Effect of kanglaite injection combined with chemotherapy on tumor factors, angiogenesis and immunoglobulin in patients with lung adenocarcinoma

Yan Chen¹, Yong-Feng Shan²

¹. Oncology Department, The Second Hospital of Traditional Chinese Medicine of Wuxi, Wuxi 214121, Jiangsu, China
². Oncology Department, The Fifth Peoples Hospital of Wuxi, Wuxi 214000, Jiangsu, China

ARTICLE INFO

Article history:
Received 17 Dec 2018
Received in revised form 22 Dec 2018
Accepted 4 Jan 2019
Available online 14 Jan 2019

Keywords:
Kanglaite injection
Chemotherapy
Lung adenocarcinoma
Tumor factor
Angiogenesis
Immunoglobulin

ABSTRACT

Objective: To explore the effect of Kanglaite injection combined with chemotherapy on the levels of tumor factors, angiogenesis and immunoglobulin in patients with lung adenocarcinoma. Method: A total of 88 patients with lung adenocarcinoma in our hospital and the Fifth Peoples Hospital of Wuxi from February 2014 to December 2017 were divided randomly into observation group and control group according to the visiting time, 44 cases for each group. The observation group was treated with chemotherapy combined with Kanglaite injection, and the control group was treated with chemotherapy only. Both groups were treated for 6 weeks and then the levels of CEA, CA125, CA199, VEGFA, VEGFB, VEGFC, and IgA, IgM, IgG after treatment in both groups were compared. Result: Before treatment, there were no significant differences in the levels of CEA, CA125 and CA199 between two groups. The level of CEA in the observation group (29.88±7.07) μg/L was lower than that in the control group, and the difference was statistically significant. The levels of CA125 and CA199 after treatment were lower than those before treatment, but with no significant difference. Between the two groups, there was no significant difference of the levels of VEGFA, VEGFB and VEGFC before treatment, the level of VEGFA after treatment in the observation group (80.49±12.29) ng/mL was lower than that in the control group and the difference was statistically significant, and the levels of VEGFB and VEGFC after treatment were also lower than those before treatment, but with no significant difference. The levels of IgA, IgM and IgG after treatment in two groups had no significant difference, The level of IgM after treatment in the observation group (1.52±0.30) g/L was lower than that in the control group, with a statistical difference. The levels of IgA and IgG after treatment were lower than those before treatment, but with no significant difference; No serious adverse reaction was observed after treatment in both groups. Conclusion: Kanglaite injection combined with chemotherapy has a good clinical effect in lung adenocarcinoma, which can effectively inhibit the high expression of tumor markers, reduce angiogenesis, enhance body immunity, and can be recommended for clinical application.

1. Introduction

Lung cancer is the most common malignant tumor in the world with the highest morbidity and mortality. Non-small cell lung cancer accounts for more than 80% of the total number of lung cancers, of which lung adenocarcinoma accounts for about 50%, and female patients are more than male[1-2]. The early symptoms of lung adenocarcinoma are atypical and easily overlooked. Once the symptoms appear, they have developed to the advanced stage and lost the chance of surgery. In the past, the treatment of advanced lung adenocarcinoma mostly used chemotherapy as the main treatment, but although chemotherapy can kill tumor cells, it also significantly inhibited the body's immune function, and the drug
has serious side effects. At present, the application of Kanglaite injection combined with chemotherapy in the treatment of lung adenocarcinoma can effectively improve clinical efficacy and reduce adverse reactions.

2. Materials and methods

2.1 Clinical data

A total of 88 patients with lung adenocarcinoma who were admitted to our hospital and the Fifth People’s Hospital of Wuxi from February 2014 to December 2017 were enrolled. They were divided into two groups according to the order of admission, 44 cases in each group, which were set as observation group and control group. There were 18 males and 26 females in the observation group, aged 40-66 years old. TNM staging: 25 cases of stage IIIB, 19 cases of stage IV; in the control group 20 males and 24 females, aged 38-65 years old, TNM staging: 23 cases of stage IIIB and 21 cases of stage IV. Inclusion criteria: a. All patients met the relevant diagnostic criteria of Chinese advanced primary lung cancer diagnosis and treatment [3], and confirmed by imaging and pathology, there is at least one measurable focus; b. estimated survival for more than 3 months; c. KPS (Ka-mofsky) score > 60 points [4], no chemotherapy contraindications; exclusion criteria: a. secondary lung malignancy; b. combined with serious heart, brain, liver, kidney and other organ damage; c. poor compliance during medical treatment, or mental, neurological disorders, do not cooperate; d. with drug allergic history. The study was agreed by the patient and their family members, signed informed consent.

2.2 Treatment method

The control group was given cisplatin (Jiangsu Haosen Pharmaceutical Co., Ltd., Approval number: H20040813) 75 mg/m², applied in 3 d, and pemetrexed was given on the first day (Qilu Pharmaceutical Co., Ltd., Approval number: H20060671) 500 mg/m². On the basis of the control group, the observation group was given 200 mL daily intravenous infusion of Kanglaite Injection (Zhejiang Kanglaite Pharmaceutical Co., Ltd., Approval number: Z10970091). The above treatments were for one course every 3 weeks, and two courses were used continuously.

