Clinical effect of Kanglaite Injection combined with paclitaxel in the management of aged patients with advanced NSCLC

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[Abstract] Objective: To investigate therapeutic effect and toxic and side reaction of Kanglaite Injection (KLT) combined with paclitaxel in treating aged patients with advanced NSCLC Methods: Paclitaxel domestically manufactured 200mg/m², iv drip, d1; Kanglaite Injection (KLT), 200ml/d, iv drip, for 15 days and repeated every 21 days. Therapeutic effect was evaluated after the second and the forth cycle respectively. Results: 30 cases were evaluated in therapeutic effects and toxic and side reaction with CR 1 case and PR 12 cases after 2 cycles, response rate: 43.7%; CR 3 cases, PR 13 cases after 4 cycles, response rate: 44.3% Conclusion: KLT combined with paclitaxel presented better effect to treat aged patients with advanced NSCLC and patient quality of life got elevated, survival period prolonged and toxic and side reaction better tolerated.

[Key words] Kanglaite Injection; Paclitaxel, Combination therapy; Advanced NSCLC

Foreword
Pulmonary carcinoma is a disease severely threatening health and life of human being and currently one of the most common malignant tumors. 70-80% NSCLC patients are already advanced when diagnosed and thus lose opportunity of surgical operation. Along with marketing of new anticancer drugs in recent years there has been new progress in chemotherapy of aged patients with advanced NSCLC. Based on characteristics of biophysical metabolism of aged patient, 32 cases with advanced NSCLC were treated by KLT combined with paclitaxel in our hospital from Aug. 2000 to Aug. 2003 to investigate therapeutic effect and toxic and side reaction with the following report.

1. Materials and methods
1.1 Clinical data
All 32 cases were in-patient at our hospital. Age: 70-83 years, median age: 73 years, male: 24 cases, female: 8 cases. All were evaluative and pathologically or histologically confirmed stage IIIb or IV advanced NSCLC with squamous carcinoma 23 cases, adeno carcinoma 9 cases; stage IIIb 21 cases, stage IV 11 cases; first visit 18 cases, return visit 14 cases; metastasis at supraclavicular lymph nodes 26 cases, at mediastinum 10 cases, at intra-lung 6 cases, at bone 5 cases, at pleura 5 cases, at pericardium 5 cases and at liver 3 cases. All return visit patients had completed radiation therapy or chemotherapy one month ago with normal blood routine, EKG and hepatic and renal functions.

1.2 Treatment methods
Paclitaxel domestically manufactured 200mg/m² added into 5% 500ml glucose injection, iv drip for 3 hours, d1, dexamethasone 10mg orally taken 12 hours and 6 hours respectively before
treatment, diphenhydramine 10mg, im and cimetidine 400mg, iv, 30 minutes before therapy to prevent allergic reaction; antiemetic ondansetron applied as routine prior to the treatment. KLT was administered as 200ml/d, iv drip for 15 days and repeated every 21 days. Therapeutic evaluation was made after the second and the forth cycle.

1.3 Observing indications
1.3.1 Objective response
Based on Response Evaluation Criteria in Solid Tumor (RECIST 2000) objective response was divided into CR, PR, SD and PD with CR+PR as total response rate.

1.3.2 Disease-related symptoms
Based on the WHO criteria for evaluation to observe patient changes after treatment in appetite, fatigue, cough, dyspnea, hemoptysis and pain.

1.3.3 Toxic and side reaction
Observation and determination were based on the WHO performance and grading criteria in acute and sub-acute toxicity of anticancer medicine. 0-4 degrees were divided.

2. Results
2.1 Clinical responses
Among 32 cases to be treated for 2 cycles (42 days) CR 1 case, PR 12 cases, SD 15 cases and PD 3 cases with CR+PR 43.7%. Response rate in first visit patients was 42.8% and 36.9% in return visit patients with 2 cases quitted due to progressive disease. 30 cases were evaluative for survival period and median survival time was 10.8 months (5-18 months). After 4 cycles (84 days) treatment, CR 2 cases, PR 13 cases, SD 13 cases and PD 2 cases with CR+PR 44.3%. Response rate in first visit patients was 45.8% and in return visit patients 39.5%. 28 cases were evaluative for survival period and median survival time was 12.2 months (7-24 months).

2.2 Disease-related symptoms
From follow-up after 2 cycles (42 days) of treatment 29 cases had symptom improved, accounting for 90.6% of the total, among whom 12 cases got appetite improved, 14 cases had mental state on the mend, 6 cases had cough relieved, 12 cases got dyspnea reduced and 8 cases had pain relieved. 23 patients had symptom improved within 2 weeks after treatment and 2 cases did not get symptom relieved. From follow-up after 4 cycles (84 days) of treatment 2 from 32 cases quitted due to progressive disease and 28 cases had symptom improved, accounting for 93.4% of the total, among whom 12 cases had appetite improved, 14 cases got mental state on the mend, 6 cases had cough relieved, 12 cases got dyspnea reduced and 8 cases had pain relieved. 2 cases did not get symptom improved.

2.3 Impact on Karnofsky score
Generally Karnofsky Performance Status (KPS) got 10-20 scores increased after treatment. From follow-up after 4 cycles (84 days) of treatment KPS got 20-30 scores elevated as compared with
those before treatment.

2.4 Toxic and side reaction
Toxic and side reaction in the whole group was comparatively slight. White cell reduction was major hematological toxicity with incidence after 2 cycles as 40.3% (grade III-IV accounting for 4.2%) and incidence after 4 cycles as 62.9% (grade III-IV accounting for 6.1%). Incidence of nausea and vomit was 13.2% and all were grade I-II. All patients had alopecia to a certain extent and 23.2% patients had pain in muscles or joints. However there was no allergic reaction among all cases.

3. Discussion
Due to its unapparent symptom pulmonary carcinoma could not be detected at early stage and most patients thus lose opportunity of operation. Along with increase in age and decrease in immunological function senile patients could not tolerate two-drug or three-drug combination chemotherapy. Platinum regimens bring dose-limited bone marrow inhibition and side reaction in digestive tract. Therefore it has been an urgent subject to select proper regimen and dosage suitable for aged cases. In recent years paclitaxel has been clinically used to treat pulmonary carcinoma especially NSCLC with acceptable therapeutic effect. Paclitaxel, a drug of anti-microtubule, has action on microtubule-tubulin system of cancer cells to promote microtubule polymerization, stop cytodiaeresis before G-M phase and also induce cell apoptosis [1].

According to report from ECOG, USA response rate of single dose paclitaxel in treating NSCLC was 28.8% [1] with lower toxic and side reaction and effective to drug resistant cases. Response rate was 22.0-47.0% if it was combined with platinum drug [2]. Kanglaite Injection (KLT) is an emulsion with anticancer active ingredient extracted from semen coicis by high-technology. KLT can improve body immune function, unspecific ability to resist diseases and survival quality. In this study response rate of KLT combined with paclitaxel reached 43.7% (2 cycles) and 44.3% (4 cycles). Median survival time was 10.8 months after 2 cycles (5-18 months) and 12.2 months after 4 cycles (7-24 months) with both therapeutic effect and patient tolerance apparently better than those from single-dose treatment regimen. Major toxic and side reaction were bone marrow inhibition and reaction in digestive tract caused by chemotherapy. Tissue and organs of senile patient have retrograde and organic affection to influence drug metabolism and reduce hematopoietic function of bone marrow so as to limit patient treatment. Supportive treatment remarkably reduces life quality and survival period [3]. This study had less case number and was not a randomized comparative trial so further study involving more cases shall be necessary.

References
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