Effects of hemoperfusion and hemofiltration combination on treating patients with acute organophosphours pesticide poisoning and influence of it on cholinesterase, dopamine and inflammatory factors

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1. Introduction

Acute organophosphours pesticide poisoning (AOPP) is one of the common emergencies in internal medicine¹,², especially is the severe poisoning³. Therapeutic methods of AOPP in clinical practice could not clearly removed free pesticide ingredients and cholinesterase compounds in human bodies, thus the fatality rate is high⁴. Currently, hemoperfusion (HP), hemofiltration (HF) and hemodialysis (HD) are methods to rescue AOPP⁵. Our research compared effects of HP+HF and HP+HD on AOPP patients and influences of them on cholinesterase, dopamine and inflammatory factors, to investigate the method which could minimize the fatality rate of AOPP patients.
2. Materials and methods

2.1 General materials

A total of 82 cases of AOPP patients treated in our hospital from Sep 2012 to Jul 2016 were selected as subjects. All the patients were met with diagnose standards of severe AOPP[6]. Excluded standards: (1) Patients who experienced disease longer than 24 h; (2) Patients who had history of cardiac, renal or other important organs dysfunction; (3) Patients with diabetes, lupus erythematosus or other severe systemic diseases; (4) Patients who had been administered immune stimulants within 3 months prior to admission. Our research had consents by patients and relatives. The research project was approved by discussion of ethic committee in our hospital. Patients were divided to be observation group and control group based on odd and even number sequence of medical record sheet (visiting time), 41 cases for each group. There were 22 male cases and 19 female cases in observation group, ages were ranged from 21-29 years old; There were 15 cases of metrifonate poisoning, 14 cases of methamidophos poisoning and12 cases of rogor poisoning. There were 21 male cases and 20 female cases in observation group, ages were ranged from 20-27 years old; There were 17 cases of metrifonate poisoning, 13 cases of methamidophos poisoning and 11 cases of rogor poisoning. No significant difference showed on genders, ages or poison types between two groups of patients ($P>0.05$).

2.2 Therapeutic methods

Routine therapies, such as intensive care and gastric lavage, were given to all the patients after admission. For observation group, HF and HP combined therapeutic project was utilized: AK200 Ultra hemofiltration machine, Polyflux filter in series with HA280 resin hemoperfusion apparatus were used to achieve the HF and HP combination therapy; The methods included first 2 h HF+HP treatment, then 2 h HP treatment. During the treatment, blood flow volume was 200 mL/min, blood exchange volume was 18 L. For control group, HD and HP combined therapeutic project was utilized: blood pathways were at first created. AK100 dialysis machine, polysulfone membrane hemodialyzer in series with HA280 resin hemoperfusion apparatus were used to achieve the HP and HD combination therapy; The methods included first 2 h HP+HD treatment, then 2 h HD treatment. During the treatment, standard carbonate dialysate flow was 500 mL/min, blood flow volume was 200 mL/min. Utilization of heparin for all the patients were decided by results of coagulation tests.

2.3 Observation indexes

Consciousness improving durations, durations of hospitalization and fatality rates between the two groups of patients were observed and compared.

Variations of cholinesterase (CHE), dopamine (DA) before treatment and 6 h, 12 h after treatment and inflammatory factors before and after treatment in two groups of patients were observed. (1) 3 mL cerebrospinal fluid were extracted by lumbar puncture for all the patients, detected by CHE measure kit and human DA ELISA kit separately; (2) 4 mL peripheral venous blood were extracted from all the patients with empty stomachs, and ELISA was utilized to detect serum tumor necrosis factor- $\alpha$ (TNF- $\alpha$), transforming growth factor-$\beta_1$ (TGF-$\beta_1$), interleukin-6 (IL-6) and interleukin-8 (IL-8).

2.4 Statistical process

SPSS 19.0 statistical software was used to analyze data results, quantity materials were indicated by average number $\pm$ SD. T test was utilized to compare between two groups. $\chi^2$ test was utilized for statistical analysis of enumeration data, $P<0.05$ showed that the difference had statistical significance.

