Effects of Yiqi Gu Ben Decoction combined with DC chemotherapy on serum tumor markers, inflammatory factors and immune function in patients with locally advanced non–small cell lung cancer

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ABSTRACT

Objective: To investigate the effects of Yiqi Gu decoction combined with DC chemotherapy on serum tumor markers, inflammatory factors and immune function in patients with locally advanced non-small cell lung cancer. Methods: A total of 95 patients with locally advanced non-small cell lung cancer were selected as the research objects, according to the random data table they were divided into control group (n=48) and observation group (n=47), patients in the control group were given DC chemotherapy, on the basis of this treatment, the patients in the observation group were given Yiqi Gu decoction treatment, Comparison of the levels of serum tumor markers [antigen (CEA) and carbohydrate antigen 19-9 (CA19-9)], inflammatory factor [C reactive protein (CRP) and tumor necrosis factor-α (TNF-α)] and immune function [CD3+, CD4+, CD8+, CD4+/CD8+].

Results: Before treatment, there were no significant difference in the levels of CEA, CA19-9, CRP, TNF-α, CD8+ between the two groups; After treatment, the CEA, CA19-9, CRP, TNF-α, CD8+ levels of two groups were significantly lower than those in the same group before treatment, and the decreased range in observation group was significantly higher than the control group, moreover the levels after treatment were obviously lower than control group; After treatment, the levels of CD3+, CD4+, CD4+/CD8+ in the observation group were (64.72±5.25)%, (39.51±5.14)% and (1.35±0.27), which were significantly higher than the same group before treatment, and significantly higher than the control group [(58.57±5.09)%, (31.34±5.06)%, (1.14±0.33)], differences were statistically significant.

Conclusion: DC chemotherapy combined with Yiqi Gu Ben Decoction in the treatment of locally advanced non-small cell lung cancer, can effectively reduce the serum tumor marker levels, decrease inflammatory stress, improve immune function, has an important clinical value.

1. Introduction

In China, the incidence and mortality of lung cancer occupy the top of malignant tumors, of which non-small cell lung cancer is the most common tissue type, accounting for more than 80%[1,2]. Early symptoms of lung cancer are more hidden, nearly 70% of patients diagnosed in the advanced stage, synchronous chemotherapy became the standard treatment of advanced lung cancer in the world[3]. DC chemotherapy is a more commonly used clinical treatment, but with the use of chemotherapy drugs, adverse drug reactions also increase, seriously affecting the quality of life of patients and the efficacy of treatment[4]. The study pointed out that the combination of traditional Chinese medicine on the basis of chemotherapy can effectively prolong the survival of patients and improve life quality of patients[5]. The purpose of this study was to investigate the clinical effects of Yiqi Gu Ben Decoction assisted DC chemotherapy.
2. Data and methods

2.1 Clinical data

A total of 95 patients with locally advanced non-small cell lung cancer admitted to Zhangbei Hospital of Traditional Chinese Medicine from February 2015 to April 2017 were enrolled in this study. All patients met the diagnostic criteria of non-small cell lung cancer[6], diagnosed by imaging and pathological examination, K-mofsky (KPS) score 60 points. 95 cases of patients were divided into control group (48 cases) and observation group (47 cases) according to random data table method. In the control group 31 males and 17 females, aged from 39 to 75 years old; cancer type: squamous cell carcinoma 24 cases, adenocarcinoma 17 cases, adenosquamous carcinoma 6 cases, large cell carcinoma 1 case; TNM staging: stage III 21 cases, stage IIb 18 cases, stage IV 9 cases. In the observation group 29 males and 18 females, aged 40-75 years old. cancer type: 25 cases of squamous cell carcinoma, 16 cases of adenocarcinoma, 5 cases of adenosquamous carcinoma and 1 case of large cell carcinoma. TNM stage: stage III 20 cases, stage IIb 17 cases, stage IV 10 cases. Exclusion: (1) with severe liver and kidney and hematopoietic disorders and other functional disorders; (2) pregnant women, patients with mental illness; (3) allergy to research drug; (4) poor compliance, failed to complete the treatment as required and the cases of self-shedding in the midway; (5) not cooperate with the treatment, and incomplete clinical information. There was no significant difference in clinical data between the two groups (P>0.05). Research content and processes follow the relevant standards of the hospital ethics committee.

