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Observation on the Improvement of Quality of Life in Patients with Advanced Non-small Cell Lung Cancer by DC-CIK Maintenance Therapy Combined with Traditional Chinese Medicine Therapy

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Abstract: To explore and observe the effect of DC-CIK maintenance therapy combined with traditional Chinese medicine treatment on the improvement of quality of life in patients with advanced non-small cell lung cancer (NSCLC). The research period was from January 2017 to April 2018. 89 patients with advanced NSCLC who were diagnosed and treated in our hospital. They were divided into observation group 49 cases and control group 40 cases. Record the improvement of the quality of life. After treatment, the short-term total effective rates of the observation group and the control group were 71.4% and 42.5% respectivel. The rate of the observation group was significantly higher than that of the control group (P<0.05). CD8+, CD3+ and CD4+ in the observation group and the control group after treatment were significantly different from those before treatment. And there was a statistically significant difference (P<0.05). DC-CIK maintenance therapy combined with traditional Chinese medicine treatment of advanced NSCLC patients can improve the quality of life, improve the body's immune ability, reduce the occurrence of adverse reactions, thereby improving the therapeutic effect.

Keywords: DC-CIK Maintenance Therapy; Chaihulonggumuli Decoction; Non-small Cell Lung Cancer; Quality of Life-verse reactions; cardiovascular events

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1. Introduction

Lung cancer is a common clinical malignant tumor, and more than 85% of it belongs to non-small-cell lung cancer (NSCLC)[1-2]. As early NSCLC has no significant clinical symptoms, it is mostly late at the time of treatment, and the opportunity for surgical treatment is lost. Moreover, surgery is a local treatment, it is difficult to remove all tumor cells of advanced NSCLC, and it is easy to relapse after surgery[3]. With the rapid development of cellular immunology and molecular biology, maintenance biological immunotherapy has been widely used for malignant tumors, which can eliminate subclinical lesions and residual tumor cells[4-5]. Basic research shows that immunotherapy can distinguish tumor cells from normal cell populations, which can promote patients with malignant tumors to have a longer survival period and promote patients with a higher quality of life[6]. DC (dendritic cell) is a cell in the body that stimulates the body's specific immune response by processing, ingesting, and presenting antigens. It can highly express MHC-II/I molecules and costimulatory molecules, and secrete a variety of cytokines. And chemokines, stimulate the body's specific immune response to tumor cells, and promote the activation and proliferation of T cells and B cells[7-8]. Cytokine-induced killer cells have many advantages, such as a broad tumor-killing spectrum, fast proliferation, and high tumor-killing activity. The effector cells are mainly CD3+CD56+ double-positive T cells, which are currently known to have the strongest killing activity[9]. Traditional Chinese medicine treats malignant tumors with emphasis on integrity, which can enhance the body's immune function, inhibit the growth of tumor blood vessels, and can also directly damage the DNA of cancer cells[11-12]. ChaihuLongguMuli Decoction aims to smooth the Qi machine, make the Qi machine smooth, the ratio of yin and yang, the ups and downs orderly, and then the yin, yang, qi and blood are reconciled, promoting the self-healing of the disease[13-14]. This article explored and observed the effect of DC-CIK maintenance therapy combined with traditional Chinese medicine treatment on the improvement of quality of life in patients with advanced NSCLC, in order to clarify the value of biological immunotherapy. The report is as follows.

2. Materials and Methods

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2.1 Research Object

Adopting retrospective summary research method, the research time is from January, 2017 to April, 2018, 89 patients with advanced NSCLC diagnosed and treated in our hospital were selected as the research objects. Inclusion criteria: pathological diagnosis of advanced NSCLC, with measurable or evaluable tumors lesions; according to the international staging standards for lung cancer revised in 2009, the staging is stage III-IV; the expected survival time is greater than 3 months; the hospital ethics committee approved the study; aged from 18 to 75 years old; the patient signed an informed consent; meet the diagnostic criteria of TCM Qi deficiency and blood stasis syndrome; complete clinical data. Exclusion criteria: lack of clinical data; pregnant or breast-feeding women; patients with heart, liver, kidney and other vital organ failure; allergic constitution, allergic to traditional Chinese medicine or biological reagents; patients with central nervous system metastasis; clinical participation in other studies. According to the different treatment methods, they were divided into control group and observation group, with 40 and 49 cases respectively. There was no statistically significant difference in the data in Table 1 between the two groups (P>0.05). See Table 1.

