Two postoperative chemotherapies for gastric cancer: FOLFOX4 vs. TPF

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Abstract. Clinical effects of FOLFOX4 and TPF chemotherapy regimen on postoperative gastric cancer patients were investigated. A total of 60 patients admitted to the First People's Hospital of Changzhou receiving gastric cancer operation were selected and they were divided into two groups at random. Thirty patients in the FOLFOX4 group were treated with oxaliplatin, fluorouracil and leucovorin, while 30 patients in the TPF group were treated with paclitaxel, fluorouracil and cisplatin. The therapeutic effects, adverse reactions, quality of life and survival time of patients in the two groups were observed. The total effective rate of the FOLFOX4 group was 73.3%, which was significantly higher than that of the TPF group (43.3%), and the difference was statistically significant (P<0.05). The proportions of neurotoxicity and thrombocytopenia in the FOLFOX4 group were 56.7 and 33.3%, while those in the TPF group were 26.7 and 60%, respectively, and the differences were statistically significant (P<0.05). The increasing proportion of postoperative scores of the FOLFOX4 group was 46.7%, which was significantly higher than that of the TPF group (20%), and the difference was statistically significant (P<0.05). The 2- and 3-year survival rates of the FOLFOX4 group were 63.3 and 50%, which were significantly higher than those of the TPF group (36.7 and 23.3%), and the differences were statistically significant (P<0.05). Therefore, the effective rate of FOLFOX4 regimen is high in the treatment of gastric cancer with relatively fewer adverse reactions, which has a certain advantage.

Introduction

Gastric cancer is one of the five major malignant tumors in the world, and surgical resection is still the preferred method of treatment of gastric cancer, but 50% patients are diagnosed with advanced gastric cancer, so the opportunity of operation is lost (1). Postoperative recurrent rate of patients with advanced gastric cancer receiving simple operative treatment is as high as 50-70% due to the high recurrent risk and metastasis (2,3). Therefore, chemotherapy occupies an important position in the comprehensive treatment of gastric cancer (4). In the past few decades, great advances have been made to treat gastric cancer, and with the emergence of the third generation of chemotherapy drugs and the development of molecular targeted drugs, many new chemotherapy drugs have been used in the treatment of gastric cancer, such as docetaxel, paclitaxel, oxaliplatin, irinotecan, capecitabine, and molecular targeted drugs, thus a number of new combined regimens are derived, which provide more individual choices in the treatment of gastric cancer.

At present, FOLFOX4 regimen is one of the most common treatments for patients who have advanced gastric cancer. 5-FU, as the preferred drug for gastrointestinal cancer, is also the basic drug of combination chemotherapy. L-OHP is a third-generation platinum-based antitumor drug that inhibits DNA synthesis and produces cytotoxic and antitumor activities by generating hydrated derivatives that act on DNA to form intra- and inter-chain cross-linking. L-OHP and 5-FU have synergistic effects. The results show that RR of the treatment of advanced gastric cancer with L-OHP combined with 5-FU and CF is 40-52%, the median PFS is 5.2-7.1 months, and the median OS is 8.1-10.6 months (5-7). REAL-2 and other studies have shown that the efficacy of L-OHP is not inferior to that of cisplatin (HR, 0.92; 95% CI, 0.80-1.10), and in terms of safety, the incidence of grade-3 and -4 neutropenia caused by L-OHP is significantly decreased, and the increasing trend of creatinine level and thromboembolism are decreased (8).

TPF (paclitaxel + cisplatin + 5-fluorouracil) is currently widely used in clinical chemotherapy. It has been reported in China and other countries that the total effective rate is 22-65% (9). Prospective randomized study confirmed that the combined application of paclitaxel, cisplatin and fluorouracil significantly improves the efficiency and survival time (10).

Chemotherapy is an effective means to consolidate the therapeutic effect of gastric cancer, but due to immunosuppression, increasingly severe drug resistance of tumor and other factors, most physically weak patients cannot receive the chemotherapy smoothly on schedule, thus, shortening the survival time and decreasing the quality of life. A total of 60 patients with gastric cancer from October 2015 to

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October 2017 were randomly divided, and the control study was conducted. Therapeutic effects, adverse reactions, quality of life and survival time of FOLFOX4 and TPF chemotherapy regimen were compared, and the effects of different chemotherapy regimens on postoperative quality of life of patients were evaluated. Now it is reported as follows.

