The effect on immune function and inflammatory factors of adjuvant antibiotic therapy through Xuebijing combined with thymopentin in elderly patients with severe pneumonia

Yi-Ya Jiang, Tie-Feng Qiu, Zhi-Fang Zhuang

Respiration Medicine of Changzhou Wujin People’s Hospital, Changzhou Jiangsu 213000

ARTICLE INFO

Objective: To investigate the effect on immune function and inflammatory factors of adjuvant antibiotic therapy through Xuebijing combined with thymopentin in elderly patients with severe pneumonia. Methods: Divided 100 cases of elderly patients with severe pneumonia into the observation group and the treatment group according to the order of serial number. Fifty patients in each group. Gave control group severe pneumonia conventional treatment, such as mechanical ventilation, antifebrile, removing phlegm and anti-infection, and gave Xuebijing by intravenous drop simultaneously; observation group was given Xuebijing combined with thymopentin by intravenous drop on the base of conventional treatment. Then compared the T lymphocyte subpopulation and serum inflammatory factors level including CRP, IL-6, IL-1 and TNF-α of two groups before treatment and 7 d, 14 d of treatment respectively. Result: (1) There was significant difference in the level of CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ in this two groups at different time points, and that the level of CD3⁺, CD4⁺, CD4⁺/CD8⁺: T2 > T1 > T0, CD8⁺ level: T2 < T1 < T0; The increasing range of CD3⁺, CD4⁺, CD4⁺/CD8⁺ level and the decreasing range of CD8⁺ in the observation group were larger than that in the control group, there was statistical significant difference. (2) The level of serum inflammatory factors CRP, IL-6, IL-1, TNF-α in two groups at different time points were statistical significant difference, all the CRP, IL-6, IL-1 and TNF-α level were T2 < T1 < T0, presenting a downward trend; The descending range of serum CRP, IL-6, IL-1, TNF-α level in the observation was larger compared with the control group, there was significant difference. Conclusion: The adjuvant antibiotic therapy through Xuebijing combined with thymopentin in elderly patients with severe pneumonia could improve the immune function and lower the inflammatory factors level.

1. Introduction

Severe pneumonia (SP) is the common respiration system critical illness in the elderly population, due to the fast progress of disease and the various complication, its mortality was as high as 15%-30% in literature reports[1]. The clinical researches showed that inflammatory factors released largely after SP attack and inhibited the body immunity at a certain extent. It had an important influence on the prognosis of this disease. Recently, the treatment of SP has made some advances along with the reasonable application of antibiotics and a part of studies have demonstrated that Xuebijing had good effect on the treatment of severe infective diseases[2]. As a new type of immunomodulatory drug, thymopentin can improve the immune function of the patients who suffered chemotherapy and infection[3]. However, the combined application research of Xuebijing with thymopentin still was rare. This adjuvant antibiotic therapy through Xuebijing combined with thymopentin in elderly patients with severe pneumonia has achieved excellent effect. The report was following:
2. Clinical data and method

2.1 Clinical data

Selected one hundred cases of elderly SP patients from June 2015 to December 2016 in the respiration medicine of hospital according to the consecutive grouping and randomly divided them into observation group and control group, 50 cases in each group, according to serial number of they went into group. Observation group: 30 males, 20 females, aged from 61 to 72 years with an average (66.18±4.36) years, course of disease 3-8 d with average (5.38±1.79) d, 15 cases of type I respiratory failure, 35 cases of type II respiratory failure, complication including 6 cases of diabetes and 7 cases of hypertensive disease; Control group: 31 males, 19 females, aged from 61 to 75 years with an average (66.39±4.55) years, course of disease 3-10 d with average (5.25±1.75) d, 16 cases of type I respiratory failure, 34 cases of type II respiratory failure, complication including 5 cases of diabetes and 8 cases of hypertensive disease; Control group: 31 males, 19 females, aged from 61 to 75 years with an average (66.39±4.55) years, course of disease 3-10 d with average (5.38±1.79) d, 15 cases of type I respiratory failure, 35 cases of type II respiratory failure, complication including 6 cases of diabetes and 7 cases of hypertensive disease. The clinical baseline data of patients in two groups was no statistical significant (P>0.05), with comparability. The ethics committee and respiratory disease panel have approved this research.

