

## RESEARCH ARTICLE

# Clinical Safety and Efficacy of Kanglaite® (Coix Seed Oil) Injection Combined with Chemotherapy in Treating Patients with Gastric Cancer

Yi-Ping Zhan<sup>1,2</sup>, Xin-En Huang<sup>1\*</sup>, Jie Cao<sup>1</sup>, Yan-Yan Lu<sup>1</sup>, Xue-Yan Wu<sup>1</sup>, Jin Liu<sup>1</sup>, Xia Xu<sup>1</sup>, Jin Xiang<sup>3</sup>, Li-Hong Ye<sup>2\*</sup>

### Abstract

**Objective:** To observe efficacy and side effects, as well as the impact on quality of life, of Kanglaite® (Coix Seed Oil) injections combined with chemotherapy in the treatment of advanced gastric cancer patients. **Method:** A consecutive cohort of 60 patients were divided into two groups: the experimental group receiving Kanglaite® Injection combined with chemotherapy and the control group with chemotherapy alone. After more than two courses of treatment, efficacy, quality of life and side effects were evaluated. **Results:** The response rate and KPS score of experimental group were significantly improved as compared with those of the control group ( $P < 0.05$ ). In addition, gastrointestinal reactions and bone marrow suppression were significantly lower than in the control group ( $P < 0.05$ ). **Conclusions:** Kanglaite® Injection enhanced efficacy and reduced the side effects of chemotherapy, improving quality of life of gastric cancer patients; use of Kanglaite® injections deserves to be further investigated in randomized control clinical trials.

**Keywords:** Kanglaite injection - chemotherapy - advanced gastric cancer treatment

*Asian Pacific J Cancer Prev*, **13** (10), 5319-5321

### Introduction

Gastric cancer is one of the most frequent cancers in the world. The highest incidence and mortality rate are in Eastern Asia (Jemal et al., 2011). In China, gastric cancer has become a significant cancer burden and one of the key issues regarding cancer prevention and treatment. It was predicted that, in 2005, 0.3 million deaths and 0.4 million new cases from gastric cancer thus would rank the third most common cancer (Yang, 2006). The main treatment modalities for gastric cancer available are: surgery, chemotherapy, radiotherapy, immunochemotherapy, multimodality therapy etc. Chemotherapy is one of the treatment options available in advanced gastric cancer. It may relieve gastric cancer-related symptoms, improve quality of life and prolong survival in some patients who respond to treatment. How to increase efficacy and decrease toxicities of chemotherapy remains a focus in this area.

Kanglaite® (Coix Seed Oil) Injection, which had been confirmed with anti-tumor activity, is one of Chinese herb Preparations that is developed and manufactured by Zhejiang Kanglaite Pharmaceutical Co., Ltd in China (Li 2005). It is mainly used for the treatment of no-small cell lung cancer, liver cancer, gastric cancer etc (Lian et al., 2006; Zhu et al., 2009). We hypothesize that it

is effective when applied with chemotherapy in the treatment of gastric cancer. Another aim of this study is to evaluate toxicities of Kanglaite® when combined with chemotherapy.

### Materials and Methods

#### Patient

All the patients were required to be pathologically diagnosed with gastric cancer, with Karnofsky performance status  $\geq 60$ , aged between 18 and 75 years, predicted survival time  $\geq 3$  months. With adequate bone marrow (white blood cell count  $> 4.0 \times 10^9$  and platelet count  $> 100 \times 10^9$ ), and liver function (bilirubin and transaminases  $< 2$  times the upper limit normal), no heart and kidney disease, and signed an informed consent before chemotherapy.

Patients excluded from this study if they failed to complete two cycles of chemotherapy, with any serious medical or psychiatric condition, or other malignancies. Pregnant or lactating women are excluded from the study.

