

Clinical effect of the concomitant administration of bevacizumab with docetaxel, 5-FU, and cisplatin on advanced gastric cancer.

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Abstract

Objective: This study aimed to explore the therapeutic effect of bevacizumab concomitantly administered with docetaxel, 5-FU, and cisplatin on patients with advanced gastric cancer.

Methods: A total of 60 patients with advanced gastric cancer were recruited and received the relevant therapy at our hospital over the period of December 2015 to December 2016. All patients were divided into two groups with 30 patients in each group. Patients in the control group received docetaxel, 5-FU, and cisplatin chemotherapy. Patients in the observation group received docetaxel, 5-FU, and cisplatin chemotherapy combined with bevacizumab. Subsequently, the therapeutic effects of the different treatments on the patients in the two groups were compared.

Results: The effective rates of the two clinical treatments were compared. The effective rate of the treatment administered to the observation group was 76.66%, which was higher than that (46.67%) of the treatment administered to the control group. The comparative difference between the two groups was statistically significant ($p < 0.05$). After treatment, the IgA and IgG levels of the patients in the observation group significantly improved relative to those of the patients in the control group ($p < 0.05$). The IgM levels of the patients in the observation group were not significantly different from those of the patients in the control group before and after treatment ($p > 0.05$). The life quality scores of the patients in the observation group were significantly higher than those in the control group, and their comparative difference was statistically significant ($p < 0.05$).

Conclusion: The concomitant application of bevacizumab with docetaxel, 5-FU, and cisplatin chemotherapy exhibited good clinical effect. In addition, the combined treatment improved the life quality of patients with advanced gastric cancer. Therefore, this therapeutic method should be further applied clinically.

Keywords: Cisplatin chemotherapy, Docetaxel, 5-FU, Advanced gastric cancer, Bevacizumab.

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Introduction

Gastric cancer is a common malignant tumor associated with high morbidity and mortality. Patients with gastric cancer are mainly treated with chemotherapy given that they cannot receive surgical therapy [1]. The concomitant application of cisplatin with 5-FU is clinically used for chemotherapy; this method, however, has barely satisfactory effect and causes toxicity, side effects, and pain [2,3]. We recruited 60 patients with advanced gastric cancer who were admitted to our hospital (Affiliated Hospital of Qingdao University). We aimed to study the therapeutic effect of the concomitant application of bevacizumab with docetaxel, 5-FU, and cisplatin chemotherapy on patients with advanced gastric cancer. We also investigated whether the treatment method improved the life quality of the patients. The specific experimental report is as follows.

Information and Methodology

General information

A total of 60 patients with advanced gastric cancer were recruited and received the relevant therapies at our hospital over the period of December 2015 to December 2016. The patients were divided into two groups, each containing 30 cases. All patients were professionally diagnosed with advanced gastric cancer. The control group consisted of 13 male and 17 female patients. In this group, the youngest patient was 30 years old, the oldest patient was 71 years old, and the average age was 51.6 ± 11.2 years old. The observation group consisted of 14 male and 12 female patients. In this group, the youngest patient was 29 years old, the oldest patient was 69 years old, and the average age was 50.2 ± 11.5 years old. The two groups exhibited similar relevant information, such as age and gender, thus indicating comparability.

Methodology

Patients in the control group received intravenous injections of 75 mg/m² docetaxel once every day, 500 mg/m² 5-FU 1–3 times every day, and 25 mg/m² cisplatin 1-3 times every day. Patients in the observation group received intravenous injections of 75 mg/m² bevacizumab once every day concomitant with the therapeutic intervention received by patients in the control group. The therapeutic effects of the two intervention methods on the patients in the two groups were observed and compared.

Observational indexes

The clinical effect and life quality of patients in the observation and control groups were observed and compared.

Evaluation criteria

Therapeutic effect was classified into complete remission, partial remission, stability, and deterioration in accordance with the relevant WHO standards. The sum of complete and partial remissions was considered as the total effective rate. The life quality of the patients was scored in accordance with the Karnofsky scoring standard. The patients were observed for half a month.

Statistical method

SPSS22.5 software was selected for statistical processing. Moreover, t- and χ^2 tests were used to evaluate the dosage and enumeration date, respectively. Statistical significance was considered at p<0.05.

Results

Clinical therapeutic effects on patients in the two groups

The effective rates of clinical treatment in the two groups were compared. The effective rate of the treatment administered to the observation group was 76.66%, which was better than that of the treatment administered to the control group (46.67%). The comparative difference between groups was statistically significant (p<0.05) (Table 1).

Table 1. Comparison of therapeutic effects on patients in the control and observation groups.

