ORIGINAL RESEARCH

Clinical impact of traditional Chinese medicine in combination with chemotherapy in the therapy of extensive-stage small cell lung cancer

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Abstract

Objective

We investigated the clinical impact of traditional Chinese medicine in combination with chemotherapy in treating extensive-stage small cell lung cancer. Methods: One hundred and two patients admitted to our hospital from October 2022 to August 2023 were included. The control group received irinotecan hydrochloride for injection. On the basis of the control group, the study group was given Kangai injection.

Results

The objective response rate and clinical benefit rate values of the study group presented higher than the control group, the decline of tumor markers was more obvious, the levels of CD4+ and CD4+/CD8+ were higher, the CD8+ level was lower. Incidence of adverse drug reactions in the study group (7.84%) presented reduction as relative to the control group (25.49%). After therapy, the elevation of quality of life score was more obvious in the study group as relative to the control group.

Conclusion

Traditional Chinese medicine in combination with chemotherapy can promote the short-term efficacy, reduce the levels of tumor markers, regulate the immune function of patients, lessen the occurrence of adverse reactions, along with help promote the quality of life of patients with extensive-stage small cell lung cancer.

Keywords: Small cell lung cancer, Chemotherapy, Traditional Chinese medicine, Kangai injection, Immune function

Introduction

As one of the most frequent malignant tumors, the incidence of lung cancer is increasing year after year because of the negative influence of modern people's bad living habits and surrounding environment[1]. According to the Global Cancer Statistics Report 2020, there are 2.2 million new lung cancer cases and 1.79 million deaths worldwide, and the disease burden is relatively serious[2]. At the same time, lung cancer belongs to also one of the most frequently occurring cancer diseases in China, and it is a difficult point in our country's cancer prevention and control[3].

Small cell lung cancer (SCLC), a kind of lung cancer tissue, originates in the bronchus and grows along the bronchial wall mucosa into the lumen, accounting for about 10% of all lung cancer[4]. It is characterized by high malignancy, rapid reproduction, and strong invasion ability[5]. The main treatment means is comprehensive chemoradiotherapy, and there has been no significant progress in drug therapy in recent 30 years[6]. At present, the treatment decision staging of SCLC follows the method of the American Veterans Lung Cancer Association: it is divided into the local period and the extensive period[7]. Due to the insidious onset of SCLC, complex pathogenesis, lack of typical clinical signs and specific manifestations in the early stage, and lack of attention to disease prevention and screening, most patients have already had distant metastasis at the time of diagnosis, which is classified as extensive stage SCLC (ES-SCLC)[8]. The prognosis of ES-SCLC patients is unsatisfactory, with a median overall survival of only 9-11 months and progression-free survival of less than 6 months and 2-year survival rate of less than 5%[9]. So far, the treatment of ES-SCLC is single, and surgery can only be performed for a few limited-stage patients[10]. Chemotherapy is still the cornerstone of treatment for ES-SCLC[11]. For first-line chemotherapy for ES-SCLC, platinum-based dual-agent chemotherapy (etoposide/Irinotecan + platinum) is recommended[12]. Although the clinical effective rate of first-line standard chemotherapy regimen for ES-SCLC can reach 50%-90%, the overall survival time along with disease-free survival time of ES-SCLC patients are not ideal, less than 2% of patients survive more than 5 years, and most patients are prone to relapse of drug resistance after chemotherapy[13].

As a crucial part of Chinese medicine, traditional Chinese medicine (TCM) has exerted a significant function in treating ES-SCLC with its characteristics of syndrome differentiation and holistic concept[14]. In the process of participating in chemotherapy, TCM can effectively play a role in decreasing toxicity and promoting efficiency, improving clinical symptoms, and improving patients' quality of life[15]. Modern medicine has proved that TCM can control the development of tumors by regulating the internal balance of immune cells, changing the tumor microenvironment, activating the active function of immune cells, and reversing the phenotypic polarization of immune cells[16]. Other studies have pointed out that TCM combined with platinum drugs in treating

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advanced lung cancer can reverse platinum resistance, reduce toxic side effects, and then enhance the efficacy to achieve the effect of synergistic treatment[17].