#### Treatment

In experimental group, Kanglaite® Injection combined with DOC regimen, which consisted of docetaxel (D), oxaliplatin (O) and capecitabine (C). Docetaxel and

<sup>1</sup>Department of Chemotherapy, Jiangsu Cancer Hospital & Research Institute, <sup>2</sup>Nanjing University of Traditional Chinese Medicine, <sup>3</sup>Department of Research, Jiangsu Cancer Hospital & Research Institute, Nanjing, China \*For correspondence: [huangxinen06@yahoo.com.cn](mailto:huangxinen06@yahoo.com.cn), [cocolihongye@126.com](mailto:cocolihongye@126.com)

**Table 1. Comparison of Treatment Efficacy in Two Groups n (%)**

Treatment	N	CR	PR	SD	PD	CR+PR	CR+PR+SD
Experimental group	30	0	12	14	4	12(40)	26(86.7)
Control group	30	0	5	15	10	5(16.7)	20(66.7)

\*N, number cases; CR, Complete Remission; PR, Partial response; SD, stable disease; PD, progressive disease; \*experimental group was chemotherapy combined with Kanglaite injection, which is developed and manufactured by Zhejiang Kanglaite Pharmaceutical Co., Ltd in China. Control group. control group was given chemotherapy alone

**Table 2. Karnofsky Performance Status Score in Two Groups\***

Treatment	Increased	Stable	Decreased
Experimental group	15	10	5
Control group	6	13	11

\*KPS, score; increased, ≥10 after treatment; stable, <10; decreased, ≥10

oxaliplatin was administered on days 1 and 8, at 60mg and 130mg/m(2)/day respectively, and capecitabine 1,000 mg/m(2) twice daily on days 1-14. Treatment was repeated every 3 weeks. While in control group, chemotherapy alone was administered. Patients in experimental group received intravenous Kanglaite Injection 100ml per day during chemotherapy. Routine blood test, blood biochemistry and tumor markers were reviewed during and after chemotherapy.

*Efficacy Observation*

Treatment efficacy was evaluated after more than two cycles of chemotherapy. Complete remission (CR), partial response (PR), stable disease (SD), and progressive disease (PD) were determined based on RECIST criteria (Eisenhauer et al., 2009). Quality of life was evaluated in accordance with the Karnofsky Scale (Clancey, 1995; Friendlander and Ettinger, 2009), designated increasing if the score increased by 10 after treatment, decreasing if the score decreased by 10 and otherwise stable.

*Toxicity Assessment*

Patients were assessed and graded for toxicity according to WHO criteria (Kaba et al., 2004).

*Statistical analysis*

The study data were analyzed by t and enumeration data by  $\chi^2$  test. Statistic significance was determined if  $p < 0.05$ . We have enough experience in conducting medical researches, and have published some results elsewhere (Huang et al., 2004; Zhou et al., 2009; Jiang et al., 2010; Yan et al., 2010; Gao et al., 2011; Huang et al., 2011; Li et al., 2011; Li et al., 2011; Li et al., 2011; Xu et al., 2011; Xu et al., 2011; Xu et al., 2011; Yan et al., 2011; Zhang et al., 2011; Gong et al., 2012; Li et al., 2012; Yu et al., 2012).

**Results**

*Efficacy*

Sixty patients fulfilled eligibility and had completed

**Table 3. Toxicity in Two Groups\***

Toxicity Grade/	Experimental group Number				Control group Number			
	I	II	III	IV	I	II	III	IV
Leukopenia	8	5	2	0	7	10	5	1
Thrombocytopenia	5	3	1	0	6	7	3	1
Nausea,vomiting	10	5	1	0	14	8	2	0
Diarrhea	7	3	0	0	10	6	2	0
Oral mucositis	6	3	0	0	8	5	1	0
Neurotoxicity	12	7	2	0	12	8	4	0
Hand-foot syndrome	10	6	1	0	12	8	2	0

at least 2 cycles of treatment. All patients were divided into two groups. No statistically significant difference was found between two groups of patients regarding age, sex, and clinical stage ( $P > 0.05$ ).

No CR was observed in all patients. The response rate in experimental group (CR+PR) was 40%, while that in control group was 16.7%, with statistically significant difference ( $p < 0.05$ ). The clinical benefit rate of two groups (CR+PR+SD) were 86.7% (in experimental group), 66.7% (in control group) respectively, without statistical significance ( $p > 0.05$ ) (Table 1).

*Quality of life before and after treatment*

KPS score of experimental group increased in 15 cases (50%), 10 cases stable and 5 cases decreased, while that of control group increased in 6 cases (20%), 13 cases stable and 11 cases decreased. The difference between two groups was statistically significant ( $p < 0.05$ ) (Table2).

