Effect of Ziyin Jiedu Yangfeitang combined with GP chemotherapy on tumor markers and sex hormones in advanced lung cancer patients with Yin deficiency inner heat

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Objective: To observe the effect of Ziyin Jiedu Yangfeitang combined with GP chemotherapy on tumor markers and sex hormone levels in yin deficiency type advanced lung cancer patients. Methods: A total of 105 patients with advanced lung cancer by Yin deficiency were divided into the observation group (55 cases) and control group (50 cases). The control group was given the standard GP chemotherapy, the observation group was given Ziyin Jiedu Yangfeitang on the basis of the control group. After 2 cycles of chemotherapy, the levels of tumor markers (CEA, CA125, CYFRA21, NES) and sex hormone (T, E2, FSH, LH) in the two groups were compared. Results: ① After treatment, the level of CA125, CEA, NES and CYFRA21 in both two groups were significantly decreased (P<0.05); CA125, CEA, NES and CYFRA21 in the observation group were (46.45±10.34) U/mL, (10.36±2.03) ng/mL, (17.35±4.56) ng/mL and (2.56±0.31) ng/mL respectively, all were significantly lower than those in the control group after treatment (P<0.05). ② After treatment, the levels of E2 and FSH were significantly decreased while T and LH were significantly increased in the observation group (P<0.05); those indexes had no obvious changes in the control group (P>0.05). E2 and FSH in the observation group were (85.71±33.57) pmol/L and (10.35±3.56) mU/mL, both were significantly lower than that in the control group after treatment; T and LH in the observation group were (12.33±3.62) nmol/L and (4.08±1.66) mU/mL, both were significantly higher than that in the control group after treatment, (P<0.05). Conclusions: Ziyin Jiedu Yangfeitang can inhibit tumor marker expression and regulate endocrine disorder.

1. Introduction

The mainly purpose is to prolong the life cycle for advanced lung cancer patients, and chemotherapy is the main treatment method to inhibit tumor progression[1]. Studies[2] shows that it exist sex hormone disorder in advanced lung cancer, which is believed to stimulate cancer cell proliferation and reduce the body’s specific immune on cancer cell and adverse to control the progress of the disease. It is necessary to regulate the sex hormone disorders in this class of patients, combination use of traditional Chinese medicine is a viable option. We used Ziyin Jiedu Yangfeitang based on GP chemotherapy for 55 patients, and by observing the changes of tumor markers and sex hormone levels to explore the application value of traditional Chinese medicine. Reports as follows.

2. Materials and methods

2.1. General information

This study was approved by the hospital committee. All cases were patients with advanced lung cancer admitted in our hospital from January 2014 to October 2015, and meet the advanced lung cancer diagnosis standard in "New criteria for diagnosis and treatment of common malignant tumors"[3]. Inclusion criteria were as follows: ① The cytology and pathology diagnosis was non small
cell carcinoma, and was in the stage III B to IV; ② In accordance with the Yin deficiency and lung cancer syndrome type standard in "guidelines for clinical research of traditional Chinese medicine new drug clinical research guidelines"[4]; ③ Without clinical surgery indications or unwilling to operate; ④ The Karnofsky score (KPS) ≥60; ⑤ The expected lifetime ≥2 months. Exclusion criteria were as follows: ① Excluded patients with serious heart, liver, kidney and blood, endocrine system diseases, or combined with serious infection; ② patients with pulmonary tuberculosis, bronchial asthma, pulmonary abscess, pulmonary interstitial fibrosis, bronchial dilation and other lung diseases; ③ Excluded non menopausal women, allergies, cognitive impairment and mental retardation; ④ Less than 2 months from the end of the last chemotherapy or used immunopotentiator treatment; ⑤ did not sign informed consent. A total of 105 cases were included in the study, and were randomly divided into the observation group and control group according to the results of the draw. In observation group, total 55 cases with male 30 cases and female 25 cases; aged from 46 to 74 years old with an average (59.06±14.52) years; the average KPS score was 72.10±9.24; Pathological types: squamous cell carcinoma in 24 cases, adenocarcinoma in 20 cases, glandular squamous cell carcinoma in 8 cases and large cell carcinoma in 3 cases; TNM stage: stage IIIB in 28 cases and stage IV in 27 cases. In control group, total 50 cases with male 30 cases and female 25 cases; aged from 46 to 74 years old with an average (60.06±13.35) years; the average KPS score was 73.01±9.56; Pathological types: squamous cell carcinoma in 22 cases, adenocarcinoma in 20 cases, glandular squamous cell carcinoma in 6 cases and large cell carcinoma in 2 cases; TNM stage: stage IIIB in 27 cases and stage IV in 25 cases. There were no significant differences in age, sex, pathological classification, TNM grade and KPS score between the two groups (P>0.05).