2.2. Incorporation and exclusion criteria

Incorporation criteria: (1) Clinical symptoms, signs, laboratory inspection conformed to 《The diagnostic criteria for severe pneumonia》 published by American Thoracic Society (ATS) in 2001[4], for example, inflammation enlarged over 50% after 48 h of hospitalization, needing mechanical ventilation, respiratory rates>30 times/min and so on; (2) Age ≥ 60 years; (3) Clinical data and laboratory inspection indexes were intact; Exclusion criteria: (1) Patients with combined malignant tumor, the other parts infection, pulmonary embolism, pulmonary tuberculosis, connective tissue disease, severe cardio-cerebro-vascular diseases; (2) Patients who were dead or complicated by other diseases in the period of research; (3) Hepatic and renal dysfunction; (4) The patients who have contraindications to Xuebijing combined with thymopentin.

2.3. Treatment methods

Gave all patients of two group comprehensive treatment including oxygen inhalation, hypothermia, anti-shock, anti-arrhythmia, diuresis and nutritional support when they were in hospital. Gave mechanical ventilation in time, such as gas hood ventilation, tracheotomy and nutritional support when they were in hospital. Gave all patients of two group comprehensive treatment including oxygen inhalation, hypothermia, anti-shock, anti-arrhythmia, diuresis and nutritional support when they were in hospital. Gave mechanical ventilation in time, such as gas hood ventilation, tracheotomy and nutritional support when they were in hospital. Gave all patients of two group comprehensive treatment including oxygen inhalation, hypothermia, anti-shock, anti-arrhythmia, diuresis and nutritional support when they were in hospital. Gave mechanical ventilation in time, such as gas hood ventilation, tracheotomy and nutritional support when they were in hospital. Gave all patients of two group comprehensive treatment including oxygen inhalation, hypothermia, anti-shock, anti-arrhythmia, diuresis and nutritional support when they were in hospital. Gave mechanical ventilation in time, such as gas hood ventilation, tracheotomy and nutritional support when they were in hospital. Gave all patients of two group comprehensive treatment including oxygen inhalation, hypothermia, anti-shock, anti-arrhythmia, diuresis and nutritional support when they were in hospital. Gave mechanical ventilation in time, such as gas hood ventilation, tracheotomy and nutritional support when they were in hospital. Gave all patients of two group comprehensive treatment including oxygen inhalation, hypothermia, anti-shock, anti-arrhythmia, diuresis and nutritional support when they were in hospital. Gave mechanical ventilation in time, such as gas hood ventilation, tracheotomy and nutritional support when they were in hospital.

2.4. Observation indexes

(1) Observed the level of T lymphocyte subgroup when the patients before treatment (T0), after 7 d of treatment (T1), after 14 d of treatment (T2) in two groups and applied DxFLEX type Flow cytometry of Beckman to detect. (2) Serum inflammatory factors levels after T0, T1, T2 of two groups were observed and the specific indexes including: C-reaction protein (CRP), Interleukin 6 (IL-6), Interleukin 1 (IL-1) and tumor necrosis factors- α (TNF- α). The immunodiffusion was used for CRP detection, IL-6, IL-1 and TNF- α were measured by enzyme linked immunosorbent assay.

2.5 Statistical methods

Using medical statistical software SPSS19.0 for statistical analysis. All the measurement data was showed by (x±s). If the data obeyed normal distribution, would adopt the single factor repeat measurement for analysis of variance and t-test. If not, would adopt revised non-parametric test, P<0.05 was defined as statistical significant difference.