2.2 Treatment method

Patients in the control group received DC chemotherapy (docetaxel combines with cisplatin): given dexamethasone tablets treatment (produced by Guangdong Sancai Shiqi pharmaceutical Co., Ltd., batch number 20141102, specification 0.75 mg 100 s ) (continuous treatment for 3 d) before 1 d of docetaxel treatment, the day of medication and after 1 d of docetaxel treatment, take orally 0.75 mg/time, once a day; 75 mg/m² of docetaxel (produced by Zhejiang Haizheng Pharmaceutical Co., Ltd., approval number H20093092, specification 0.5 mL: 20 mg/s) was added in 250 mL of 0.9% sodium chloride injection, infusion after fully mixing, the time did not exceed 1 h; cisplatin (produced by Qilu Pharmaceutical Co., Ltd., batch number 20150409) drip infusion treatment (75 mg/mL diluted in 5% dextrose solution) for more than 2 h; hydration, diuresis and antiemetic medications were also given to patients during treatment. 21 d as a chemotherapy period, after stopping medication for 1 week, started the next period of treatment, at least 2 periods of treatment.

On the basis of the DC chemotherapy in the control group, the observation group was treated with Yiqi Guben decoction. The full prescription consisted of 30 g of Astragalus root, 25 g of Radix Codonopsis pilosulae, 6 g of Radix Glycyrrhiza, Atractylodes, Houttuynia, Radix Ophiopogonis and Radix Hedyotis diffusa respectively 15 g, Yam, Poria, Rehmannia, Angelica, Cortex Moutan and mulberry each 12 g, once a day, decoction and took in the morning and evening twice. Treatment time was same with the control group.

2.3 Index test

Before treatment and after 2 period of treatment, fasting peripheral venous blood was extracted from both groups and centrifuged to detect serum. The indicators included: (1) tumor markers: carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9), respectively using the electrochemical luminescence (instrument was the electrochemical luminescence apparatus) and the ELISA method for detection, detection kits were purchased from Shanghai Meilian Bio-technology company; (2) Inflammatory factors: C-reactive protein (CRP) and tumor necrosis factor-α (TNF-α) were detected by ELISA and CRP/TNF-α ELISA kits were purchased from Shanghai Meilian Bio-technology company; (3) Immune function: CD3⁺, CD4⁺, CD8⁺, CD4⁺/CD8⁺ levels were detected by Beckman Coulter automatic biochemical analyzer; all the above operations were strictly with the instructions.

2.4 Statistical analysis

SPSS 7.0 statistical software was used to analyze the original data obtained from the study. The levels of tumor markers, inflammatory factors and immune function in the study were all in accordance with the normal distribution through validation, presenting by Mean SD. t test were used to comparison of intergroup and intragroup levels, the difference was statistically significant presented by P<0.05.

3. Results

3.1 Comparison of tumor markers before and after treatment

There was no significant difference in CEA and CA19-9 levels between the two groups before treatment (P>0.05). The levels of CEA and CA19-9 in the control group after treatment were (12.73±2.78) ng/mL and (37.53 ± 8.03) U/mL respectively, which were significantly lower than those before treatment in the same group (P<0.05); Levels in observation group were respectively (6.94±1.53) ng/mL and (15.63 ±3.72) U/mL respectively, which were significantly lower than those before treatment in the same group (P<0.05).


± 1.69) ng/mL and (24.32 ± 6.43) U/mL, which were significantly lower than before treatment in the same group, moreover obviously lower than those of the control group after treatment \((P<0.05)\). As shown in Table 1.

Table 1.

Comparison of tumor markers level before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>CEA (ng/mL)</th>
<th>CA19-9 (U/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>48</td>
<td>Before treatment</td>
<td>25.98±5.05</td>
<td>65.15±14.38</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>12.73±2.78*</td>
<td>37.53±8.03*</td>
</tr>
<tr>
<td>Observation</td>
<td>47</td>
<td>Before treatment</td>
<td>26.24±7.05</td>
<td>65.41±14.54</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td>After treatment</td>
<td>6.94±1.69*</td>
<td>24.32±6.43*</td>
</tr>
</tbody>
</table>

Note: compared with before treatment \(^p<0.05\), compared with control group after treatment \(^p<0.05\).