3. Results

3.1 Comparison of effects between two groups of patients

Consciousness improving durations in observation group were (1.12±0.30) d, in control group were (2.36±0.47) d, which showed significant difference ($P<0.05$); Durations of hospitalization in observation group were (7.92±1.01) d, in control group were (13.76±1.73) d, which showed significant difference ($P<0.05$); Fatality rate in observation group was 9 cases (21.95%), in control group was 13 cases (31.71%), no significant difference showed ($P>0.05$).

3.2 Variations of CHE, DA levels in cerebrospinal fluids of two groups of patients

Before treatment, no significant difference showed in CHE, DA levels between two groups of patients ($P>0.05$); 6 h and 12 h after treatment, CHE levels in both the two groups were significantly higher than the same group before treatment ($P<0.01$), and levels in observation group at the same phase were significantly higher than in control group ($P<0.05$, $P<0.01$); 6 h and 12 h after treatment, DA levels in observation group were significantly lower than the same group before treatment ($P<0.01$), and were significantly lower than in control group ($P<0.01$), while only DA levels in control group 12 h after treatment were significantly lower than the same group before.
Note: Compared with the same group before treatment, $P<0.05$, $\alpha P<0.01$; Compared between two groups at the same phase, $P<0.05$, $\alpha P<0.01$.

Table 1

Variations of CHE and DA levels in two groups before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>CHE (U/L)</th>
<th>DA (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>41</td>
<td>Before treatment</td>
<td>543.16±29.95</td>
<td>27.61±3.70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 h after treatment</td>
<td>1,534.4±87.23**</td>
<td>14.61±3.08**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 h after treatment</td>
<td>1,093.71±99.70**</td>
<td>13.02±2.27**</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>Before treatment</td>
<td>547.27±31.03</td>
<td>27.43±4.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 h after treatment</td>
<td>893.05±59.62**</td>
<td>21.01±3.94**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12 h after treatment</td>
<td>1,215.08±103.72**</td>
<td>18.34±2.76**</td>
</tr>
</tbody>
</table>

Note: Compared with the same group before treatment, $P<0.05$, $\alpha P<0.01$; Compared between two groups at the same phase, $P<0.05$, $\alpha P<0.01$.

Table 2

Comparison of serum inflammatory factors levels in two groups (ng/L).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>TGF- $\beta$ 1</th>
<th>TNF- $\alpha$</th>
<th>IL-6</th>
<th>IL-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>41</td>
<td>Before treatment</td>
<td>3,287.70±109.42</td>
<td>79.24±9.81</td>
<td>151.35±41.57</td>
<td>76.93±10.17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>742.56±59.83**</td>
<td>40.53±5.62**</td>
<td>68.12±9.09*</td>
<td>40.21±7.53**</td>
</tr>
<tr>
<td>Control</td>
<td>41</td>
<td>Before treatment</td>
<td>3,254.33±115.06</td>
<td>78.77±10.01</td>
<td>155.60±37.83</td>
<td>78.54±9.58</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>978.50±64.35**</td>
<td>53.38±8.90**</td>
<td>91.67±11.06*</td>
<td>57.32±8.40**</td>
</tr>
</tbody>
</table>

Note: Compared with the same group before treatment, $P<0.05$, $\alpha P<0.01$; Compared between two groups at the same phase, $P<0.05$.

3.3 Variations of serum inflammatory factors in two groups of patients

Before treatment, no significant difference showed on serum TGF- $\beta$1, TNF- $\alpha$, IL-6, IL-8 between two groups of patients ($P>0.05$). After treatment, serum TGF- $\beta$1, TNF- $\alpha$, IL-6, IL-8 levels in both the two groups of patients were significantly decreased comparing with the same group before treatment, significant difference existed ($P<0.05$ or $P<0.01$); In observation group, GF- $\beta$1, TNF- $\alpha$, IL-6, IL-8 levels were (742.56±59.83) ng/L, (40.53±5.62) ng/L, (68.12±9.09) ng/L, (40.21±7.53) ng/L, which were significantly lower than in control group ($P<0.05$). See table 2.

