after treatment, both P-values were less than 0.05.

main reason is postsynaptic nerve–muscle junction dysfunction, which causes myasthenia, respiratory muscle paralysis, and dyspnea, further leading to hypoxia and then bringing about disturbance of consciousness, coma, and even death. Therefore, it is vital for severe AOPP patients to have dissociative and protein- or lipid-combined toxic substances in the blood removed and recover their cholinesterase activities. At present, the main drugs for AOPP are cholinesterase reactivators (pralidoxime, pralidoxime chloride, etc.) and anticholinergic drugs (atropine). It is difficult for cholinesterase reactivators to play a role in the treatment of patients with intermediate syndrome. Due to the low permeability rate of the blood–brain barrier, cholinesterase reactivators do not have a significant effect on the treatment of symptoms caused by neurological disorders (central respiratory failure, etc.). Anticholinergics (atropine) have more side effects, such as a blurred mind, coma, and convulsions, and a significant effect on muscarinic action, while they have no alleviating effect on nicotine action (14). Hemoperfusion could remove toxic substances and purify the blood via extracorporeal circulation and solid adsorbents. The hemoperfusion apparatus in this study could not only absorb dissociative organic phosphorus in the blood but could also get rid of organic phosphorus that had combined with protein or lipids (15). It was demonstrated in the study that hemoperfusion in the treatment of severe AOPP could obviously shorten the recovery time of cholinesterase activity, significantly reduce the incidence of intermediate syndrome and mortality, and enhance cure rates.

Organic phosphorus pesticide is absorbed into the blood through the gastrointestinal tract and skin and is then excreted via the kidney. Due to residual toxic substances in patients' gastrointestinal tracts on admission, there were still some toxic substances absorbed into the blood at the early stage of treatment. Therefore, cholinesterase activity within 1 day after patients were admitted to the hospital decreased to a certain degree compared to that on admission. Cholinesterase activity of patients gradually recovered after they were treated with drugs. On the basis of drug therapy, patients in the hemoperfusion group were also treated with hemoperfusion to quickly purify their blood and eliminate toxic substances. This could reduce the successive injury to patients' bodies caused by residual toxic substances, boost the recovery of cholinesterase activity, and shorten the recovery time of cholinesterase activity. Blood glucose concentrations of patients with severe AOPP in the two groups increased, but then decreased after treatment. Nevertheless, hemoperfusion has no advantages in the treatment of blood glucose concentrations.

Hemoperfusion not only reduces the complications for patients significantly after admission and shortens hospital stays (16,17), but also decreases fees for nutrition support, postoperative management, and treatment of complications. Hemoperfusion can be implemented by the side of a bed in the hospital, which is simple, economical, and effective. Due to the significant effect on AOPP, hemoperfusion improves cure rates, reduces the pain of patients, and increases hospital income. Hemoperfusion in the treatment of AOPP is worthy of promotion in clinics.

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