Table 1: Comparison of General Data of Observation Group and Control Group

Group	Number of Cases (n)	Gender(Male/Female)	Age(year)	Pathological Type(Squamous Cell Carcinoma/Adenocarcinoma)	Stage(Stage III/Stage IV)	Course of Disease (Month)	Body Mass Index (kg/m2)
Observation Group	49	29/20	59.14±3.28	28/21	20/29	4.09±0.44	20.33±1.74
Control Group	40	25/15	59.00±5.09	24/16	13/27	4.11±0.28	20.23±1.88
X^2 or t		0.567	0.188	0.036	0.289	0.155	0.413
P		0.555	0.832	0.978	0.813	0.823	0.651

2.2 Treatment Methods

Control Group: DC-CIK was given maintenance treatment, blood was collected from the patient, the lymphatic cells were separated and cultured in vitro. And then DC subcutaneous injection and CIK intravenous infusion were performed, 28 days as a cycle, treatment observation for 2 cycles. DC reinfusion method: subcutaneous injection into the accumulating area, cell number ≧ 5×106 (2mL dilution), injection at 2-3 points, and injection treatment on 7d, 14d, 21d, 28d. CIK reinfusion method: intravenous reinfusion, cell volume> 600×106 (100mL dilution), injection in the cubital vein reinfusion site, 30 drops for min, and reinfusion treatment on 12d, 14d, 16d, 18d, and 20d.

Observation Group: On the basis of the treatment of the control group, the traditional Chinese medicine Chaihulonggumuli Decoction was given orally. The prescriptions were: Bupleurum spp. 10 g, Scutellariae 10 g, Codonopsis 15 g, Guizhi 6 g, Poria 15 g, Pinellia 10 g, Cooked Rhubarb 6 g, Raw Longgu 15 g, oyster 15 g, ochre 20 g, jujube 10 g, dried ginger 3 g, 1 dose/d, decocted in water, divided into two warm servings, 150-200 ml each time, 28d as a cycle, and 2 cycles of treatment observation were carried out.

2.3 Observation Index

(1) Efficacy criteria: complete remission: the tumor lesion disappeared and the maintenance time was ≧ 4 weeks; partial remission: the total length of the tumor lesion was reduced by ≧ 30%, and the maintenance time was ≧ 4 weeks. Stable: the total length of tumor lesions increased but did not worsen or decreased but did not achieve partial remission, and the maintenance time was ≧ 4 weeks. Deterioration: the appearance of new lesions or the total length of tumor lesions increased by >20%, and the maintenance time was ≧ 4 weeks. Complete remission + partial remission / number of cases in the group × 100.0% = total effective rate. (2) Flow cytometry was used to detect the content of peripheral blood T lymphocyte subsets before and after treatment. (3) Record the adverse reactions of the two groups during the treatment period, mainly skin reactions, liver and kidney function reactions, blood system reactions, and digestive tract reactions. (4) To evaluate the quality of life of the two groups of patients before and after treatment, select four indicators of physical strength, sleep, appetite, and weight for comparison. The higher the score, the better the quality of life.

2.4 Statistical Methods

The selected application analysis software is SPSS22.00, and the inspection level is α=0.05.

3.Results

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Table 2: Comparison of Short-term Prognostic Efficacy between the Observation Group and the Control Group (n)

Group	Number of Cases (n)	Deterioration	Stable	Complete Remission	Partial Remission	Total Effective Rate
Observation Group	49	3	11	16	19	35(71.4%)
Control	40	8	15	10	7	17(42.5%)
X^2						7.587
P						0.006

3.1 The Comparison of Short-term Efficacy

In terms of total effective rate, the control group and the observation group were 42.5% and 71.4% respectively, and the rate of the observation group was significantly higher than that of the control group (P<0.05). See table 2.

3.2 The Comparison of Immune Index Changes

After treatment, the CD8+, CD3+ and CD4+ of the control group and the observation group were significantly different before treatment. There was statistical significance (P<0.05). The difference between the two groups after treatment was statistically significant (P<0.05). See table 3.

