Evaluation of the prognosis as well as tumor marker levels and immune function of Fuzheng Xiaoliu decoction combined with paclitaxel treatment of advanced breast cancer

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ABSTRACT

Objective: To analyze the effect of Fuzheng Xiaoliu decoction combined with paclitaxel treatment of advanced breast cancer on the prognosis as well as tumor marker levels, immune function and so on. Methods: A total of 40 patients with advanced breast cancer were randomly divided into observation group and control group (n=20), control group received conventional chemotherapy + paclitaxel treatment and observation group received conventional chemotherapy + paclitaxel + Fuzheng Xiaoliu decoction treatment. The survival of two groups of patients was followed up, and serum levels of tumor markers and sex hormones as well as immune function indexes were determined. Results: Progression-free survival and overall survival of observation group were longer than those of control group; after one course of treatment, serum VEGF-A, TK1, IGF-1, CerbB-2, CEA, CA15-3, CA125, E1 and E2 levels of observation group were significantly lower than those of control group while LH and FSH levels were significantly higher than those of control group; CD3+CD4+, CD8+CD28+, CD19+ and CD16+CD56+ expression levels in peripheral blood of observation group were significantly higher than those of control group while CD4+CD25+ and CD8+CD28- expression levels were significantly lower than those of control group. Conclusion: Fuzheng Xiaoliu decoction combined paclitaxel treatment of advanced breast cancer can reduce tumor malignancy and improve the body's immune function, and is of positive significance in optimizing treatment prognosis.

1. Introduction

Breast cancer is clinically common, patients at advanced stage can mostly accept conservative treatments such as radiotherapy and chemotherapy, and the long-term prognosis is poor. Cytotoxic effect of paclitaxel has been clinically recognized, has been widely used in treatment of many kinds of advanced malignant tumors, and is good for prolonging patients’ survival[1,2]. The application effect of paclitaxel in advanced breast cancer has also been reported by many scholars, but studies have found that with the extended time of paclitaxel treatment, its treatment effectiveness declines, which may be associated with paclitaxel resistance. In view of the limitations of western medicine, some scholars recommend the use of traditional Chinese medicine in anticancer treatment, and Fuzheng Xiaoliu decoction is the widely recognized prescription of traditional Chinese medicines. Fuzheng Xiaoliu decoction can regulate qi and remove blood stasis, disperse tumor and dissipate binds, clear heat and resolve toxin, etc, it is effective for a variety of malignant tumors, and the study of CHEN Zhi-gang[3] has found that Fuzheng Xiaoliu decoction has definite therapeutic effect on ovarian cancer. In order to break the bottleneck of advanced breast cancer treatment, Fuzheng Xiaoliu decoction combined with paclitaxel therapy was used in the study for patients with advanced breast cancer in our hospital, and the effect of combined treatment of traditional Chinese medicine and western medicine on tumor cell toxicity, immunity and prognosis was mainly elaborated.
2. Information and methods

2.1. General information

A total of 40 patients with advanced breast cancer treated in our hospital from September 2010 to September 2015 were included, and inclusion criteria were: 1) confirmed by pathological biopsy; 2) without radiotherapy and chemotherapy 1 month before included; 3) the patients and families signed informed consent; 4) not associated with the primary tumor of other parts; 5) with complete clinical data. 40 patients were divided into observation group and control group (n=20) according to random number table. Control group were 45-71 years old and (64.38±7.14) years old in average, and tumor typing was as follows: 6 cases with intraductal carcinoma, 7 cases with invasive lobular carcinoma, 4 cases with infiltrating ductal carcinoma and 3 cases with mucous carcinoma; observation group were 43-73 years old and (65.12±6.89) years old in average, and tumor typing was as follows: 5 cases with intraductal carcinoma, 8 cases with invasive lobular carcinoma, 5 cases with infiltrating ductal carcinoma and 2 cases were with mucous carcinoma. Two groups of patients were not statistically different in age and tumor typing distribution (P>0.05), and could be subsequently compared.

