Effect of TCM Combined with Chemotherapy on Immune Function and Quality of Life of Patients with Non-small Cell Lung Cancer in Stage III-IV

YANG Zu-yi (杨祖贻), WU Xue-mei (吴雪梅), OU Ya-long (欧亚龙), YU Ping (余萍), LUO Jie (罗洁), and SONG Xiu-yun (宋秀云)

ABSTRACT  Objective: To observe and compare the effect of traditional Chinese medicine (TCM) combined with chemotherapy (CT) on immune function and quality of life (QOL) of patients with non-small cell lung cancer (NSCLC) in stage III-IV. Methods: One hundred cases with stage III-IV NSCLC were randomly divided into two groups. The treated group (n=50) received CT combined with TCM, and the control group received CT alone. The percentage of T lymphocyte subset in peripheral blood and the change of natural killer (NK) cell count were observed after treatment. The QOL and tolerance of CT were also compared between the two groups after treatment. Results: In the treated group, CD3 cell count, CD4 cell count, CD4/CD8 ratio and NK cell activity were higher than those in control group, while CD8 cell count in the treated group was lower than that in the control group (P<0.05), and QOL and tolerance of CT in the treated group were also better (P<0.05). Conclusion: TCM combined with CT could raise the patients' ability in tolerating CT in stage III-IV NSCLC.

KEY WORDS non-small cell lung cancer in stage III-IV, traditional Chinese medicine combined with chemotherapy, immune function, quality of life

When comprehensive treatment is given to tumor patients, how to effectively control the development of local tumor, and also how to elevate the immune function, the quality of life (QOL), the tolerance of the patients to chemotherapy (CT) should be considered. Therefore, in designing the comprehensive therapeutic regimen of tumor, the problem of protecting and elevating the patients' immune function, improving and raising the patients' QOL, strengthening the patients' tolerance to tumor treatment attracts more and more attention. In the above-mentioned aspect, TCM possesses unique function.

The T lymphocyte subset percentage in peripheral blood and natural killer (NK) cell count are the appropriate parameters in judging immune function of tumor patients. In the course of routine tumor treatment, determining the T lymphocyte subset and NK cell count could provide a basis for multiple aspects such as selecting different treating modality for clinicians, but at the same time, it was of vital significance to pay attention to such aspects as the prognosis judgment, therapeutic effect observation, assessment of the patients' tolerance to the treatment, and the effect of treatment regimen to the patients' QOL. The present study was a multicentric randomized and controlled clinic trial on 106 patients with III-IV stage non-small cell lung cancer (NSCLC) from Sichuan Provincial Tumor Hospital, Clinical Medicine College of Chengdu University of TCM, and Affiliated Hospital to Sichuan Academy of TCM, in order to observe and compare the effect of TCM combined with CT and that of CT alone on the immune function, QOL and the tolerance to CT of III-IV stage NSCLC, the result is reported as follows.

METHODS

Patients' Inclusion Criteria

(1) The patients were pathologically and cytologically confirmed as NSCLC patients; (2) According to International Union against Cancer (UICC) TNM staging, all the cases belong to T3-4, N1-3, M0-1 or P3-4, PNI-a, PM0-1 (III-IV stage); (3) They were of

1. Sichuan Tumor Hospital, Chengdu (610041), China; 2. Clinical Medicine College, Chengdu University of TCM; 3. Affiliated Hospital to Sichuan Academy of TCM
Correspondence to: YANG Zu-yi, Tel: 028-85420351, Fax: 028-85553169, E-mail: chianghm@163.com
ages of 20–70 years old; (4) Their general condition scoring KPS ≥ 60 points; (5) Granulocyte ≥ 4.0 × 10⁹/L, platelet ≥ 100 × 10⁹/L, hemoglobin (Hb) ≥ 90 g/L; (6) Their heart, liver, kidney function were basically normal (SGPT, SGOT, SCr, BUN increase did not exceed the normal upper limit of 1.5 times); (7) The patients had had no CT administration in recent 3 months, and never used immune preparations; (8) Expected survival period more than 3 months.

**Patients' Exclusion Criteria**

(1) I - II stage NSCLC patients who could carry on and were willing to accept surgical operation for treatment; (2) Pregnant and lactation women; (3) Those with apparent heart, liver and kidney dysfunction, diabetes mellitus, and with hematological diseases; (4) With non-tumor immunodeficiency disorders; (5) Those having used immune preparation recently.

**Exclusion Criteria of Patients during the Course of Treatment**

(1) Their CT program did not comply with the present protocol; (2) Those who were unable to complete the clinical study; (3) In the experimental period, other regimens that affect the immune function agent has been used.

**Experiment Design**

The present experiment started from March 1999 to August 2003, Sichuan Tumor Hospital, Clinical College of Chengdu University of TCM, and Affiliated Hospital to Sichuan Academy of TCM accomplished 46, 40 and 20 cases respectively, altogether 106 cases. The method of simple randomization was used to divide the patients into treated and control group, each 53 cases, TCM plus CT were given to the treated group, while CT alone was given to the control group. Besides, 50 healthy subjects were selected as healthy normal control group, who were chosen from healthy volunteers of 20–70 years old, male 38 and female 12 cases, mean age 54.6 years old.

**General Data**

The present study included 106 patients, and with 6 cases excluded because of the question of compliance (3 cases in the treated and the control group each), 100 cases were included in the evaluation of immune function and QOL evaluation, male 72 cases and female 28 cases; ages 28–70 years old, mean 56.3 years. According to staging criteria of UICC in 1997: In III A stage 32 cases, in III B stage 40 cases, and in IV stage 28 cases. Among them, squamous cancer were in 31 cases, adeno-carcinoma in 53 cases, large cell cancer in 7 cases, and adeno-squamous cancer in 9 cases. Comparison of the treated and the control group in sex, age, pathological type, clinical staging, and KPS scoring showed insignificant difference (P > 0.05).

**Treatment Method**

Regimen of CT is composed of NVB 40 mg/m² d₁₋₈, DDP 50 mg/m² d₁₋₈, or GEMZ 1.2/m² d₁₋₈, and DDP 50 mg/m² d₁₋₃. Treated group and control group both used the same CT regimen and the same dose, 21 days as one cycle, and consecutively 2 cycles were used. The treated group on CT d₁₋₈ Astragalus injection (Chengdu Diaojiu Hong Pharmaceutical Factory produced, 10 ml/amp) 60 ml was given through intravenous dripping, once a day, Shenmai injection (Ya'an Sanjiu Pharmaceutical Co., Ltd., 10 ml/amp) 60 ml was given through intravenous dripping, once a day, and at the same time TCM (Asiabell root 30 g, Milkvetch root 30 g, Indian bread 20 g, Bighead Atractylodes 15 g, Angelica root 15 g, Chuanxiong rhizome 12 g, Prepared Rehmannia root 15 g, White Peony root 30 g, Licorice 10 g, Barbary Wolfberry fruit 20 g, Chinese Dates 15 g, Dodder seed 15 g) was also given orally, 1 dose daily.

Other treatment: (1) According to practical condition, hydrolyzed, anti-emetic agents and other symptomatic treatment