Therefore, this study was designed to explore the efficacy as well as safety of TCM in combination with chemotherapy in treating ES-SCLC, to offer data support for clinical application.

Methods

General data

One hundred and two patients with ES-SCLC admitted to our hospital from October 2022 to August 2023 were chosen, followed by dividing into study group (SG) and control group (CG) according to different treatments, with 51 cases in each group. The CG contained 31 males and 20 females, aged 33~74 years, with an average age of (58.62±15.62) years. The SG contained 32 males and 19 females, ranging in age from 31 to 76 years, with an average age of 58.78±15.72 years. No difference was seen in general data between 2 groups (P>0.05).

Inclusion criteria: (1) SCLC diagnosed pathologically or histologically according to Western diagnostic criteria; (2) Patients who were initially diagnosed with an extensive stage and did not receive prior treatment; (3)

Patients received standard chemotherapy and TCM treatment. Exclusion criteria: (1) Patients with serious lack of medical history data; (2) Patients had other primary tumors; (3) Patients with symptomatic brain metastases and bone metastases requiring simultaneous radiotherapy; (4) Patients with serious diseases of the heart, liver, kidney, blood and other systems.

Treatments

In the CG, irinotecan hydrochloride for injection (Manufacturer: Jiangsu Hengrui Pharmaceutical Company, Specification: 100 mg/piece) was injected intravenously, 350 mg/m2 of irinotecan hydrochloride was dissolved into 100 mL of normal saline, and the administration was completed in 60 minutes. At the same time, carboplatin for injection (Manufacturer: Qilu Pharmaceutical Co., LTD., specification 0.1 g) was injected intravenously at a dose of 5× (creatinine clearance +25), dissolved into 5% glucose 250 mL, and the administration was completed in 60 minutes.

On the basis of the CG, the SG was given Kangai injection, 40 mL of Kangai injection was dissolved in 250 mL of normal saline. The course of treatment was 10 days, repeated every 21 days. Patients in both groups underwent 6 courses.

Observation indicators

(1) Chest CT was re-examined every 2 courses of chemotherapy to evaluate the changes of lung tumors. The efficacy was evaluated according to WHO standards. Complete response (CR): all target lesions disappeared; Partial response (PR): Target lesion reduction ≥30%; Stable disease (SD): the target lesion had a reduction but not PR or an increase but not disease progression (PD); PD: New lesions or target lesions increased by ≥20%. Objective response rate (ORR) = (CR+PR)/total cases. Clinical benefit rate (CBR) = (CR+PR+SD)/total cases.

(2) Tumor markers: Fasting peripheral blood of patients was collected in the morning to detect the levels of carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199) along with carbohydrate antigen 125 (CA125).

(3) Immune function: Fasting venous blood of 2 groups was collected, and CD4+ and CD8+ were measured by FACSCalibur flow cytometer (BD Company of the United States), and CD4+/CD8+ was calculated.

(4) The incidence of adverse drug reactions, including myelosuppression, thrombocytopenia, diarrhea along with neutropenia was recorded in 2 groups.

(5) The score of Generic Quality of Life Inventory-74 (GQOLI-74) was compared between 2 groups 18, which contained 4 dimensions of social function, psychological function, physical function, wlong with material life status. The higher the score of patients, the better the quality of life was.

Table 1 Clinical efficacy in 2 groups

Groups	Cases	CR	PR	SD	PD	ORR	CBR
Control group	51	10	21	10	10	31 (60.78%)	41 (80.39%)
Study group	51	20	22	7	2	42 (82.35%)	49 (96.08%)
χ^2						5.83	6.04
P						0.01	0.01

Table 2 Incidence of adverse drug reactions in 2 groups

Groups	Cases	Myelosuppression	Thrombocytopenia	Diarrhea	Neutropenia	Total incidence rate
Control group	51	3	3	4	3	13 (25.49%)
Study group	51	1	1	1	1	4 (7.84%)
χ^2						5.72
P						0.02