All patients received oral folic acid preparation 400 μg/d one week before the administration of pemetrexed and continued until the end of treatment. 1 mg Vitamin B12 intramuscular injection was given within one week before the administration, oral administration of dexamethasone tablets 4.5 mg on one day before medication, the current day and the second day, 2 times a day.

2.3 Analysis of efficacy

Tumor markers, angiogenesis and immunoglobulin levels were compared between the two groups. Tumor markers include CEA (carcinoembryonic antigen), CA125 (carbohydrate antigen 125), CA199 (carbohydrate antigen 199), detected by electrochemiluminescence [5]; angiogenesis factors including VEGFA (vascular endothelial factor-A) VEGFB (vascular endothelial factor-B) and VEGFC (vascular endothelial factor-C) were detected by enzyme-linked immunosorbent assay [6]; immunoglobulins include IgA (mucosal immune secretion antibody), IgM (primary immune response antibody), IgG (re-immunization antibody), was determined by immunoturbidimetry [7].

2.4 Statistical methods

All data were statistically processed using SPSS 20.0. The measurement data were expressed as mean ± standard deviation (Mean ± SD), Using t test, \( P < 0.05 \) was considered statistically significant.

3. Results

3.1 Comparison of tumor marker levels before and after treatment in both groups

The levels of CEA, CA125 and CA19 in the two groups were the similar before treatment, the difference was not statistically significant (\( P > 0.05 \)). The CEA level (29.88±7.07) μg/L in the observation group was lower than that in the control group, the difference was statistically significant (\( P < 0.05 \)), the levels of CA125 and CA199 after treatment were lower than those before treatment, but there was no significant difference between the two groups and before treatment (\( P > 0.05 \)), as shown in Table 1.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>CEA (μg/L)</th>
<th>CA125 (U/mL)</th>
<th>CA199 (U/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>44</td>
<td>Before</td>
<td>55.2±10.63</td>
<td>42.48±14.34</td>
<td>36.14±8.49</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>29.88±7.07*</td>
<td>40.66±7.11</td>
<td>34.45±8.07</td>
</tr>
<tr>
<td>Control group</td>
<td>44</td>
<td>Before</td>
<td>55.27±11.03</td>
<td>42.92±15.04</td>
<td>36.07±9.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>40.36±11.26*</td>
<td>41.47±10.43</td>
<td>33.55±6.30</td>
</tr>
</tbody>
</table>

Note: Compared with this group before treatment, *\( P < 0.05 \); compared with the control group after treatment, \( *P < 0.05 \).
Table 2.
Comparison of angiogenesis index levels before and after treatment in both groups (ng/mL).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>VEGFA</th>
<th>VEGFB</th>
<th>VEGFC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>44</td>
<td>Before</td>
<td>100.5±29.66</td>
<td>85.19±14.87</td>
<td>79.78±10.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>80.49±12.29*</td>
<td>75.79±9.66</td>
<td>71.92±9.37</td>
</tr>
<tr>
<td>Control</td>
<td>44</td>
<td>Before</td>
<td>100.87±27.27</td>
<td>84.73±15.57</td>
<td>79.67±18.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>87.44±21.47*</td>
<td>79.38±10.12</td>
<td>70.12±12.44</td>
</tr>
</tbody>
</table>

Note: Compared with this group before treatment, *P<0.05; compared with the control group after treatment, *P<0.05.

Table 3.
Comparison of immunoglobulin indexes before and after treatment in both groups (g/L).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>IgA</th>
<th>IgM</th>
<th>IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>44</td>
<td>Before</td>
<td>2.71±0.30</td>
<td>1.25±0.18</td>
<td>12.27±1.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>2.75±0.62</td>
<td>1.52±0.20</td>
<td>12.60±1.72</td>
</tr>
<tr>
<td>Control</td>
<td>44</td>
<td>Before</td>
<td>2.69±0.28</td>
<td>1.28±0.20</td>
<td>12.31±2.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After</td>
<td>2.72±0.43</td>
<td>1.30±0.21</td>
<td>12.54±1.25</td>
</tr>
</tbody>
</table>

Note: Compared with this group before treatment, *P<0.05; compared with the control group after treatment, *P<0.05.

3.2 Comparison of angiogenesis indicators before and after treatment in both groups

The levels of VEGFA, VEGFB and VEGFC were similar in the two groups before treatment, the difference was not statistically significant (P>0.05). The VEGFA level (80.49±12.29 ng/mL in the observation group after treatment was lower than that in the control group, the difference was statistically significant (P<0.05), the levels of VEGFB and VEGFC after treatment were decreased than those before treatment, but there was no significant difference compared with before treatment and comparison between both groups (P>0.05), as shown in Table 2.