*Toxicity*

All patients underwent toxicity assessment. Treatment related side effects were reversible, and no termination of chemotherapy or death caused by adverse events occurred. the main adverse effects were bone marrow suppression, gastrointestinal symptoms, neurotoxicity, oral mucositis, and hand-foot syndrome etc. The statistical significance differences were discovered between two groups in terms of leukopenia (50% in experimental vs. 63.3% in control group), thrombocytopenia (30% in experimental vs. 43.3% in control group), diarrhea (33.3%in experimental vs. 46.7% in control group) and nausea/vomiting (53.3% in experimental vs. 66.7% in control group) (Table3).

**Discussion**

Gastric cancer chemotherapy was still not normalized and standardized. Chemotherapy could reduce the rate of recurrence and metastasis, and prolongs survival time. But, chemotherapy often brings about serious side effects. Therefore, how to reduce side effects of chemotherapy, in the meantime increase efficacy and improve quality of life have aroused more and more attention. It is a distinguishing feature of traditional Chinese medicine to contribute in this area.

The main ingredient of Kanglaite® Injection is Coix seed oil, which has been used to treat cancers in Chinese traditional medicine (Yu et al., 2008; Yu et al., 2008). It can induce tumor cell apoptosis, block tumor cell mitosis, improve immune function, reduce the toxicity of chemotherapy, and relieve cancer pain etc.

Kanglaite® Injection has been developed and manufactured by Zhejiang Kanglaite Pharmaceutical Co., Ltd in China. Study of anti-tumor mechanism of Kanglaite® Injection has been performed in many research centers of China, and demonstrated a blockage of tumor cell mitosis at the boundary of G2 and M phases of the cell cycle, an increase in tumor cell apoptosis and expression of Fas/Apo-1 gene and a decrease in expression of Bel-2 gene ( Li, 2005; Lian et al., 2006; Zhu et al., 2009).

Our study suggested that Kanglaite® Injection combined with Chemotherapy could enhance efficacy of chemotherapy, reduce side effects caused by chemotherapy, and improve quality of life. Thus, Kanglaite® Injection deserves to be further investigated by randomized controlled clinical trails.

## Acknowledgements

Dr. Xin-En Huang is supported in part by a grant from Jiangsu Provincial Administration of Chinese Medicine (LZ11091), and in part from a special research fund of Organization Department of Jiangsu Provincial Party Committee, Talent Work Leading Group of Jiangsu Province (333 High-level Talents Training Project).