3.2 Comparison of inflammatory factor levels before and after treatment.

There was no significant difference in CRP and TNF-\(\alpha\) levels between the two groups before treatment \((P>0.05)\). The levels of CRP and TNF-\(\alpha\) in the control group after treatment were \((13.32 ± 3.94)\) mg/L and \((19.46 ± 4.63)\) ng/L respectively, which were significantly lower than those before treatment in the control group \((P<0.05)\), the difference was significant \((P<0.05)\), levels in observation group were \((11.25 ± 2.51)\) mg/L and \((12.42 ± 3.49)\) ng/L respectively, which were significantly lower than those before treatment in the same group and significantly lower than those in control group after treatment \((P<0.05)\). As shown in Table 2.

Table 2.

Comparison of inflammatory factor levels before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>CRP (mg/L)</th>
<th>TNF-(\alpha) (ng/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>48</td>
<td>Before treatment</td>
<td>15.19±3.61</td>
<td>23.27±5.79</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>13.32±3.94*</td>
<td>19.46±6.63*</td>
</tr>
<tr>
<td>Observation</td>
<td>47</td>
<td>Before treatment</td>
<td>17.55±3.86</td>
<td>23.53±5.29</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td>After treatment</td>
<td>11.25±2.51*</td>
<td>12.42±3.49*</td>
</tr>
</tbody>
</table>

Note: compared with before treatment \(^p<0.05\), compared with control group after treatment \(^p<0.05\).

3.3 Comparison of immune function before and after treatment.

There was no significant difference between the two groups before treatment \((P>0.05)\). Compared with before treatment in the group, the levels of CD3\(^+\), CD4\(^+\), CD4\(^+\)/CD8\(^+\) in the control group and the observation group after treatment were significantly higher than those in the control group \((58.57 ± 5.09)%\), \((31.34 ± 5.06)%\), \((1.14 ± 0.33)\), \((64.72 ± 5.25)\)%, \((39.51 ± 5.14)%\) and \((1.35 ± 0.27)\) in the observation group were significantly higher than those in the control group \((P<0.05)\). After treatment, the level of CD8\(^+\) in the observation group was \((26.42 ± 4.07)\) which was significantly lower than that of the same group before treatment and lower than level in the control group after treatment \((30.91±3.94)%\), the difference was statistically significant \((P<0.05)\). As shown in Table 3.

Table 3.

Comparison of immune function before and after treatment.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Treatment time</th>
<th>CD3(^+) (%)</th>
<th>CD4(^+) (%)</th>
<th>CD4(^+)/CD8(^+) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>48</td>
<td>Before treatment</td>
<td>54.38±4.86</td>
<td>26.85±4.31</td>
<td>33.58±5.23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>58.57±5.09*</td>
<td>31.34±5.06*</td>
<td>30.91±3.94*</td>
</tr>
<tr>
<td>Observation</td>
<td>47</td>
<td>Before treatment</td>
<td>24.27±4.84</td>
<td>27.03±4.33</td>
<td>33.67±5.48</td>
</tr>
<tr>
<td>group</td>
<td></td>
<td>After treatment</td>
<td>64.72±5.25*</td>
<td>39.51±5.14*</td>
<td>26.42±4.07*</td>
</tr>
</tbody>
</table>

Note: compared with before treatment \(^p<0.05\), compared with control group after treatment \(^p<0.05\).