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

3.3 The Comparison of Adverse Reactions

The adverse reactions during the treatment period of the two groups were mainly liver and kidney function reactions, skin reactions, digestive tract reactions, blood system reactions, etc. There was no statistically significant data comparison between the two groups (P>0.05). See table 4.

3.4 The Comparison of Changes in Quality of Life Scores

The scores of physical strength, weight, appetite, and sleep quality of the observation group and the control group after treatment were higher than those before the treatment. And the Scores of the observation group was also higher than that of the control group. The comparison between the two groups was statistically significant (P<0.05). See table 5.

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

Table 3: Comparison of Changes in Immune Ondex between the Two Groups before and after Treatment (%, mean ± standard deviation)

Group	Number of Cases(n)	CD3+ Before Treatment	CD3+ After Treatment	CD4+ Before Treatment	CD4+ After Treatment	CD8+ Before Treatment	CD8+ After Treatment
Observation Group	49	48.78±2.73	60.32±5.11*^	33.18±2.84	40.11±2.47*^	32.67±2.67	25.13±3.09*^
Control Group	40	48.22±4.57	54.99±4.17*	33.78±2.84	37.44±3.11*	32.14±2.47	28.55±2.47*

Table 4: Comparison of Adverse Reactions between the Two Groups during Treatment (n)

Group	Number of Cases (n)	Liver and Kidney Function Reaction	Skin Reaction	Digestive Tract Reaction	Blood System Reaction
Observation Group	49	4(0.08%)	5(0.10%)	11(0.22%)	8(0.16%)
Control Group	40	5(1.25%)	5(1.25%)	10(0.20%)	9(0.22%)
X^2		0.782	0.562	0.034	0.144
P		0.384	0.513	0.988	0.899

4. Discuss

At present, the most effective method for the treatment of NSCLC is surgery. However, most patients are already at an advanced stage when confirmed and cannot be effectively treated[15]. The treatment of advanced NSCLC is mainly to carry out consolidation therapy or sequential therapy after first-line treatment to better maintain the efficacy, to further extend the survival time and further improve the quality of life. The treatment principle is to maximize the efficacy of killing tumor cells. Try to kill tumor

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Table 5: Comparison of Changes in Quality of Life Scores between the Two Groups before and after Treatment (points, mean ± standard deviation)

Group	Number of Cases (n)	Physical Strength Before Treatment	After Treatment	Body Weight Before Treatment	After Treatment	Appetite Before Treatment	After Treatment	Quality of Sleep Before Treatment	After Treatment
Observation Group	49	45.11±2.74	67.33±5.44*^	37.98±2.77	67.20±4.17*^	41.56±5.72	75.13±6.28*^	48.11±4.58	74.16±5.27*^
Control Group	40	45.09±3.33	54.00±5.15*	38.34±3.48	48.67±5.18*	40.14±5.55	59.33±4.17*	48.22±6.15	56.33±4.38*

cells before the emergence of drug resistance[16].

DC is an important antigen-presenting cell in the body, which is mainly transmitted to the body's immune cells through antigen presentation, and induces a large number of effector T cells, cytokines, secretion of chemokines to play anti-cancer effects[17]. CIK cells are a new type of immunocompetent cells that are simultaneously labeled with CD3 and CD56 and have powerful anti-tumor cell activity. Compared with other NK cells, CIK cells have the ability to dissolve a variety of tumor cells and isolate tumor cells in the body, and will not affect the bone marrow. The hematopoietic function can function normally, and some tumor cells that are resistant to multi-drug resistance can still behave sensitively. It does not require exogenous IL-2. And it will not be affected by immunosuppressive agents[18-19-20]. This study showed that the total short-term effective rates of the observation group and the control group after treatment were 71.4% and 42.5% respectively. The rate of the observation group was significantly higher than that of the control group ($P<0.05$); the adverse reactions during the treatment period of the two groups were mainly liver and kidney function reactions, skin reaction, digestive tract reaction, blood system reaction, etc. There was no statistically significant difference between the comparison of the two groups($P>0.05$). It indicates that the application of DC-CIK maintenance therapy combined with traditional Chinese medicine can improve the treatment effect and reduce the occurrence of adverse reactions. Analyzed from the mechanism, Bupleurum and Scutellaria clears the lungs and resolves phlegm, eliminates phlegm and disperses phlegm, to treat phlegm and dampness; Codonopsis, Guizhi, Poria nourishes the lungs and kidneys, removes the roots of phlegm; Pinellia and Rhubarb are healthy I nvigorate spleen, cultivate soil and produce gold, block the source of phlegm; grow keel, oyster, and replace ocher to make blood stasis and regenerate; jujube, dried ginger detoxify and fight cancer. The combination of various medicines can benefit qi, invigorate the spleen, and remove blood stasis,resolve phlegm, nourish yin and promote body fluid[21-22].

