The clinical value of Fufangkushen injection in the treatment of stomach cancer: A meta-analysis

ABSTRACT

Objective: The purpose of this meta-analysis was to evaluate the effects of Fufangkushen injection combined with chemotherapy in the treatment of stomach cancer.

Materials and Methods: The relevant clinical trials about Fufangkushen injection combined with chemotherapy in the treatment of stomach cancer were searched in the databases of Pubmed, EMBASE, Cochrane, and CNKI. The data related to objective response rate, Karnofsky (KPS) score, and toxicity were extracted and pooled using the Stata 11.0 software. Dichotomous data was presented as risk ratio (RR) and its 95% confidence interval (95% CI).

Results: Thirteen relevant trials were included in this meta-analysis. Heterogeneity test indicated there was no statistical heterogeneity among the studies, thus the fixed effects model was used to calculate the results. Pooled results indicated that the objective response rate (ORR) and KPS score improvement in Fufangkushen chemotherapy group was significant higher than that of control group (RR = 1.24, P < 0.05). Synthesis data also demonstrated the Fufangkushen injection can significantly decrease the risk of developing granulocytopenia in stomach cancer patients treated with chemotherapy (RR = 0.67, P < 0.05).

Conclusion: Fufangkushen injection combined with chemotherapy can increase the objective response rate, improve the quality of life and decrease the risk of developing granulocytopenia in patients with stomach cancer.

KEY WORDS: Chemotherapy, Fufangkushen injection, meta-analysis, stomach cancer

INTRODUCTION

A total of 989,600 new stomach cancer cases and 738,000 deaths are estimated to have occurred in 2008, accounting for 8% of the total cases and 10% of total deaths.[1] Over 70% of new cases and deaths occur in developing countries. In year 2011, an estimated 21,320 new cases was diagnosed and 10,540 cases eventually died of the stomach cancer in the United States.[2] In China, stomach cancer is one of the most common gastrointestinal carcinomas.[3] Surgery is the main treatment strategy in patients with early stage with relative acceptable prognosis. Complete resection with adequate margins is widely considered as a standard goal, whereas the type of resection along with extent of lymphadenectomy remains controversial. But the prognosis of this disease was relative poor in patients with advanced clinical stages or recurrence disease. According to the National Comprehensive Cancer Network (NCCN) guideline for gastric cancer, chemotherapy can provide palliation, improved survival and quality of life compared to best supportive care in patients with advanced and metastatic disease.[4] But the chemotherapy itself has drawbacks such as it impairs the patient's immune system, increase the risk of develop severe chemotherapy drug toxicity such as nausea and vomiting, hematologic toxicity, lipsotrichia etc. Thus, how to improve the chemotherapy effects and decrease its toxicity in the same time is the key points for chemotherapy treatments. Traditional Chinese medicine (TCM) had the advantages of improving the immune system and quality of life. Several trials about the Fufangkushen injection in the treatment of gastric cancer indicated that Fufangkushen injection plus chemotherapy can increase the clinical efficacy and decrease the side effects related to chemotherapy drugs.[5,6] But the results of the studies were not in consistent with each other. So, we performed this meta-analysis to further demonstrate the effects of Fufangkushen injection in the treatment of stomach cancer.

MATERIALS AND METHODS

Search strategy

The relevant clinical trials about Fufangkushen injection combined with chemotherapy in the treatment of stomach cancer were search in the
data bases of Pubmed, EMBASE, Cochran and CNKI. The search terms were “Fufangkushen”, “stomach cancer”, “stomach carcinoma”, “gastric cancer”, “gastric carcinoma”. All searches were retrieved and checked for other possible studies. The search procedure was done by two reviewers independently.

**Data extraction**
All of the data were extracted independently by two reviewers (Jin Li and Mingdong Wu) according to the pre-specified selection criteria. Any disagreements among the authors were resolved by discussion. The following data were extracted: Study design and period, year of publication, number of patients included in each studies, clinical stages, Karnofsky (KPS) score, chemotherapy regimen and Fufangkushen injection administration.

**Statistical analysis**
Dichotomous data were expressed as the risk ratio (RR) and its 95% confidence interval (95% CI). Statistical heterogeneity was evaluated by Q-statistic and I². A fixed effects model was used if no statistical heterogeneity across the studies in the aspects of effect size; otherwise, the random effects model was purchased. Begg’s rank correlation method and Egger’s weighted regression method were also used to statistically assess the publication bias.

**RESULTS**

**General characteristics**
By searching the related data bases, thirteen relevant studies[5-17] were finally included in this meta-analysis [Table 1]. All of the patients included in the trails were from China. The clinical stage for the patients range from II to IV and all the patients’ KPS score were more than 60 points. The most common chemotherapy drugs were cisplatin (DDP), 5-fluorouracil (5-FU) and Oxaliplatin (L-OPH). The Fufangkushen injection regimen was 20 ml intravenously guttate (ivggt) range from 10–21 days.

**Quantitative data synthesis**
Thirteen trials report the objective response rate (ORR) in the Fufangkushen plus chemotherapy group and the control group. The synthesis results demonstrated that the ORR in Fufangkushen chemotherapy group was significant higher than that of control group (RR = 1.24, P < 0.05) [Figure 1].

Eleven studies providing the data of KPS score improvement. Results indicated that patients in the Fufangkushen plus chemotherapy group are more likely to have the life quality improvement than the control group (RR = 1.41, P < 0.05), [Figure 2].