4. Discussion

Lung cancer is the malignant tumor that causes most incidence and death in the world, epidemiological studies have pointed out that the incidence showed an upward trend year by year, and tend to be younger, can attack in all ages, seriously threatening human life[7,8]. Surgical treatment is important program for non-small cell lung, but because most patients already were in advanced stage, cannot treat with operation, and coupled with most patients still existed recurrence and metastasis risk after treatment, therefore, chemotherapy is key to locally advanced non-small cell lung cancer[9,10]. However, due to the emergence of adverse drug reactions, seriously affecting the quality of life of patients, therefore, the overall effect was still not satisfactory, to be further improved. The motherland medicine believes that lung cancer belongs to the categories of "lung accumulation", "hemoptysis" and "obstruction". The main causes are the deficiency of righteousness, the invasion of lungs and the accumulation of sputum and silt, of which phlegm is its basic pathogenesis, meanwhile also the main pathological changes of lung cancer, Chinese medicine mainly treated through nourishing the blood, nourishing the liver and kidney and spleen and stomach, aiming to Fu Zheng guben, meanwhile eliminating the adverse effects of chemotherapy drugs, to improve patient quality of life and control development of cancer[11,12].

Yiqi Guben Decoction combined syndrome differentiation and disease differentiation, balance of strengthening the body resistance to eliminate pathogenic factors was basis, full prescription consisted of the Astragalus, Houttuynia, Codonopsis, Ophiopogon, Atractylodes, Hedysotis, Yam, Angelica, Poria, Rehmannia, Moutan, mulberry and licorice, of which astragalus, Codonopsis, Atractylodes and Poria have effect of nourishing Qi, can supplement spleen and lung Qi; Houttuynia, Hedysotis diffusa have effect of detoxification, with exact anti-tumor effect; Yam, Rehmannia, Moutan bark, mulberry can mainly tonify kidney-Qi and reinforce kidney, angelica can promote blood circulation, all kinds of medicine with effect of nourishing Qi and strengthening the body and anti-tumor[13,14]. Modern pharmacological study showed that Astragalus, Codonopsis, Glycyrrhiza glabra and Poria have effect of increasing leukocyte, NK cells and monocyte-macrophage activity, inducing interferon synthesis, improving immune function, anti-tumor, alleviate adverse drug reactions caused by chemotherapy drugs in patients[15,16]; Angelica has significant anti-cancer, dilate blood vessels and improve microcirculation effects[17]. In this study, serum tumor markers, inflammatory cytokines and immune function were analyzed in order to clarify the therapeutic effect of Yiqi-Guben decoction combined with DC chemotherapy.
Serum tumor marker-related index detection is an important indicator of assessing the degree of malignancy, treatment efficacy and prognosis[18]. CRP and TNF-α are critical detection indexes of inflammatory factors, and CRP as an important acute phase reaction protein plays an important role in acute infection and injury. In recent years, numerous studies have demonstrated that CRP was closely related to tumor stage and prognosis in cancer patients, a number of studies have pointed out that elevated serum CRP level can be used as an important indicator of tumor diagnosis[19,20]. TNF-α belonging to the cytokine with multiple biological effects, mainly secreted by monocytes macrophages, and its relationship with tumors mainly presented as that one hand can kill tumor cells directly, non-toxic to normal cells, but also on the other hand promote tumor cell transfer and growth[21,22]. Cellular immunity mediated by T lymphocytes plays an important role in tumor prevention and removal process, development of malignancy suppressed immune function, and with the degree of malignancy increased, the suppression of immune function was more significant[23,24].

The results of this study showed that after treatment of both regimens, the serum tumor markers, serum inflammatory factors and immune function were significantly improved, and the improvement of each index after treatment with Yiqi Guben decoction was better. The results revealed that Yiqi Guben decoction can effectively reduce the level of serum tumor markers, with significant anti-tumor effect, reduce the level of CRP and TNF-α and the inflammatory response, thereby decreasing the body damage, more conducive to recovery, in addition, it can effectively relieve the immunosuppression brought by malignant tumor and with great significance of the reconstruction of the immune system and the restoration of tumor immune surveillance. The improvement of various indexes may be related to the supplement of qi and blood, anti-cancer and immune regulation of Yiqi Guben decoction.

In conclusion, the combination of Yiqi Guben decoction combined with DC chemotherapy in the treatment of locally advanced non-small cell lung cancer had significant clinical effect, can effectively improve serum tumor markers, inflammatory factors and immune function, has important clinical significance.

Reference


[22] De Simone V, Franze E, Ronchetti G. Th17-type cytokines, IL-6 and TNF-α synergistically activate STAT3 and NF-kB to promote colorectal cancer cell growth. Oncogene 2015; 34(27): 3493-3503.