Group	Number of cases	Complete remission	Partial remission	Stability	Deterioration	Total effective rate
Control group	30	5	18	5	2	76.66
Observation group	30	3	11	6	10	46.67
χ^2						5.681
P						<0.05

Variation of the immunologic functional indexes of patients in the two groups after treatment

After treatment, the IgA and IgG levels of the patients in the observation group improved relative to those in the control group, and the comparative difference between the two groups was significant (p<0.05). The IgM level of the patients in the observation group was not significantly different from that of the patients in the control group before and after treatment (p>0.05). Specific data are shown in Table 2.

Table 2. Variation of the immunological functional indexes of patients in the control and observation groups after treatment.

Group	Number of cases	Time	IgA	IgG	IgM
Control group	30	Before treatment	2.87 ± 3.56	18.51 ± 1.47	0.81 ± 0.12
		After treatment	2.91 ± 2.64*	19.36 ± 2.54*	1.08 ± 0.16*
Observation group	30	Before treatment	2.85 ± 1.44	18.54 ± 1.70	0.94 ± 0.42
		After treatment	3.98 ± 2.11*	22.87 ± 1.77*	1.12 ± 0.08*
*t			2.002	7.171	1.414
*P			0.048	0.000	0.161

Comparison of the life quality of patients in the two groups

The life quality scores of the patients in the observation group were significantly higher than those of the patients in the control group. The comparative difference of the scores between groups was statistically significant (p<0.05), as shown in Table 3.

Table 3. Life quality scores of patients in the control and observation groups.

Group	Number of cases	Before treatment	After treatment	T value	P value
Control group	30	51.24 ± 2.63	66.82 ± 12.3	15.285	<0.05
Observation group	30	52.14 ± 22.33	79.56 ± 1.28	31.416	<0.05
t		0.178	8.374		
P		>0.05	<0.05		

Discussion

Gastric cancer is a common neoplasm of the digestive system. Epigastric discomfort is the most common initial symptom of early-stage gastric cancer and is experienced by approximately 80% of patients. Similar to dyspepsia, epigastric discomfort

manifests as mild, irregular stomachache that does not remit after eating [4,5]. These symptoms do not attract considerable concern from patients because they are easily mistaken for symptoms of gastritis or ulcer. Therefore, to avoid misdiagnosis, middle-aged patients with the following conditions should receive further examination [6]: no history of stomach illness but with recent noncausal epigastric discomfort or pain with ineffective treatment; or history of ulcer with recent regular change in epigastric pain in an increasingly aggravated degree. Patients with somewhat remitted symptoms and recent seizure should consider the possibility of gastric cancer and should thus receive timely examination. Nearly 50% patients with gastric cancer exhibit symptoms of evident anorexia or inappetence. Some patients autonomously restrict food because of abdominal distension or stomachache due to excessive eating [7,8]. Noncausal anorexia and emaciation are probably initial symptoms of early-stage gastric cancer and must receive further attention. Patients with early-stage gastric cancer generally show no evident positive signs, only experiencing deep-pressing epigastric pain and general weakness. Patients may experience persistent and acute that radiates toward the lower back as the gastric tumor develops and expands, especially when it infiltrates and penetrates into the serosa and infringes upon the pancreas [9,10]. As the tumor grows, patients may suffer from increasing emaciation, debility, anemia, and finally cachexia, as well as obstruction symptoms. Carcinomas of the cardiac or gastric fundus may cause difficulty swallowing. Gastric antrum cancer will cause pyloric obstruction symptoms, and the stomach may come into contact with the tumor. Hematemesis and melena will occur when the tumor becomes ulcerous [11,12]. Metastatic lesions, such tumors in the rectum, umbilical region, and supraclavicular lymph node, and ascites, are evidence of advanced gastric cancer.

Drug administration concomitant with 5-FU, capecitabine, oxaliplatin, and tegafur chemotherapy is the main therapeutic method for advanced gastric cancer that cannot be treated through surgical excision. Oxaliplatin, a novel platinum-based anticancer drug, can generate hydration derivatives that inhibit DNA synthesis, exert cytotoxic effects, and generate antitumor activity [13,14]. However, when independently used, oxaliplatin will cause severe gastrointestinal reactions, liver and kidney damage, and bone marrow suppression. 5-FU, a fluorouracil drug commonly used in chemotherapy to hinder tumorigenesis, can generate F-dUMP and FUMP. The former can combine with thymidylate synthetase to inhibit enzymatic activity and decrease deoxynucleotide synthesis to hinder DNA synthesis [15]. 5-FU metabolites will influence the cell functions of RNA and DNA and exert cytotoxic effects to inhibit RNA synthesis. The therapeutic effect of 5-FU improves when combined with calcium folinate. Cisplatin, also a basic chemotherapy drug, can interfere with DNA replication and has better antitumor effects than 5-FU. Docetaxel is synthesized from the effective constituents of yew, a precious medicinal plant, and has the effects of resisting and treating cancer. Nevertheless, docetaxel is a rare precious medicinal material. Bevacizumab can inhibit tumor growth and obstruct

the metastasis of tumor cells. The present research results showed that the clinical effect and life quality of patients in the observation group are significantly better than those of patients in the control group ($p < 0.05$).