DC-CIK biological immunotherapy is currently the most effective treatment method. Compared with chemotherapy, radiotherapy and surgery, it has many characteristics such as non-cytotoxicity and tropism[23]. Studies have found that DC can also be used as the initiating factor of immune response. After obtaining antigens from peripheral tissues, it gradually matures and enters the secondary lymphatic organs from the blood and (or) lymphatic circulation. It plays a key role in the generation and mediation of tumor immunity[24]. In particular, the co-culture of tumor antigen-sensitized DCs and T cells can increase the anti-tumor activity of T cells, regulate cells to reduce endocytosis and phagocyte receptor activity[25-26]. Tumor immunity is centered on T cell immunity. For CD4+, Th cells play a very important role in the immune response of tumors, and can effectively regulate anti-tumor immunity to achieve a certain therapeutic effect[27]. This study showed that the CD3+, CD4+, and CD8+ values of the observation group and the control group after treatment were significantly different from those before the treatment ($P<0.05$). And the difference between the observation group and the control group after treatment was also statistically significant ($P<0.05$). From a mechanism analysis, Scutellaria baicalensis can inhibit inflammatory exudation and hyperplasia by inhibiting bacteria and fighting toxins, and exert analgesic effects. The keel, Pseudostellaria, and Oyster rise and fall, and the qi mechanism is unobstructed, which can normalize the qi reduction of the lung meridian; Pinellia can relieve phlegm, relieve pain and relieve vomiting[28]. Basic research shows that Chaihu Longgu Muli Decoction can enhance the body's natural immunity by enhancing the phagocytic activity of NK cells. DC-CIK cells can directly kill tumor cells, and have the powerful anti-tumor activity of T lymphocytes, which can regulate the body's immune function and induce tumor cell apoptosis[29].

There are many dendritic protrusions on the surface of DC, which can load certain tumor antigens and present

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them to CIK cells, and can also secrete IL-12 and other cytokines, thereby promoting the anti-tumor activity of CIK. NSCLC belongs to the categories of Chinese medicine such as “pimentia”, “lung accumulation” and “chest pain”. The leading idea of Chinese medicine in adjuvant treatment of advanced NSCLC is to hope to achieve the purpose of eliminating evil by restoring and adjusting the body’s own defense mechanism[30]. The anti-tumor function of Chaihulonggumuli Decoction is mainly reflected in reducing the viscosity of whole blood and inhibiting DNA synthesis of cancer cells[31-32]. This study showed that the scores of physical strength, weight, appetite, and sleep quality of the observation group and the control group after treatment were higher than those before the treatment, and the scores of the observation group was also higher than that of the control group. the difference between the data was statistically significant (P<0.05). Relevant studies have also shown that Chaihulonggumuli Decoction can regulate the tumor-bearing body to a certain extent, and can also enhance the body’s immune function and regulate endocrine function, and improve the body’s immunity[33]. Related studies have also shown that Chaihu Longgumuli Decoction can improve the natural immunity of mice by enhancing the killing activity of NK cells and the phagocytic activity of macrophages; it can also reduce blood viscosity, resist tumor invasion and metastasis, improve microcirculation, and inhibit tumors neovascularization[34-35]. However, this study also has certain shortcomings, and animal studies have not specifically elaborated, an1d will be further analyzed in the next step.

4In short, DC-CIK maintenance therapy combined with traditional Chinese medicine treatment of patients with advanced NSCLC can improve the quality of life, improve the body’s immune capacity, reduce the occurrence of adverse reactions, and thus improve the therapeutic effect.

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