Patients and methods

General data. Under the condition of Ethics Committee approval of the First People's Hospital of Changzhou, (Changzhou, China) 60 patients who were admitted to the hospital and received gastric cancer operation from October 2015 to October 2017 were selected, including 12 cases of cardiac cancer and 48 cases of gastric antrum cancer. According to the international staging method, there were 15 cases of stage II, 24 cases of stage III and 21 cases of stage IV. The patients were divided into two groups at random, and the balance of patients' conditions between the two groups was ensured with the consent of patients. Thirty patients in the FOLFOX4 group were treated with FOLFOX4 chemotherapy regimen, including 18 males and 12 females aged 40-72 years with an average age of 56.3±1.2 years. Thirty patients in the the TPF group were treated with TPF chemotherapy regimen, including 17 males and 13 females aged 42-72 years with an average age of 53.8±1.4 years. There were no significant differences in the general data, such as sex, age, pathological pattern and staging of patients between the two groups (P>0.05), and the data were comparable.

Treatment methods. All patients underwent chemotherapy after all stitches were removed at 10 days after operation. The FOLFOX4 group received intravenous drip of 85 mg/m^2 oxaliplatin on the first day, intravenous infusion of 400 mg/m^2 fluorouracil on day 1-2, and then intravenous drip of 600 mg/m^2 fluorouracil for 22 h continuously, and intravenous drip of 200 mg/m^2 leucovorin at 2 h before the injection of fluorouracil on day 1-2; one course of treatment lasted for 14 days, and four courses of treatment were applied continuously. The TPF group received intravenous drip of 135 mg/m^2 paclitaxel added into the 500 ml normal saline for 3 h on the first day, intravenous drip of 500 mg/m^2 fluorouracil for 6-8 h on day 1-5, and intravenous drip of 20 mg/m^2 cisplatin for 2 h on day 1-5; one course of treatment lasted for 28 days, and two courses of treatment were applied continuously.

Evaluation of therapeutic effects. According to the evaluation criterion of WHO, therapeutic effects include complete remission (CR), partial remission (PR), stable disease (SD) and progressive disease (PD), and CR+PR are regarded as effective.

Evaluation of quality of life. Quality of life was evaluated using Karnofsky Performance Scale (11), including 11 levels of performance status with 10 points for each level. The decrease of 10 points or more was regarded as decrease, the decrease or increase within 10 points was regarded as stable, and increase of 10 points after treatment was regarded as increase.

Statistical analysis. SPSS 13.0 software (SPSS, Inc., Chicago, IL, USA) was used for processing of all data. χ^2 test was used for enumeration data. P<0.05 was defined as statistically significant.

Table I. Comparison of clinical effects on patients between the two groups.

Groups	Cases	CR	PR	SD	PD	Effective rate (%)
FOLFOX group	30	14	8	5	3	73.3
TPF group	30	8	5	11	6	43.3
χ^2		2.584	0.884	3.068	1.176	5.554
P-value		0.108	0.347	0.08	0.278	0.018

CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease.

Results

Comparison of clinical effects on patients between the two groups. The total effective rate of the FOLFOX4 group was significantly higher than that of the TPF group, and the difference was considered as statistically significant (P<0.05) (Table I).

Comparison of adverse reactions of patients between the two groups. The proportion of neurotoxicity in the FOLFOX4 group was significantly higher than that in the TPF group, but the proportion of thrombocytopenia in the FOLFOX4 group was significantly lower than that in the TPF group, and the differences were statistically significant (P<0.05). The proportions of hepatic and renal functional lesion, gastrointestinal reaction and leucopenia in the FOLFOX4 group were lower than those in the TPF group, but the differences were not statistically significant (P>0.05) (Table II).

Comparison of improvement of life quality between the two groups at 6 months after operation. The difference in the increasing proportion of postoperative scores between the FOLFOX4 and TPF groups indicated a statistical significance (P<0.05), but there were no statistically significant differences in stable and decreasing proportions of postoperative scores between the FOLFOX4 and TPF groups (P>0.05) (Table III).

Comparison of survival rates of patients between the two groups. The 2- and 3-year survival rates of the FOLFOX4 group were higher than those of the TPF group, and the differences were statistically significant (P<0.05). Meantime, the 1-year survival rate of the FOLFOX4 group was higher than that of the TPF group, but the difference was not statistically significant (P>0.05) (Table IV).

Discussion

Gastric cancer is a common malignant tumor originating in gastric mucosal epithelial cells, which causes serious harm to human health (12,13). More than 70% gastric cancers have no symptom in the early stage, and upper abdominal pain, pyloric obstruction, metabolic disorders, gastrointestinal bleeding, fatigue, emaciation and tumor spread and metastasis will occur in the middle and advanced stage. According to the demographic survey, the incidence rate of gastric cancer is

Table II. Comparison of adverse reactions of patients between the two groups.

Groups	Cases	Neurotoxicity	Thrombocytopenia	Hepatic and renal functional lesion	Gastrointestinal reaction	Leucopenia
FOLFOX group	30	17 (56.7%)	10 (33.3%)	11 (36.7%)	11 (36.7%)	12 (40%)
TPF group	30	8 (26.7%)	18 (60%)	16 (53.3%)	14 (46.7%)	14 (46.7%)
χ^2		5.554	4.286	1.684	0.617	0.271
P-value		0.018	0.038	0.194	0.432	0.602

Table III. Comparison of improvement of life quality between the two groups at 6 months after operation.