2.2. Treatment methods

2.2.1. Control group
The control group were given the standard GP scheme, including: ① Gemcitabine (manufacturer: Harbin Yu Heng Pharmaceutical Co., Ltd. Chinese medicine standard word: H20040958), usage: 1.0 g/m², intravenous infusion the first and 8 days; ② Cisplatin (manufacturer: Qilu Pharmaceutical Co., Ltd. Chinese medicine standard word: H20023460), usage: 80 g/m², intravenous infusion the first day after chemotherapy. Given orally dexamethasone before chemotherapy and given dexamethasone and ondansetron during the treatment. One period was 3 weeks of treatment add 1 week stopping medicine, observation therapeutic effect after 2 periods.

2.2.2. The observation group
The observation group was given Ziyin Jiedu Yangfeitang based on the standard GP scheme of the control group. It included Radix Glehniae 12 g, Ophiopogon root 12 g, Radix Rehmanniae Preparata 9 g, Artemisia annua 15 g, medlar 12 g, dandelion 12 g, turtle shell 12 g, skullcap 12 g, Oldenlandia diffusa 9 g, dangshen 15 g, Lily 12 g, Radix Astragali 30 g, yam 15 g, Platycodon grandiflorum 9 g, white peony root 12 g. One dose per day, take 2 times in the morning and evening.

2.3. Observation of indexes

2.3.1. Tumor markers
Serum carbohydrate antigen -125 (CA125), carciinoembryonic antigen (CEA), neuron specific enolase (NSE) and cytokeratin fragment 21-1 (CYFRA21) were detected by Roche Elecsys2010 chemiluminescence detector.

2.3.2. Sex hormones
Serum estradiol (E₂), testosterone (T), luteinizing hormone (LH) and follicle stimulating hormone (FSH) were detected by Double anti detection method, the reagent kits were purchased from Sino American Joint Venture Tianjin Depp company.

2.4. Statistical analysis
SPSS 17.0 software was used for statistical analysis, the measurement data were compared by t test, P <0.05 was considered as significant difference.

3. Results

3.1. Tumor marker levels of two groups before and after treatment
Before treatment, there were no significant differences in the level of CA125, CEA, NES and CYFRA21 between the two groups (P>0.05). After treatment, both two groups’ indexes were significantly decreased (P<0.05); CA125, CEA, NES and CYFRA21 in the observation group were significantly lower than those in the control group after treatment, (P<0.05) (Table 1).

3.2. Sex hormone levels of two groups before and after treatment
Before treatment, there were no significant differences in the level of E₂, T, LH and FSH between the two groups (P>0.05). After treatment, the levels of E₂ and FSH in the observation group were significantly decreased while T and LH were significantly increased (P<0.05); those indexes had no obvious changes in the control group (P>0.05). E₂, FSH and FSH in the observation group were significantly higher than that in the control group after treatment (P<0.05) (Table 2).
4. Discussion

Data[5] shows that the incidence of lung cancer has increased year by year in China, and most of the patients are in the advanced stage at the time of diagnosis. The chances of surgical treatment are slim, the main therapeutic purpose is to extend the life and improve the quality of life[6]. Chemotherapy is the main treatment method for malignant tumors and the GP regimen is the first-line treatment for patients with advanced non-small cell lung cancer[7], but also with poor improvement of the clinical symptoms, toxic side effects and other issues. Studies[7] have shown that chemotherapy combined with traditional Chinese medicine has attenuated and synergistic effect in the treatment of advanced non-small cell lung cancer, but the specific mechanism is still under exploration. Due to the Yin deficiency heat type accounted for about 70%-80% in advanced lung cancer[8], we choose this type of patients as the research object, which has important practical significance.