Conclusion

The concomitant administration of bevacizumab, 5-FU, and cisplatin can improve the clinical effect of the individual drugs and improve the life quality of patients with advanced gastric cancer. Therefore, this therapeutic method is worthy of further clinical applications.

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References

1. Pimentel-Nunes P, Libânio D, Dinis-Ribeiro M. Evaluation and Management of Gastric Superficial Neoplastic Lesions. *GE Port J Gastroenterol* 2017; 24: 8-21.
2. Hu N, Hu Y, Zhu XF. Synthesis and Evaluation of Tetrahydroisoquinoline Derivatives against Human Hepatoma Carcinoma Cell Lines. *Lat Am J Pharm* 2017; 36: 192-195.
3. Oh SJ, Oh SH, Jun JY, Park JH, Lee JH, Lee DY, Lee JH, Yang JM. Paraneoplastic atypical scleromyxedema with advanced gastric cancer. *JAAD Case Rep* 2017; 3: 376-378.
4. AL-Yahya AAI, Asad M. Antiulcer activity of gum Arabic and its interaction with antiulcer effect of ranitidine in rats. *Biomed Res-India* 2016; 27: 1102-1106.
5. Song W, Teng W, Shi X, Liu X, Cui Z, Tian Z. The Relationship between RUNX3 Expression, Nursing Strategies and Nutritional Status in Elderly Patients with Advanced Gastric Cancer. *Iran J Public Health* 2017; 46: 762-770.
6. Ghorab MM, Alsaïd MS, Alqasoumi SI, Abdel-Kader MS. Semisynthesis of Some Novel Urea, Thiourea, Carbamimidothioic Acid and Dihydrooxazole Derivatives as a New Class of Anticancer Agents. *Lat Am J Pharm* 2017; 36: 380-385.
7. Shimodate Y, Mizuno M, Doi A, Nishimura N, Mouri H, Matsueda K, Yamamoto H. Gastric superficial neoplasia: high miss rate but slow progression. *Endosc Int Open* 2017; 5: E722-E726.
8. Gopal B, Rajagopal S. Localization of neurodegenerative brain MRI image for gene expression evaluation. *Biomed Res-India* 2017; 28: 539-548.
9. Li X, Meng Q, Sun S, Zhan Z, Zhang L, Sun B, Zhang Y. Histological transformation from gastric mucosa-associated lymphoid tissue lymphoma to gastric diffuse large B-cell lymphoma. *Oncol Lett* 2017; 14: 2244-2248.
10. Hamad A, Singhi AD, Bahary N, McGrath K, Amarin R, Zeh HJ, Zureikat AH. Neoadjuvant Treatment With

- Trastuzumab and FOLFOX Induces a Complete Pathologic Response in a Metastatic ERBB2 (HER2)-Amplified Duodenal Cancer. *J Natl Compr Canc Netw* 2017; 15: 983-988.
11. Colak MC, Colak C, Erdil N, Sandal S. Potential risk factors for early large pleural effusion after coronary artery bypass grafting surgery. *Biomed Res-India* 2017; 28: 625-629.
 12. Madabhavi I, Modi G, Patel A, Anand A, Panchal H, Parikh S. Pulmonary toxicity following bleomycin use: A single-center experience. *J Cancer Res Ther* 2017; 13: 466-470.
 13. He L, Luo L, Zhu H, Yang H, Zhang Y, Wu H, Sun H, Jiang F, Kathera CS, Liu L, Zhuang Z, Chen H, Pan F, Hu Z, Zhang J, Guo Z. FEN1 promotes tumor progression and confers cisplatin resistance in non-small-cell lung cancer. *Mol Oncol* 2017; 11: 1302-1303.
 14. Wang JM, Ju BH, Pan CJ, Gu Y, Li MQ, Sun L, Xu YY, Yin LR. MiR-214 inhibits cell migration, invasion and promotes the drug sensitivity in human cervical cancer by targeting FOXM1. *Am J Transl Res* 2017; 9: 3541-3557.
 15. Tan L, Peng J, Zhao Q, Zhang L, Tang X, Chen L, Lei M, Qian Z. A Novel MPEG-PDLLA-PLL Copolymer for Docetaxel Delivery in Breast Cancer Therapy. *Theranostics* 2017; 7: 2652-2672.

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