Original Article

Adjuvant Effects of Fermented Red Ginseng Extract on Advanced Non-Small Cell Lung Cancer Patients Treated with Chemotherapy*

JIANG Shu-long1,2,△, LIU Hong-jie3,△, LIU Zhao-chun1, LIU Ning4, LIU Rui5, Young-Reep Kang6, Joong-Gu Ji6, ZHANG Chao3, HUA Bao-jin†, and Shin-Jyung Kang®

ABSTRACT Objective: To investigate the adjuvant therapeutic effects of fermented red ginseng (FRG) extract on non-small cell lung cancer (NSCLC) patients treated with chemotherapy. Methods: A total of 60 patients with advanced NSCLC were assigned to two groups using a random number table, i.e., the gemcitabine plus cisplatin (GP) chemotherapy alone group (26 patients) and the FRG + GP chemotherapy group (34 patients), for 60-day treatment. Patients were then assessed according to the Fatigue Symptom Inventory, Chinese medicine symptoms score, Self-Rating Anxiety Scale, Self-Rating Depression Scale, Karnofsky Performance Status Scale, and Functional Assessment of Cancer Therapy-Lung. In addition, chemotherapy toxicity and tumor biomarkers were measured. Results: For NSCLC patients after chemotherapy, FRG extract significantly improved the FSI score, CM symptoms score, psychological status, physical conditions, and quality of life and reduced chemotherapy toxicity (P<0.01), but the expression levels of carcinoembryonic antigen, cytokeratin-19 fragments, and neuron-specific enolase were not significantly different between the chemotherapy alone and the FRG + chemotherapy groups or between pre- and post-treatments (P>0.05). Conclusions: This study demonstrated that FRG extract had an adjuvant effect on advanced NSCLC patients treated with chemotherapy. Further studies with a larger sample size will verify the current findings.

KEYWORDS Lung cancer, Korean red ginseng, fermented red ginseng extract, chemotoxicity, tumor adjuvant therapy, Chinese medicine

Lung cancer was one of the most commonly diagnosed cancers and the leading cause of cancer-related death in the world in 2008, accounting for 1.6 million new cancer cases and 1.4 million deaths. In China, lung cancer rate is increasing significantly, although the incidence is decreasing in most Western countries. Non-small cell lung cancer (NSCLC) accounts for 75%–80% of all lung cancers; and the five-year survival rate is still only 8%–15% because most lung cancer patients are diagnosed at the advanced stages of disease, at which curable surgery is impossible, while chemotherapy and radiotherapy are ineffective in curing the disease.

Most recently, targeted therapy may lead to a bright future for lung cancer patients. To date, more than half of surgical patients will develop postoperative tumor recurrence and distant metastasis and require nonsurgical management. Moreover, the most effective chemotherapy for advanced NSCLC has only a 30% remission rate, and complete clinical remission is rare. The reason may be that intolerance of chemotherapy induces toxicity in patients; thus, adjuvant treatment of these NSCLC patients after chemotherapy could reduce chemotoxicity but improve the effects of chemotherapy and the quality of life.

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1. Department of Oncology, Guang’anmen Hospital, China Academy of Chinese Medical Sciences, Beijing (100053), China; 2. Department of Oncology, Jining First People’s Hospital, Jining, Shandong Province (272000), China; 3. School of Medicine, Jinan University, Guangzhou (510632), China; 4. Institute of International Education, Shandong University of Traditional Chinese Medicine, Jinan (250000), China; 5. Industry-Academic Cooperation Foundation (IACF), Joongbu University, Daejeon (990007), Republic of Korea; 6. Department of Oriental Health Care, Joongbu University, Daejeon (990007), Republic of Korea; 7. Department of Stomatology, Jining First People’s Hospital, Jining, Shandong Province (272000), China; 8. Department of Herbal Pharmaceutical Science, Joongbu University, Daejeon (990007), Republic of Korea