3. Results

3.1 Comparison of T lymphocyte subgroup level at T0, T1, T2 between two groups

The difference of CD3+, CD4+, CD8+, CD4/CD8+ levels in two groups were statistical significant (CD3+ Fgroup=10.726, CD4+ Fgroup=8.482, CD8+ F group=7.268, CD4+/CD8+ F group=6.325, P<0.05). The CD3+, CD4+, CD8+, CD4/CD8+ levels at different time points were significant difference (CD3+ Ftime=11.006, CD4+ Ftime=9.164, CD8+ Ftime=8.115, CD4/CD8+ Ftime=7.092, P<0.05). And that, CD3+, CD4+, CD4/CD8+ levels: T2>T1, CD8+ level: T2<T1, CD8+ levels: T2>T1, CD8+ level: T2<T1, CD8+ levels: T2>T1, CD8+ level: T2<T1, CD8+ levels: T2>T1, CD8+ level: T2<T1, CD8+ levels: T2>T1, CD8+ level: T2<T1. The increasing range of CD3+, CD4+, CD4/CD8+ level and the decreasing range of CD8+ level in observation group were larger than in the control group (CD3+Finteraction =11.879, CD4+ F interaction=8.442, CD8+ F interaction=7.163, CD4+/CD8+ F interaction =6.008, P<0.05), see table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>Indexes</th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
</tr>
</thead>
<tbody>
<tr>
<td>The observation group (n=50)</td>
<td>CD3+ (%)</td>
<td>50.12±6.22</td>
<td>53.61±6.72</td>
<td>57.29±6.91</td>
</tr>
<tr>
<td></td>
<td>CD4+ (%)</td>
<td>34.22±5.38</td>
<td>35.15±5.05</td>
<td>36.75±6.17</td>
</tr>
<tr>
<td></td>
<td>CD8+ (%)</td>
<td>21.09±2.41</td>
<td>19.17±3.29</td>
<td>17.76±3.15</td>
</tr>
<tr>
<td></td>
<td>CD4/CD8+</td>
<td>1.68±0.24</td>
<td>1.88±0.17</td>
<td>1.98±0.23</td>
</tr>
<tr>
<td>The control group (n=50)</td>
<td>CD3+ (%)</td>
<td>50.46±6.74</td>
<td>51.92±6.33</td>
<td>55.22±6.56</td>
</tr>
<tr>
<td></td>
<td>CD4+ (%)</td>
<td>34.51±5.35</td>
<td>33.87±5.23</td>
<td>35.14±5.33</td>
</tr>
<tr>
<td></td>
<td>CD8+ (%)</td>
<td>21.17±2.62</td>
<td>20.68±3.02</td>
<td>19.09±2.97</td>
</tr>
<tr>
<td></td>
<td>CD4/CD8+</td>
<td>1.71±0.23</td>
<td>1.78±0.17</td>
<td>1.88±0.19</td>
</tr>
</tbody>
</table>

Note: compared with the control group: P<0.05.
Table 2.
Comparison of serum inflammatory factors level after T0, T1, T2 between two groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>CRP (mg/L)</th>
<th>IL-6 (pg/mL)</th>
<th>IL-1 (pg/mL)</th>
<th>TNF-α (ng/mL)</th>
<th>CRP (mg/L)</th>
<th>IL-6 (pg/mL)</th>
<th>IL-1 (pg/mL)</th>
<th>TNF-α (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The observation group (n=50)</td>
<td>102.35±25.63</td>
<td>213.84±41.28</td>
<td>176.93±39.67</td>
<td>228.62±46.87</td>
<td>107.06±31.06</td>
<td>211.85±42.31</td>
<td>180.06±40.11</td>
<td>231.02±45.49</td>
</tr>
<tr>
<td>The control group (n=50)</td>
<td>81.44±19.67</td>
<td>175.67±35.09</td>
<td>144.08±31.44</td>
<td>182.37±39.82</td>
<td>90.44±22.79</td>
<td>188.09±38.72</td>
<td>162.17±33.47</td>
<td>191.08±40.32</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>102.35±25.63</td>
<td>213.84±41.28</td>
<td>176.93±39.67</td>
<td>228.62±46.87</td>
<td>107.06±31.06</td>
<td>211.85±42.31</td>
<td>180.06±40.11</td>
<td>231.02±45.49</td>
</tr>
</tbody>
</table>

Note: compared with the control group: P<0.05.

3.2 Comparison of serum inflammatory factors level after T0, T1, T2 between two groups

There was significant difference in serum inflammatory factors CRP, IL-6, IL-1, TNF-α levels between two groups (CRP group=22.638, IL-6F group=37.118, IL-1F group=35.065, TNF-α F group=41.772, P<0.05). Serum inflammatory factors CRP, IL-6, IL-1, TNF-α level at different time points were statistical significant difference (CRP time=34.286, IL-6F time=45.773, IL-1F time=42.728, TNF-α F time=55.083, P<0.05). All the serum inflammatory factors CRP, IL-6, IL-1, TNF-α level were T2<T1<T0, showing a decreased trend; The decreased range of serum inflammatory factors CRP, IL-6, IL-1, TNF-α in the observation group was outstandingly larger than the control group (CRP interaction =35.452, IL-6F interaction =40.771, IL-1F interaction =42.182, TNF-α F interaction =50.773, P<0.05), see table 2.