Groups	Cases	Decrease	Stable	Increase
FOLFOX group	30	7 (23.3%)	9 (30%)	14 (46.7%)
TPF group	30	11 (36.7%)	13 (43.3%)	6 (20%)
χ^2		1.27	1.148	4.8
P-value		0.26	0.284	0.028

Table IV. Comparison of survival rates of patients between the two groups.

Groups	Cases	1-year survival rates	2-year survival rates	3-year survival rates
FOLFOX group	30	20 (66.7%)	19 (63.3%)	15 (50%)
TPF group	30	17 (56.7%)	11 (36.7%)	7 (23.3%)
χ^2		0.635	4.267	4.593
P-value		0.426	0.039	0.032

different in different ages, which increases with the increase of age, and the peak is at the age of 50-70 years (14). Most patients are diagnosed with intermediate or advanced gastric cancer, and chemotherapy is used in clinical treatment as an important means. For some patients with early gastric cancer, chemotherapy is still needed after surgical resection to prevent the postoperative recurrence and metastasis. Related literature reports have pointed out that chemotherapy can effectively extend the median survival time from 3-5 to 7.5-12 months, improving the quality of life of patients (15,16). Chemotherapy regimens and chemotherapy-sensitive drugs for postoperative gastric cancer still need further study.

Oxaliplatin and taxane drugs promote the development of gastric cancer chemotherapy to a certain extent. The resistance mechanism and antitumor activity spectrum of oxaliplatin and cisplatin are not exactly the same, and there is no cross resistance without renal toxic and side-effects compared with cisplatin (17,18). Paclitaxel is a semi-synthetic drug that forms stable non-functional microtubules by inhibiting tubulin depolymerization and promoting tubulin polymerization, thus, tumor cell division and proliferation are inhibited, and cells are blocked in the G2/M stage. The effective rate of paclitaxel monotherapy in the treatment of gastric cancer is 27-40%, the effective rate of combined treatment is up to 68%, and the median survival time is 6.5-7.5 months (19). In FOLFOX4 regimen, the combined application of fluorouracil and leucovorin can replace doxorubicin, and calcium folinate is a biochemical regulator of fluorouracil without anticancer effects, and it will be converted into tetrahydrofolate, strengthens the inhibition capacity of 5-fluorouracil for DNA synthesis, and improve the efficacy without increasing the toxicity (20).

The research data in this report showed that the total effective rate of the FOLFOX4 group was significantly higher than that of the TPF group, and applying FOLFOX4 regimen can obtain a higher effective rate and successfully consolidate the curative effect after operative treatment. Adverse reactions of chemotherapy mainly include gastrointestinal reactions, bone marrow suppression and neurotoxic effects and in order to avoid possible gastrointestinal reactions during chemotherapy, such as nausea and vomiting, patients should be advised to eat lightly and regularly during the chemotherapy, so as to reduce the occurrence of nausea, vomiting and other uncomfortable symptoms. Fluid-supplement therapy should be given in time for symptoms of severe vomiting. In this study, the proportion of neurotoxicity in the FOLFOX4 group was significantly higher than that in the TPF group, but the proportion of thrombocytopenia in the FOLFOX4 group was significantly lower than that in the TPF group, showing that FOLFOX4 regimen has a higher neurotoxicity on patients, but the incidence rates of hepatic and renal functional lesion, gastrointestinal reaction and leucopenia in the FOLFOX4 group were lower than those in the TPF group, and the overall incidence rate of side-effects of the FOLFOX4 group were lower than that of the TPF group. Low incidence rate of adverse reactions can reduce the pain caused by the treatment, so that patients can successfully complete the treatment. The difference in the increasing proportion of postoperative scores between the FOLFOX4 and TPF groups indicated a statistical significance. The FOLFOX4 group had a higher Kanrofsky score after treatment, and FOLFOX4 played a role in improving the quality of life of patients. The 2- and 3-year survival rates of the FOLFOX4 group were both higher than those of the TPF group, and the differences were significant. FOLFOX4 regimen is effective in reducing adverse reactions, relieving patient's pain and improving -quality of life, so it can effectively improve the long-term survival rate of patients.

In conclusion, chemotherapy of gastric cancer can improve the prognosis and quality of life of patients to a certain extent, but the appropriate regimen still needs developing combined

with the actual situation of patients, so as to improve the curative effect and reduce the pain caused by treatment. The effective rate of FOLFOX regimen is high in the treatment of gastric cancer with relatively fewer adverse reactions, so it is worthy of clinical promotion.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

HX and QL designed the study and performed the experiments. HW, XZ and ZG collected the data. HX and HW analyzed the data. HX and QL prepared the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First People's Hospital of Changzhou (Changzhou, China). Signed informed consents were obtained from the patients or guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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