2.2. Treatment methods

Both groups of patients received NP chemotherapy, cisplatin injection 70 mg/m², intravenous drip in 3 d; vinorelbine injection 25 mg/(m²•d), on d1 and d8, 4 weeks as one course of treatment. Based on NP chemotherapy, control group received paclitaxel treatment, specifically as follows: paclitaxel 100 mg/m² in 500 mL saline, intravenous drip, speed of drip 2.8 mL/min and 30 d as one course of treatment. The NP chemotherapy was the same as above. Based on NP chemotherapy, observation group received paclitaxel + Fuzheng Xiaoliu decoction treatment, specifically as follows: each 30 g of astragalus, atractylodes macrocephala, radix actinidiae, coix seed and oldenlandia diffusa, 15 g each of grifola, dendrobe, each 30 g of astragalus, atractylodes macrocephala, radix actinidiae, + Fuzheng Xiaoliu decoction treatment, specifically as follows: paclitaxel 8.39±0.91 (pg/mL), CD25 8.28±0.8 and CD8 17.34±1.92 (pg/mL). Test was done by Student’s t test and P<0.05 indicated statistical significance.

2.3. Serum index determination methods

After one course of treatment, 2 mL of fasting peripheral venous blood was collected and centrifuged to get supernatant for subsequent testing. ELISA kits were used to detect vascular endothelial growth factor-A (VEGF-A), thymidine kinase 1 (TK1), insulin-like growth factor 1 (IGF-1) and CerbB-2; full automatic biochemical analyzer was used to determine serum carcino-embryonic antigen (CEA) and carbohydrate antigen 15-3 (CA15-3), carbohydrate antigen 125 (CA125), estradiol (E2), estrone (E1), luteinizing hormone (LH) and follicle-stimulating hormone (LSH) levels.

2.4. Peripheral blood immune function index determination methods

After 1 course of treatment, 2 mL of fasting peripheral venous blood was collected to incubate fluorescent antibody of CD3, CD4, CD8, CD28, CD19, CD16 and CD56 respectively, and then flow cytometer was used to determine CD3+CD4+, CD8+CD28+, CD19+, CD16+CD56+, CD4+CD25+ and CD8+CD28- expression levels.

2.5. Statistical methods

SPSS 23.0 was used to input and analyze the data obtained in the study, measurement data was in terms of Mean ± SD, comparison between groups was by t test and P<0.05 indicated statistical significance in differences.

3. Results

3.1. Prognosis of two groups

Progression-free survival of observation group was (11.59±1.85) months and overall survival was (19.55±2.75) while progression-free survival of control group was (7.54±0.93) months and overall survival was (13.25±2.25) months. After t test, t values were 7.695 and 8.583 respectively, and P values were all <0.05.

3.2. Serum tumor markers

After one course of treatment, analysis of serum antigen markers CEA, CA15-3 and CA125 levels was shown in Table 1: serum CEA, CA15-3 and CA125 levels of observation group were significantly lower than those of control group; analysis of serum malignant molecules VEGF-A, TK1, IGF-1 and CerbB-2 levels was shown in Table 2: serum VEGF-A, TK1, IGF-1 and CerbB-2 levels of observation group were significantly lower than those of control group. Differences in serum CEA, CA15-3, CA125, VEGF-A, TK1, IGF-1 and CerbB-2 levels were statistically significant between two groups after treatment (P<0.05).

Table 1. Comparison of serum antigen marker levels between two groups after treatment (U/L).

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CEA</th>
<th>CA15-3</th>
<th>CA125</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>20</td>
<td>8.39±0.91</td>
<td>19.23±2.41</td>
<td>40.73±4.81</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>14.17±1.89</td>
<td>45.67±5.18</td>
<td>72.45±8.13</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>7.192</td>
<td>8.934</td>
<td>8.632</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 2. Comparison of serum malignant molecule levels between two groups after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>VEGFA (pg/mL)</th>
<th>TK1 (pmol/L)</th>
<th>IGF-1 (ng/mL)</th>
<th>CerbB-2 (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>20</td>
<td>143.28±17.12</td>
<td>0.67±0.08</td>
<td>195.47±20.13</td>
<td>10.28±1.65</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>229.73±24.84</td>
<td>1.51±0.19</td>
<td>258.35±30.17</td>
<td>17.34±1.92</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>9.384</td>
<td>5.182</td>
<td>7.283</td>
<td>6.293</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
3.3. Serum sex hormone levels

After one course of treatment, analysis of serum sex hormones E1, E2, LH and FSH of two groups was as follows: serum E1 and E2 levels of observation group were significantly lower than those of control group while LH and FSH levels were significantly higher than those of control group. Differences in serum E1, E2, LH and FSH levels were statistically significant between two groups after treatment ($P<0.05$), shown in Table 3.