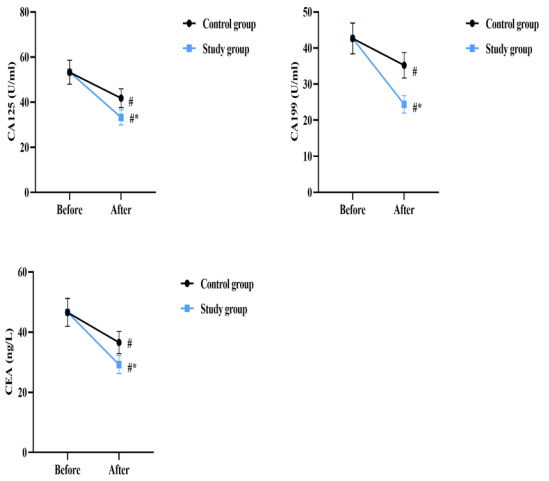

Figure 1 Levels of tumor markers in 2 groups. In comparison with before therapy, # meant P<0.05. In comparison with CG, * meant P<0.05.

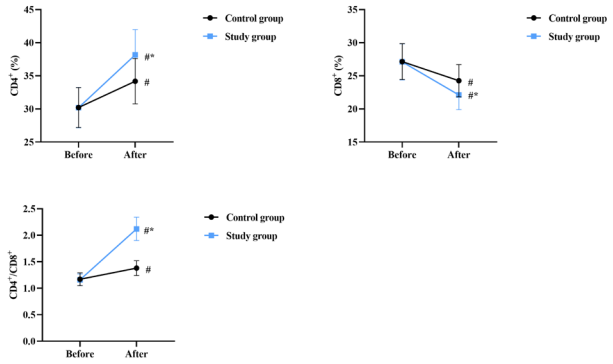

Figure 2 Immune function in 2 groups. In comparison with before therapy, # meant P<0.05. In comparison with CG, * meant P<0.05.

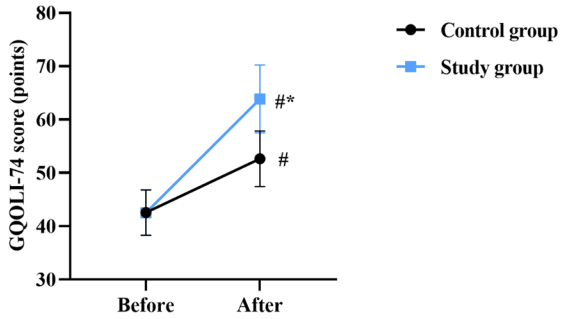

Figure 3 Quality of life in 2 groups. In comparison with before therapy, # meant P<0.05. In comparison with CG, * meant P<0.05..

Statistical analysis

SPSS 24.0 statistical software was adopted for data analysis. Measurement data were exhibited to be (x±s), and t-test was adopted for comparison. Count data were exhibited to be (n, %), and χ2 test was implemented for comparison. P<0.05 meant statistical significance.

Results

Clinical efficacy in 2 groups

In the CG, the ORR was 60.78%, CBR was 80.39%. In the SG, the ORR was 82.35%, CBR was 96.08%. The ORR and CBR values of the SG presented higher as comparing with the CG (P<0.05, Table 1).

Levels of tumor markers in 2 groups

Prior to therapy, no difference was seen in levels of CA125, CA199 along with CEA between 2 groups (P>0.05). After therapy, CA125, CA199 long with CEA levels were declined in 2 groups, and the decline was more obvious in the SG as comparing with the CG (P<0.05, Figure 1).

Immune function in 2 groups

Prior to therapy, no difference was seen in CD4+, CD8+ long with CD4+/CD8+ levels between 2 groups (P>0.05). After therapy, the levels of CD4+ and CD4+/CD8+ were elevated in both groups, whereas CD8+ level was decreased. Compared with the CG, the levels of CD4+ along with CD4+/CD8+ in the SG presented higher after treatment, and the CD8+ level was lower (P<0.05, Figure 2).

Incidence of adverse drug reactions in 2 groups

Table 2 displayed the incidence of adverse drug reactions in the SG (7.84%) presented reduction as comparing with the CG (25.49%) (P<0.05).

Quality of life in 2 groups

Prior to therapy, no difference was seen in GQOLI-74 score between 2 groups (P>0.05). After therapy, the GQOLI-74 score was elevated in 2 groups, and the elevation was more obvious in the SG (P<0.05, Figure 3).