These two authors contributed equally to this work

Correspondence to: Prof. Shin-Jyung Kang, Tel: 82-41-7506720, Email: sjkang@joongbu.ac.kr; Prof. HUA Bao-jin, Tel: 86-10-88001192, E-mail: huabaojin@sohu.com

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Towards this end, ginseng is one of the most valuable herbs and has been used for more than 5,000 years in Chinese and Oriental medicines. It has been used as a treatment drug and nourishing medicine in many countries, including China, Japan, and Korea.\(^{\text{(7)}}\) There are two types of ginseng: white ginseng produced by sun drying and red ginseng (RG) produced by steaming and drying. RG is the most common form in traditional Korean medicine. The production process of RG includes infiltration, cleaning, sorting, steaming, and drying. Chemically, ginseng has a complex composition, including ginsenoside, saponins, polysaccharides, volatile oils, trace elements, and others. The main active ingredient in ginseng is ginsenoside, which accounts for 4%–7% of ginseng ingredients. In the early 1960s, the total saponins were first extracted from ginseng root and named as ginsenosides Rx. Using the relative front (Rf) values of thin layer chromatography, ginsenosides Rx were separated from low to high separations and named as ginsenoside R0, Ra1, Ra2, Rb1, Rb2, Rb3, Rc, Rd, Re, Rf, Rg1, Rg2, Rhl, etc. The fundamental skeleton of ginsenosides is a dammarane-type tetracyclic triterpene; more than 25 dammarane-type saponins have been identified to date.\(^{\text{(8)}}\) Pharmacologically, the activities of ginsenosides are extremely broad, e.g., modulating activities in the human central nervous, cardiovascular, immune, and digestive systems, and affecting bodily anabolic and gonadal functions.\(^{\text{(9)}}\)

In this study, we collaborated with researchers from Korea Joongbu University to explore the adjuvant effects of fermented red ginseng (FRG) extract on NSCLC patients treated with chemotherapy.

### METHODS

#### Study Population

Sixty patients with pathologically diagnosed NSCLC were enrolled from the Department of Oncology, Jining First People’s Hospital (Jining, Shandong, China) between April 2011 and December 2012. This study was approved by the Review Board of Jining First People’s Hospital, and each patient signed an informed consent form. In this study, the patients were randomly divided into the FRG + chemotherapy group (34 patients) and the chemotherapy alone group (26 patients) using a random number table method and treated for 60 days.

Medical staff working in this study was unaware of patients’ group allocations. The schematic diagram of this study process is summarized in Figure 1.

![Figure 1. Schematic Diagram of the Study Process](image)

#### Treatment Protocol

FRG extracts were obtained from Korea Joongbu University (Seoul, Korea, No. 081005). The study group contained 34 patients who received 3,000 mg of FRG extract daily for 60 days, and the first dose was given 7 days before chemotherapy. On the 1st day and the 60th day of FRG administration, the observation indices were accurately recorded in a clinical observation table. Both groups of patients were treated with gemcitabine (1.0 g/m\(^2\), days 1 and 8) plus cisplatin (25 mg/m\(^2\), days 1 to 3) chemotherapy every 3 weeks for 60 days. Questionnaires including the Fatigue Symptom Inventory (FSI), Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), Chinese medicine (CM) symptoms, Karnofsky Performance Status Scale (KPS), and Functional Assessment of Cancer Therapy-Lung (FACT-L) were used to assess the effects of FRG on lung cancer patients.

#### Self-Test Fatigue Assessment

FSI, which is a 14-item questionnaire, was utilized to measure fatigue.\(^{\text{(10)}}\) The FSI was designed to evaluate fatigue frequency and severity, perceived interference associated with fatigue, the daily pattern of fatigue for a week, the degree of fatigue, the influence of fatigue on the QOL, and fatigue duration in the last week. The scores were recorded before and after treatment.

#### CM Syndrome Degree

CM symptoms questionnaire was used to measure cough, bloody sputum, fever, chest pain,