3.4. Cellular immune indexes

Analysis of immune cell surface molecules CD3$^+$CD4$^+$, CD8$^+$CD28$^+$, CD19$^+$, CD16$^+$CD56$^+$, CD4$^+$CD25$^+$ and CD8$^+$CD28$^+$ expression levels in peripheral blood of two groups was as follows: CD3$^+$CD4$^+$, CD8$^+$CD28$^+$, CD19$^+$ and CD16$^+$CD56$^+$ expression levels in peripheral blood of observation group were significantly higher than those of control group while CD4$^+$CD25$^+$ and CD8$^+$CD28$^+$ expression levels were significantly lower than those of control group. Differences in immune cell surface molecules CD3$^+$CD4$^+$, CD8$^+$CD28$^+$, CD19$^+$, CD16$^+$CD56$^+$, CD4$^+$CD25$^+$ and CD8$^+$CD28$^+$ expression levels in peripheral blood were statistically significant between two groups ($P<0.05$), shown in Table 4.

4. Discussion

The survival extension in patients with advanced breast cancer mostly depends on the radiotherapy and chemotherapy and other conservative treatments, but with the extension of treatment time, multidrug resistance may occur in many patients, and the survival extension in patients with advanced breast cancer is to extend the survival time and prolong the survival time. Detection of serum tumor markers is a common method to evaluate the malignant degree and prognosis of tumor, carcino-embryonic antigen (CEA), carbohydrate antigen 15-3 (CA15-3) and carbohydrate antigen 125 (CA125) are the antigen marker molecules associated with breast cancer[7]. Studies have shown that CEA is highly expressed in more than 70% of patients with colon cancer, 55% of patients with ovarian cancer and some patients with breast cancer; CA125 is actively expressed in the majority of patients with breast cancer; CA15-3 level is high in the circulation of more than 45% of patients with breast cancer[8]. The sensitivity and specificity are not high when the above three indicators are detected alone, but the combined detection of the three has significantly increased directivity for breast cancer, and can objectively reflect the illness and treatment effect of breast cancer. In the study, detection of serum antigen marker molecules showed that serum CEA, CA15-3 and CA125 levels of observation group were significantly lower than those of control group. This means that Fuzheng Xiaoliu decoction combined with paclitaxel therapy can effectively kill the cancer cells and reduce the levels of antigen markers.

In the progression of malignant tumor, a variety of malignant molecules are involved in the malignant biological behavior of tumor cells, and determination of serum malignant molecule levels can reflect the malignant degree of tumor. Vascular endothelial growth factor-A (VEGF-A) level is directly related to tumor angiogenesis activity, and also one of the objective indicators to reflect tumor malignancy[10]; thymidine kinase 1 (TK1) is the key enzyme involved in DNA precursor synthesis, its serum concentration is associated with cell cycle regulation, and it is regarded as a cell proliferation marker[11]. Insulin-like growth factor 1 (IGF-1) can regulate cancer cell proliferation, differentiation and apoptosis, it is the independent risk factor of tumor diseases, and relevant study has confirmed that IGF-1 level is positively correlated with the

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>E1 (pg/mL)</th>
<th>E2 (pg/mL)</th>
<th>LH (IU/L)</th>
<th>FSH (IU/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>20</td>
<td>30.27±3.52</td>
<td>45.72±5.09</td>
<td>36.38±3.12</td>
<td>18.58±2.42</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>53.91±5.88</td>
<td>69.83±7.12</td>
<td>22.47±2.58</td>
<td>11.03±1.52</td>
</tr>
<tr>
<td>$P$</td>
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<td>&lt;0.05</td>
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<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
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</table>