Discussion

Lung cancer belongs to one of the most frequent malignant tumors in our country, among which SCLC accounts for about 15%[19]. According to the American veteran staging standard, it can be divided into local period and the extensive period[20]. Due to the high degree of malignancy, rapid growth and poor prognosis of SCLC, more than 2/3 of patients with SCLC are in the extensive stage at the time of treatment[21]. Chemotherapy is the standard therapy for ES-SCLC[22].

As a DNA topoisomerase I inhibitor, irinotecan can prevent topoisomerase I from linking DNA by forming a firm complex with topoisomerase I and DNA, causing irreversible DNA single strand break, hindering DNA replication and synthesis, and ultimately leading to tumor cell death[23]. Irinotecan is currently widely used for treating rectal, gastric along with small cell lung cancers[24]. Carboplatin is the second generation of platinum drugs, belonging to cell cycle non-specific drugs[25]. By acting on guanine of DNA, DNA molecules are destroyed, thus interfering with DNA synthesis, and finally producing cytotoxic effects[26]. Myelosuppression is the main toxic side effect of carboplatin[27]. Delayed diarrhea and neutropenia are the main adverse effects of irinotecan, which limits its clinical use[28].

TCM believes that the essence of the tumor is "positive deficiency", both positive and evil qi throughout the tumor development, when the patient's body positive energy is insufficient, the evil qi is extremely easy to invade the body, resulting in phlegm coagulation, heat toxicity, qi stagnation, wet accumulation, blood stasis and other symptoms appear at the same time, aggregate in the body, and form a tumor over time[29]. When patients receive chemotherapy treatment, tumor cells will be killed, and normal cells will also be killed, resulting in the failure of the patient's organs, deficiency of healthy qi, and inability to resist evil[30]. Therefore, in TCM, the treatment of tumor is mostly based on the principle of supporting the healthy energy[31].

Kangai injection is composed of astragalus, ginseng and matrine[32]. The main components of astragalus include

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astragalus polysaccharide, which can improve the activity of macrophages, improve the immunity of patients, induce diuresis to alleviate edema, tonify qi and strengthen the immune system, improve hematopoietic function and promote the development of bone marrow cells [33]. Matrine and ginseng are mainly used in patients with qi and blood deficiency, lung qi deficiency, which can strengthen qi, nourish stomach and spleen and blood[34,35]. The combination of the three can strengthen spleen and tonify qi, support the healthy energy and enhance the therapeutic effect[36].

In our study, it was discovered that after therapy, the ORR together with CBR values of the SG presented higher as comparing with the CG, the decline of CA125, CA199 and CEA was more obvious in the SG as comparing with the CG, suggesting that Kangai injection in combination with chemotherapy could promote the short-term efficacy along with reduce the levels of tumor markers of patients with ES-SCLC. Consistently, Zhu et al. have conducted a meta-analysis to prove that the combination treatment of Kangai injection and platinum-based chemotherapy is more conductive to advanced non-small-cell lung cancer patients as comparing with chemotherapy alone, which can significantly promote the clinical efficacy[37].

Besides, our study also manifested that after treatment, compared with the CG, the levels of CD4+ along with CD4+/CD8+ in the SG presented higher after treatment, whereas the CD8+ level was lower, suggesting that Kangai injection in combination with chemotherapy could promote the immune function of ES-SCLC patients, which was in accordance with previous studies[38].

In addition, our study indicated that the incidence of adverse drug reactions in the SG (7.84%) presented reduction as comparing with the CG (25.49%), and the elevation of GQOLI-74 score was more obvious in the SG as comparing with the CG, implying that Kangai injection combined with chemotherapy could decrease the adverse drug reactions and promote the quality of life of patients with ES-SCLC. Consistently, Wu et al. have proposed that Kangai injection in combiantion with concurrent chemoradiotherapy has a better impact on promoting performance status as well as repressing adverse reactions against nasopharyngeal carcinoma[39].

Conclusion

TCM in combination with chemotherapy can promote the short-term efficacy, reduce the levels of tumor markers, regulate the immune function of patients, decrease the occurrence of adverse reactions, along with help promote the quality of life of ES-SCLC patients.

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