Tumor markers can be used to evaluate the therapeutic effect of malignant tumors, CA125, CEA, NES and CYFRA21 were all markers that highly correlated with non small cell lung cancer[9]. A number of studies have shown that[10,11] those markers highly expressed in the rapid progression of tumors and decreased significantly when the tumor was effectively controlled. Sex hormone disorder is very common in malignant tumor, and its stimulation malignant tumor progress has been confirmed with the progress of the disease, the sex hormones E2, T, LH and FSH that are significantly when the tumor was effectively controlled. Sex hormone disorder is very common in malignant tumor, and its regulation sexual hormone level especially lower E2 level in patients control group, which indicated that Ziyin Jiedu Yangfeitang could effectively inhibit cancer cells; the levels of sex hormone E2, FSH decreased significantly and T, LH increased significantly in the observation group while those indexes had no obvious changes in the control group, which indicated that Ziyin Jiedu Yangfeitang main due to Yin deficiency lung cancer.

Modern pharmacology proved that traditional Chinese medicine is beneficial to malignant tumor. Such as: artemisinin, arteannuin B derivatives can improve the lymphocyte transformation rate and enhance macrophage’s phagocytosis ability[12,13]; Turtle shell preparation can enhance the activity of NK cells and promote the formation of immunoglobulin[14]; ophiopogon polysaccharide can enhance the function of humoral immunity and cellular immune[15]; turtle shell and Herba Hedyotis can promote cancer cell apoptosis[16]. We can see that the prescription in our study can inhibit

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\text{Tumor marker levels of the two groups before and after treatment.}
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<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>CA125 (U/mL)</th>
<th>CEA (ng/mL)</th>
<th>NSE (ng/mL)</th>
<th>CYFRA21 (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group(55 cases)</td>
<td>Before treatment</td>
<td>57.7±12.45</td>
<td>17.84±4.45</td>
<td>35.66±15.63</td>
<td>5.44±0.45</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>46.4±10.34</td>
<td>10.36±2.03</td>
<td>17.35±4.56</td>
<td>2.56±0.31</td>
</tr>
<tr>
<td>Control group(50 cases)</td>
<td>Before treatment</td>
<td>58.3±13.45</td>
<td>18.13±4.05</td>
<td>35.51±13.40</td>
<td>5.41±0.42</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>53.6±11.49</td>
<td>14.44±3.35</td>
<td>24.32±7.45</td>
<td>3.46±0.73</td>
</tr>
</tbody>
</table>

Ps: Compared with the same group before treatment, \( ^\Delta P<0.05 \); Compared with the control group after treatment, \( ^\Delta P<0.05 \).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time</th>
<th>T (nmol/L)</th>
<th>E2 (pmol/L)</th>
<th>FSH (mU/mL)</th>
<th>LH (mU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group (55 cases)</td>
<td>Before treatment</td>
<td>9.07±4.08</td>
<td>135.43±45.24</td>
<td>13.64±3.02</td>
<td>3.65±1.53</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>12.33±3.62</td>
<td>85.71±33.57</td>
<td>10.35±3.56</td>
<td>4.08±1.66</td>
</tr>
<tr>
<td>Control group (50 cases)</td>
<td>Before treatment</td>
<td>9.14±3.95</td>
<td>136.02±50.83</td>
<td>13.57±3.16</td>
<td>3.59±1.61</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>9.63±4.23</td>
<td>130.51±47.25</td>
<td>13.31±3.40</td>
<td>3.51±1.48</td>
</tr>
</tbody>
</table>

Ps: Compared with the same group before treatment, \( ^\Delta P<0.05 \); Compared with the control group after treatment, \( P<0.05 \).
cancer cells in many ways, and regulating hormone level should also be beneficial to the inhibition of cancer cells, like the Chinese traditional medicine treating yin deficiency has the role in regulating hypothalamic pituitary gonadal axis\(^{[20]}\) and inhibiting the high level of E\(_2\) in patients with advanced malignant tumor.

In summary, Ziyin Jiedu Yangfeitang can inhibit tumor marker expression, regulate endocrine disorders and improve the prognosis of patients with advanced non small cell lung cancer due to yin deficiency and interior-heat.

References