3.3 Comparison of immunoglobulin indexes before and after treatment in both groups

The levels of IgA, IgM and IgG were the same in the two groups before treatment, the difference was not statistically significant (P>0.05). The IgM level in the observation group was (1.52±0.30) g/L higher than that in the control group, the difference was statistically significant (P<0.05), although the levels of IgA and IgG were increased than those before treatment, but there was no significant difference compared with before treatment and comparison between both groups (P>0.05), as shown in Table 3.

3.4 Comparison of adverse reactions between two groups of patients

In the observation group, there were 15 cases of digestive tract reaction, 18 cases of myelosuppression, 2 cases of dizziness, in the control group 18 cases of digestive tract reaction and 21 cases of myelosuppression, all of which were grade I-III. There was no grade IV adverse reaction in the whole group.

4. Discussion

In recent years, the incidence of lung cancer in China has been increasing year by year. Lung adenocarcinoma is the most common form of lung cancer with a five-year survival rate of less than 15%[8,9]. The disease is concealed, and there is no obvious clinical manifestation in the early stage. When it is diagnosed, it has developed to the middle and late stage, and the chance of surgery is lost. Chemotherapy is the main treatment, but the data showed that patients often had serious side effects due to drugs. For example, narrow suppression, digestive tract reaction and hair loss, eventually forced to terminate treatment, which can not achieve the desired therapeutic goals, but also reduce the quality of life, causing more serious psychological and physiological effects on patients[10,11]. Since the beginning of the new century, the Chinese medicine industry has been greatly developed, and the combination of Chinese and Western medicine has been widely recognized. Many reports have shown that some Chinese herbal extracts have obvious anti-tumor effects and can effectively enhance the body’s immunity and better relieve chemotherapy related toxic side effects[12-14]. For example, in our hospital's current treatment of lung adenocarcinoma, chemotherapy combined with Kanglaite injection, Kanglaite injection is a new type of anti-tumor traditional Chinese medicine preparation, no cytotoxicity, currently used for the treatment of non-small cell lung cancer, its sensobilization of adjuvant chemotherapy kill tumors is affirmed[15]. The natural and effective anti-tumor active ingredient in Kanglaite injection is extracted from coix seed. The effect of eliminating stagnation, tonifying qi and yin is obvious. At the same time, it has been reported that the drug is a two-way anticancer drug, which can effectively reduce the pain caused by cancer, control cancer growth and spread, induce cancer cell apoptosis, and improve immune function. It has multiple targets, multiple links and multiple effects, can effectively alleviate the toxic and side effects during chemotherapy, prolong survival and improve quality of life[16]. Tumor markers are important indicators for tumor diagnosis, treatment and prognosis assessment. They show dynamic changes during tumorigenesis and development and are related to tumor status and outcome. Like most malignant tumors, lung adenocarcinoma has no specific tumor markers. In most patients, the CEA level is often
increased during the development of the disease. In a small number of patients, the levels of CA125 and CA199 are also abnormally elevated. The later the disease, the serum CEA level is higher[17]; both CA125 and CA199 are carbohydrate antigens, which are highly expressed in many malignant tumors, and the later the tumor stage, the higher the level[16-23]; in this study, CEA level in the observation group after treatment was significantly lower than that of the control group, and the difference was statistically significant. The decrease of CA125 and CA199 levels was also better than that of the control group. Although it was not statistically significant, it showed that Kanglaite injection combined with chemotherapy can be better adjusted than chemotherapy alone. The level of tumor markers in lung adenocarcinoma may have affected the progression of the tumor through some unknown mechanism.

VEGF, vascular endothelial cell growth factor, has high stability through some unknown mechanism. Lung adenocarcinoma may have affected the progression of the tumor of CA125 and CA199 levels was also better than that of the control group after treatment was significantly lower than that of the control group. Although it was not statistically significant, it showed that Kanglaite injection combined with chemotherapy can be better adjusted than chemotherapy alone. The level of tumor markers in lung adenocarcinoma may have affected the progression of the tumor through some unknown mechanism.

The VEGF level in the observation group was significantly lower than that in the control group. The difference was statistically significant. The VEGFβ and VEGFα levels in the observation group were also significantly lower than in the control group. Although it was not statistically significant, it showed that Kanglaite injection combined chemotherapy can inhibit tumor angiogenesis in lung adenocarcinoma more effectively compared with chemotherapy alone.

The improvement of immunity is especially important for patients with advanced cancer. The higher the level of immunoglobulin, the stronger the defense and immunity of the body. The IgM level in the observation group was significantly higher than that in the control group. The difference was statistically significant, IgA and IgG level also increased after treatment, and the observation group was slightly higher than the control group. Although it was not statistically significant, it was sufficient to show that the combination of Kanglaite injection in the chemotherapy of lung adenocarcinoma can help improve the body immunity of patients. It is conducive to tumor outcome.

In summary, the application of Kanglaite injection combined with chemotherapy in lung adenocarcinoma can effectively down-regulate tumor marker levels, inhibit tumor angiogenesis, and enhance the body's immunity, which is worthy of clinical application.

References