## References

- Clancey JK (1995). Karnofsky performance scale. *J Neurosci Nurs*, **27**, 220.
- Eisenhauer EA, Therasse P, Bogaerts J, et al (2009). New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer*, **45**, 228-47.
- Friendlander AH, Ettinger RL (2009). Karnofsky performance status scale. *Spec Care Dentist*, **29**, 147-8.
- Gao LL, Huang XE, Zhang Q, et al (2011). A Cisplatin and vinorelbine (NP) regimen as a postoperative adjuvant chemotherapy for completely resected breast cancers in China: final results of a phase II clinical trial. *Asian Pac J Cancer Prev*, **12**, 77-80.
- Gong P, Huang XE, Chen CY, et al (2012). Comparison on complications of peripherally inserted central catheters by ultrasound guide or conventional method in cancer patients. *Asian Pac J Cancer Prev*, **13**, 1873-5.
- Huang XE, Li CG, Li Y, et al (2011). Weekly TP regimen as a postoperative adjuvant chemotherapy for completely resected breast cancer in China: final result of a phase II trial. *Asian Pac J Cancer Prev*, **12**, 2797-800.
- Jiang Y, Huang XE, Yan PW, et al (2010). Validation of treatment efficacy of a computer-assisted program for breast cancer patients receiving postoperative adjuvant chemotherapy. *Asian Pac J Cancer Prev*, **11**, 1059-62.
- Kaba H, Fukuda H, Yamamoto S, Ohashi Y (2004). [Reliability at the National Cancer Institute-Common Toxicity Criteria version 2.0]. *Gan To Kagaku Ryoho*, **31**, 1187-92.
- Lian Z, Lu Y, Hou E, Wang X (2006). [Combination of GP regimen and Kanglaite in the treatment of advanced non-small cell lung cancer]. *Zhongguo Fei Ai Za Zhi*, **9**, 74-7.
- Li CG, Huang XE, Li Y, et al (2011). Clinical observations on safety and efficacy of OxyContin® administered by rectal route in treating cancer related pain. *Asian Pac J Cancer Prev*, **12**, 2477-8.
- Li CG, Huang XE, Li Y (2011). Phase II trial of irinotecan plus nedaplatin (INP) in treating patients with extensive stage small cell lung cancer. *Asian Pac J Cancer Prev*, **12**, 487-90.
- Li CG, Huang XE, Xu L, et al (2012). Clinical application of serum tumor associated material (TAM) from non-small cell lung cancer patients. *Asian Pac J Cancer Prev*, **13**, 301-4.
- Li D (2005). [The anticancer drug Kang-Lai-Te emulsion for infusion]. *Vestn Ross Akad Med Nauk*, **9**, 32-7.
- Liu W, Li SY, Huang XE, et al (2012). Inhibition of tumor growth in vitro by a combination of extracts from *rosa roxburghii* tratt and *fagopyrum cymosum*. *Asian Pac J Cancer Prev*, **13**, 2409-14.
- Li Y, Yan PW, Huang XE, et al (2011). MDR1 gene C3435T polymorphism is associated with clinical outcomes in gastric cancer patients treated with postoperative adjuvant chemotherapy. *Asian Pac J Cancer Prev*, **12**, 2405-9.
- Shu J, Li CG, Liu YC, et al (2012). Comparison of serum tumor associated material (TAM) with conventional biomarkers in cancer patients. *Asian Pac J Cancer Prev*, **13**, 2399-403.
- Xu HX, Huang XE, Li Y, et al (2011). A clinical study on safety and efficacy of Aidi injection combined with chemotherapy. *Asian Pac J Cancer Prev*, **12**, 2233-6.
- Xu HX, Huang XE, Qian ZY, et al (2011). Clinical observation of Endostar® combined with chemotherapy in advanced colorectal cancer patients. *Asian Pac J Cancer Prev*, **12**, 3087-90.
- Xu JW, Li CG, Huang XE, et al (2011). Ubenimex capsule improves general performance and chemotherapy related toxicity in advanced gastric cancer cases. *Asian Pac J Cancer Prev*, **12**, 985-7.
- Xu T, Xu ZC, Zou Q, Yu B, Huang XE (2012). P53 Arg72Pro polymorphism and bladder cancer risk--meta-analysis evidence for a link in Asians but not Caucasians. *Asian Pac J Cancer Prev*, **13**, 2349-54.
- Yan PW, Huang XE, Jiang Y, et al (2010). Clinical comparison of safety and efficacy of vinorelbine/epirubicin (NE) with fluorouracil/epirubicin/cyclophosphamide (FEC). *Asian Pac J Cancer Prev*, **11**, 1115-8.
- Yan PW, Huang XE, Yan F, et al (2011). Influence of MDR1 gene codon 3435 polymorphisms on outcome of platinum-based chemotherapy for advanced non small cell lung cancer. *Asian Pac J Cancer Prev*, **12**, 2291-4.
- Yao CY, Huang XE, Tang JH, et al (2010). Clinical observation on safety of fixed dose rate gemcitabine chemotherapy by intravenous infusion. *Asian Pac J Cancer Prev*, **11**, 553-5.
- Yu DS, Huang XE, Zhou JN, et al (2012). A Comparative Study on the Value of Anal Preserving Surgery for Aged People with Low Rectal Carcinoma in Jiangsu, China. *Asian Pac J Cancer Prev*, **13**, 2339-40.
- Zhang LQ, Huang XE, Wang J (2011). The cyclin D1 G870A polymorphism and colorectal cancer susceptibility: a meta-analysis of 20 populations. *Asian Pac J Cancer Prev*, **12**, 81-5.
- Zhang XZ, Huang XE, Xu YL, et al (2012). A Phase II study on voriconazole for treatment of Chinese patients with malignant hematological disorders and invasive aspergillosis. *Asian Pac J Cancer Prev*, **13**, 2415-8.
- Zhou JN, Huang XE, Ye Z, et al (2009). Weekly paclitaxel/Docetaxel combined with a platinum in the treatment of advanced non-small cell lung cancer: a study on efficacy, safety and pre-medication. *Asian Pac J Cancer Prev*, **10**, 1147-50.
- Zhu L, Yang Z, Wang S, Tang Y (2009). [Kanglaite for Treating Advanced Non-small-cell Lung Cancer: A Systematic Review.]. *Zhongguo Fei Ai Za Zhi*, **12**, 208-15.