4. Discussion

SP not only led to injury of lungs or respiratory failure, but also usually induced the multi-organ deficiency syndrome (MODS), especially in the elderly patients, mortality was high[5,6]. The international and domestic clinical researches revealed that SP could induce neutrophile granulocyte, macrophage, endothelial cells and NK cells release much of inflammatory factors, such as CRP, IL-1, IL-6, TNF-α, it would injury body cells severely and result in “cascade of inflammation reaction” and heavy unbalance of “pro-inflammatory–anti-inflammatory” cytokines[7,8]. At the same time, all of these reactions could damage body immune system function seriously, the ratio of CD3+, CD4+ cells that represents lymphocyte-mediated immunity and assists T lymphocyte to execute the immune function decreased, and the proportion of CD8+ cells that was cytotoxic increased, CD4+/CD8+ declined, distribution of T lymphocyte subgroup was out-of-balance[9,10].

Xuebijing was a Chinese materia medica preparation that applied to clinic recently, the main ingredient was extract of Traditional Chinese medicinal materials including Flos carthami, Red peony root, Rhizoma Chuanxiong, Red-rooted salvia and Angelica sinensis. It could promote blood circulation to remove blood stasis, dredge the channel and make toxin factors collapsed. Xuebijing possessed anti-endotoxin effect and inhibited the endogenous inflammatory medium uncontrolled release that infected and caused systemic inflammatory response syndrome[11,12]. Chinese Lv Shi[13] reported that Xuebijing could improve body microcirculation and organ perfusion, inhibit platelet aggregation and sharpened inflammatory factors of septicopyemia, correct anoxia and ischemia condition, improve immune function level. Results of this study demonstrated that trend of inflammatory factors CRP, IL-1, IL-6, TNF-α dropped totally and the trend of distribution of T-lymphocyte subpopulation was improved.

For the past few years, thymopentin was an immune-enhanced preparation that applied to patients who were in perioperative period, serious infected and chemotherapy[12], Domestic researcher, Li Hailong et al used thymopentin for severe pneumonia and results displayed that the method could lower CRP level, enhance the level of IgG, IgM, IgA and possess favorable benefit of improving immune function. Through T lymphocyte distributed condition of patients who were adjuvant antibiotics by Xuebijing combined with thymopentin, found that increasing range of CD3+, CD4+, CD4+/CD8+ and decreasing range of CD8+ after one week and two weeks of treatment was higher than the patients who were treated with adjuvant antibiotics only by Xuebijing. It revealed that thymopentin was good for improving balance of T lymphocyte distribution and enhancing body immunity from this discovery. It showed that the falling range of CRP, IL-1, IL-6 and TNF-α of patients who were treated with thymopentin was remarkable after one and two weeks of treatment respectively through furtherly observing change of serum inflammatory factors level, reflected that thymopentin contributed to ameliorate the inflammation of elderly patients with SP.

Through analyzing the reasons, found that, on the one hand, thymopentin that consist of various body essential amino-acids can mediate the T lymphocyte differentiation, induce intracellular reactions, enhance phagocytic function of macrophage and improve the body immunity through combining with T lymphocyte.
receptors in peripheral blood and aggrandize cAMP level[15,16]. On the other hand, thymopentin also can enhance phagocytic function of macrophage and extend the lifetime of T-cells[17]. In zoological experiment, Lan Zhiwei et al proved that thymopentin could effectively advance the ratio of CD3<sup>+</sup>, CD4<sup>+</sup> cells in rat with liver cancer, perfect immune microenvironment of rat with cancer, furthermore they considered that thymopentin could promote differentiation and maturation of T-cells.

In conclusion, Xuebijing and thymopentin were able to improve body immunity through different mechanism, decrease inflammatory reaction. The effect on promoting the distribution of T-cells balanced and lowering inflammatory factors level was better through combined application of this two to assist antibiotics for treating elderly patients with SP, therefore, it was worthy of clinical application.

Reference