Table 3.
Serum sex hormone levels of two groups after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>CD3$^+$CD4$^+$</th>
<th>CD8$^+$CD28$^+$</th>
<th>CD8$^+$CD28$^+$</th>
<th>CD19$^+$</th>
<th>CD16$^+$CD56$^+$</th>
<th>CD4$^+$CD25$^+$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>20</td>
<td>35.96±5.23</td>
<td>29.14±3.52</td>
<td>22.42±2.95</td>
<td>14.58±1.85</td>
<td>17.85±2.24</td>
<td>2.52±0.35</td>
</tr>
<tr>
<td>Control</td>
<td>20</td>
<td>29.24±3.96</td>
<td>22.53±2.95</td>
<td>28.14±3.52</td>
<td>9.29±1.03</td>
<td>11.39±1.59</td>
<td>3.86±0.76</td>
</tr>
<tr>
<td>$T$</td>
<td></td>
<td>9.38</td>
<td>7.483</td>
<td>6.184</td>
<td>5.859</td>
<td>6.482</td>
<td>8.183</td>
</tr>
<tr>
<td>$P$</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Table 4.
Cellular immune function indexes in peripheral blood of two groups after treatment.
incidence of malignant tumor[12]. CerbB-2 is a new type of tyrosine kinase gene, it is in the inactive state in normal tissues, and CerbB-2 activation caused by combined action of internal and external factors can lead to tumorigenesis[13]. In the study, analysis of the above malignant molecules showed that serum VEGF-A, TK1, IGF-1 and CerbB-2 levels of observation group were significantly lower than those of control group. This means that Fuzheng Xiaoliu decoction combined with paclitaxel therapy has inhibiting effect on the malignant biological behavior of breast cancer. Breast cancer belongs to hormone-dependent tumor, estrogen has promoting effect on the development of tumor[14,15], and analysis of the sex hormone levels in the study showed that serum E1 and E2 levels of observation group were significantly lower than those of control group while LH and FSH levels were significantly higher than those of control group. This means that Fuzheng Xiaoliu decoction combined with paclitaxel can not only directly regulate the malignant biological behavior of breast cancer, but can also regulate the sex hormone levels in patients.

There is common immunosuppression in patients with malignant tumor, and because the cellular immune function is the main system involved in tumor immunity, the cellular immune function state in patients with malignant tumor has received universal attention. Chemotherapy can cause damage to patients’ own cellular immune function, astragalus and atractylodes macrocephala in Fuzheng in patients with malignant tumor immunity, the cellular immune function state is the main system involved in tumor immunity, the cellular immune function is the main system involved in tumor immunity, the cellular immune function state in patients with malignant tumor has received universal attention. Chemotherapy can cause damage to patients’ own cellular immune function, astragalus and atractylodes macrocephala in Fuzheng Xinyu decoction can specifically supplement Qi and nourish Yin, foster root and solidify vigor, improve resistance, etc. and can reduce the inhibiting effect of disease itself and chemotherapy on cellular immune function, and meanwhile, the optimized immune status can further kill tumor cells, forming a virtuous cycle. CD3+CD4+ is the surface marker of helper T cells, and can assist the differentiation and maturation of other immune cells[16]. CD8+CD28+ is the surface marker of cytotoxic T cells, and has the function of killing abnormally proliferated cells[17]. CD19+ and CD16+CD56+ are the surface markers of B cells and NK cells respectively, and they mediate humoral immunity and nonspecific immunity respectively; CD8+CD28+ and CD4+CD25+ are the surface markers of suppressor T cells and regulatory T cells respectively, and they have inhibiting effect on the immune response[18]. In the study, analysis of immune function proved that CD3+CD4+, CD8+CD28+, CD19+ and CD16+CD56+ expression levels in peripheral blood of observation group were significantly higher than those of control group while CD4+CD25+ and CD8+CD28+ expression levels were significantly lower than those of control group. This means that after Fuzheng Xiaoliu decoction combined with paclitaxel treatment, the cellular immune function is enhanced in patients with advanced breast cancer, indicating that the activity of malignant tumor cells is contained and it is the direct sign of good treatment effect.

In conclusion, Fuzheng Xiaoliu decoction combined paclitaxel treatment can reduce the tumor malignancy of advanced breast cancer and improve the body's immune function, it is a reliable way to optimize the prognosis of patients with advanced breast cancer, and it is worth popularization and application in clinical practice in the future.

References