Ten studies reported granulocytopenia frequency in Fufangkushen plus chemotherapy and chemotherapy alone. Synthesis data indicated that Fufangkushen injection can significant decrease the risk of developing granulocytopenia in stomach cancer patients treated with chemotherapy (RR = 0.67, P < 0.05) [Figure 3].

**Heterogeneity**
Heterogeneity among the included trials was calculated using the Q-statistic (Q > 0.10) and the I² statistic (I² = 0.0%). No significant heterogeneity was found for the above three effect size (for ORR I² = 0.0%, P = 0.74; for KPS I² = 0.0%, P = 0.96 and for granulocytopenia, I² = 0.0%, P = 0.83).

**Publication bias**
Begg’s funnel plot and Egger’s test were performed to assess the publication bias of the included studies, and no statistical publication was found in this meta-analysis (data not shown).

**DISCUSSION**
In this meta-analysis, thirteen clinical trials about the Fufangkushen injection combined with chemotherapy in the treatment of stomach cancer were finally included. Heterogeneity test indicated there was statistical heterogeneity among the studies, thus the fixed effects mode was used to calculate the results. Pooled results indicated that the objective response rate (ORR) and KPS score improvement in Fufangkushen chemotherapy group was significant higher than that of control group (RR = 1.24, P < 0.05). Synthesis data also demonstrated the Fufangkushen injection can significant decrease the risk of developing granulocytopenia in stomach
Li, et al.: Fufangkushen and stomach cancer

C44 Journal of Cancer Research and Therapeutics - Volume 10 - Special Issue 1- 2014

The pooled data indicated that Fufangkushen injection combined with chemotherapy can increase the ORR objective response rate, improve the quality of life and decrease the risk of developing granulocytopenia in patients with stomach cancer.

Although the results of this study demonstrated that Fufangkushen injection combined with chemotherapy can increase the objective response rate, improve the quality of life and decrease the risk of developing granulocytopenia in patients with stomach cancer, there are still several limitations.
of this meta-analysis. Firstly, all of the studies are come from China with relative poor methodology quality; Secondly, the number of patients included in each trials was relatively small with limited statistical power; Third, the pooled overall survival and disease-free survival were not calculated for the included 13 studies not providing the long-term follow up data.

In conclusion, this meta-analysis indicated that Fufangkushen injection combined with chemotherapy can increase the objective response rate, improve the quality of life and decrease the risk of developing granulocytopenia in patients with stomach cancer. But with several limitation of this meta-analysis, the conclusion should be drawn with caution.

REFERENCES

1. Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011;61:69-90.
2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62:10-29.
3. Zhang RF, Sun HL, Jin ML, Li SN. A comprehensive survey of etiologic factors of stomach cancer in China. Chin Med J (Engl) 1984;97:322-32.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Gastric Cancer; V1.2013.
5. Lin CL. Clinical research of gastric cancer at the late stage treated with compound spophora flavescens injection combined with chemotherapy. World J Integr Tradit West Med 2011;6:316-8.
6. Han QL, Li JY, Tang HL. Curative effect observation of compound matrine Injection combined with chemotherapy in treatment of gastric cancer. China Med Her 2011;8:68-9.
7. Hung ZF, Lu XA, Huang CJ. The life quality and immune function improvement by Fufangkushen injection combined with chemotherapy in the treatment of stomach cancer[C]. 2008 the first international cancer research BBS Chinese and western medicine, 2008,414.
8. Zhou YQ, Yuan L. An observation of Fufangkushen injection combined with small dosage chemotherapy in the treatment of advanced gastric cancer. Chin J Pract Chin Mod Med 2007;21:415-7.
9. Xiong LG. Clinical observation of yanshu injection combined with paclitaxel and oxaliplatin in the treatment of advanced gastric cancer. Pract J Cancer 2008;23:276-7.
10. Huang ZF, Li HZ. Fufangkushen injection combined with chemotherapy in the treatment of advanced gastric cancer: Report of 30 cases. West China Med J 2009;24:2883-4.
11. Lu SB. Fufangkushen injection combined with chemotherapy in the treatment of stomach cancer with 120 case report. Shandong J Tradit Chin Med 2009;20:210-1.
12. Liu SL, Gu XX. Chemotherapy combined with Fufangkushen injection in the treatment of advanced gastric cancer. Chin J Coal Ind Med 2009;12:1566-7.
13. Wang JW, Wang ZX. Fufangkushen injection combined with DCF regimen in the treatment of advanced gastric carcinoma. Chin J N Drugs 2010;19:1585-8.
14. Clinical observation of compound kushen injection combined with ECF project for advanced gastric carcinoma. Guangxi Med J 2010;32:533-5.
15. Zhang MJ. Observation of clinical efficacy of Yanshu injection combined with NP chemotherapy in treatment of advanced gastric cancer. Chin J Clin Oncol Rehabil 2010;17:531-3.
16. Hong YG. Clinical observation on treating advanced gastric cancer with Fufangkushen injection plus chemotherapy. Chin J Clin Med 2010;2:63-4.
17. Yuan CJ, Wang JR. An observation of Fufangkushen combined with chemotherapy in the treatment of advanced stomach cancer. Shandong Med J 2012;52:51-2.
18. Zhu AL, Wang F, Fan QX, He W, Wang LX, Zhao PR. Apoptosis and growth arrest of human esophageal squamous cell carcinoma cell EC9706 induced by Fufangkushen injection. Zhonghua Yi Xue Za Zhi 2011;91:2797-800.