4. Discussion

Organophosphorus pesticides (OPPs) poisoning is a common pesticide poisoning in our country. It could enter bodies through respiratory tract, alimentary tract or skin contact to induce AOPP[7]. The OPPs poisoning mechanism is to mainly suppress CHE activity[8,9]. Acetyl choline could be accumulated since it could not be effectively decomposed, thus effects of continuous impulse and failure after excitation of nervous system could be induced. Even death could be induced in some serious cases[10]. OPPs is a neurotropic toxic pesticide. The toxic symptoms would be appeared after absorption for about 10 min by alimentary tract. Therefore, timely rescue is crucial for AOPP patients. Currently, AOPP therapeutic methods mainly were anticholinergic drugs administration, supportive therapies, etc. They could not radically eliminate free OPPs ingredients and CHE compounds. The fatality rate is still high[11]. Our research compared effects of two therapeutic methods, HP+HF and HP+HD, on treating AOPP patients, in order to get the methods to enhance successful rate of AOPP rescue, and to minimize fatality rate.

The strong adhesive function of HP to macromolecular resin was received widely utilization on clinic. It could effectively eliminate lipid soluble OPPs and organophosphorus CHE compounds, and eliminate respiratory muscles paralysis. However, some disadvantages still exist, for instance, HP could not completely eliminate toxins, and symptoms would be aggravated after therapy discontinued. Therefore, therapeutic effects could not be good enough by when using HP alone[12,13]. Theory of HF is to use pressure difference generated by outside, body self or pumps, filter out solute, liquid and replenish electrolyte by filter, thus to achieve blood purification. HD is aim to clear away micromolecule soluble toxins in blood. It has a certain supplement for HP. Our research compared therapeutic effects of HP+HF and HP+HD on AOPP and found that, consciousness improving durations and hospitalized durations in observation group were significantly shorter than in control group ($P<0.05$), while no significant difference showed on fatality rates between two groups ($P>0.05$). Possible reason might be that the eliminate effects of HP+HF on toxins were better than HP+HD, but no big difference showed on damage to bodies between the two methods, and no difference showed on the generated complications. Hence, compared with HP+HD, patients who received HP+HF treatment showed shorter consciousness improving durations and hospitalized durations. While no significant difference showed on fatality rates between the two groups.

Activity of serum CHE is a special index to diagnose AOPP. It could reflect the severity of poisoning, therapeutic effects and prognosis in the patients[14-16]. Our research found that two therapeutic methods were significantly enhanced activity of CHE...
(P<0.05, P<0.01), but HP+HF showed a more significant influence. After treatment, CHE were significantly increased, which showed diminish of poisoning degree. It was in accordance with previous researches[15]. DA is an important monoamine neurotransmitter. It could regulate emotions and mental activities. And it is closely related with schizophrenial[17]. AOPP patients could experience abnormal mental symptoms. In that way, were metabolic changes of DA levels appeared in AOPP patients induced mental abnormal? Two therapeutic methods in our research were both significantly diminish DA levels (P<0.05, P<0.01). Influence of HP+HF was more significant. Yuan HJ, etc.[18] found that the increased of DA levels in AOPP patients might be related with the appearance of mental abnormal. In addition, an animal experiment found that rats with AOPP who experienced memory or other disorders were along with increase of DA levels[19]. Based on conclusions from previous researches, the significant decrease of DA levels in our research indicated that the mental abnormal symptoms were also weakened. However, it needs further verification.

TGF-β1, TNF-α, IL-6 and IL-8 play important roles on appearance and development of multiple organ dysfunction syndrome (MODS) induced by AOPP[20,21]. Our research found that, the filter effects of HP+HF on serum inflammatory factors were better than HP+HD. The possible reason might be the absorption of HF to inflammatory factors could achieve better eliminate effects than HD micromolecule filtration. Both of the two blood purification therapeutic methods could improve internal environment, suppress MODS appearance. Only HP+HF showed more significant functions.

Above all, effects of blood purification therapeutic methods on treating AOPP were for sure. However, effects of HP and HF combination were more significant. Furthermore, the improvement of HP+HF for CHE, DA and inflammatory factors were better than HP+HD.

References