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Predictive Role of Plasma Fluorouracil Concentration Monitoring in Further Improving the Effects of Chemotherapy on Advanced Gastric Cancer and Relieving Adverse Reactions

Shuwen Deng, Hongxing Xia*

ABSTRACT

Objective: To study the predictive role of plasma fluorouracil concentration monitoring in further improving the effects of chemotherapy on advanced gastric cancer and relieving adverse reactions.

Methods: A total of 90 patients with advanced gastric cancer who received DCF (docetaxel + cisplatin + fluorouracil) chemotherapy in our hospital from October 2018 to October 2019 were enrolled as research objects and assigned into control group (n=45) and observation group (n=45) according to the random number table method. In control group, the dosage of chemotherapy drugs was calculated according to the body surface area. Meanwhile, in observation group, the dosage of chemotherapy drugs was calculated in accordance with the body surface area in the first chemotherapy cycle, and it was adjusted in the second chemotherapy cycle according to the monitoring results of plasma fluorouracil concentration in the previous chemotherapy cycle. The short-term therapeutic efficacy, cancer-related symptom scores, serum tumor marker levels, incidence rate of adverse reactions, and quality of life score were compared between the two groups.

Results: The disease control rate of observation group was higher than that of control group (71.11% *vs.* 48.89%, P<0.05). The cancer-related pain and cancer-related fatigue scores of the two groups were decreased after treatment compared with those before treatment (P<0.05), and they were lower in observation group than those in control group after treatment (P<0.05). Compared with those before treatment, the levels of serum carcinoembryonic antigen (CEA), CA125 and CA199 in both groups declined after treatment (P<0.05), and they were lower in observation group than those in control group after treatment (P<0.05). The incidence rate of adverse reactions such as nausea and vomiting, diarrhea, bone marrow suppression and mucositis was lower in observation group in comparison with that in control group (P<0.05). Besides, compared with that before treatment, the quality of life score rose in both groups after treatment (P<0.05), and it was higher in observation group than that in control group after treatment (P<0.05).

Conclusion: Monitoring plasma fluorouracil concentration has a good guiding effect on the chemotherapy for patients with advanced gastric cancer, which can improve the efficacy and reduce the adverse reactions of chemotherapy, thus improving the quality of life of patients.

KEYWORDS: advanced gastric cancer; fluorouracil; plasma concentration; chemotherapy; adverse reaction

INTRODUCTION

Chemotherapy is the main therapy in clinical practice for advanced gastric cancer, but there is some toxicity to chemotherapy, and patients are which adjust the effect and prognosis ofprone to adverse reactions during chemotherapy, chemotherapy [1, 2]. Fluorouracil is commonly used during chemotherapy for the treatment of advanced gastric cancer [3].]. Monitoring plasma

Department of General Surgery, Affiliated Nanhua Hospital, University of South China, Hengyang 421002, Hunan Province, China
**Correspondence to: Hongxing Xia Email: 70762478@qq.com*
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fluorouracil concentration in patients with malignant tumors during chemotherapy to maintain a stable plasma concentration can reduce the toxic and side effects caused by chemotherapy [4]. The current randomized controlled trial was therefore conducted in 90 patients with advanced gastric cancer who received DCF chemotherapy to investigate the effects of plasma fluorouracil monitoring in improving the efficacy of chemotherapy and reducing adverse reactions in the treatment of advanced gastric cancer.

MATERIALS AND METHODS

General data

In total, from October 2018 to October 2019 90 patients who receive DCF (docetaxel + cisplatin + fluorouracil) chemotherapy from our hospital were registered with the control group (n=45) and the observational group (n=45) in the form of an allocation to research objects by a routine number table. The control group had an average age 24 (27) males and 21 (12) females aged between 27 and 74 years (49.35 ± 12,54) and a mean disease age of three to five years (4.02 ± 0,67), while the observation Group had an average disease age of 23 (49.03 ± 12.47) males and 22 (022 ± 26.73) and an average disease age of (4.07 ± 0.64) years. (12.04). There were no statistically significant differences and comparable differences between the two groups of patients with gender, age and disease course (P>0.05). The study was approved by the Committee on Medical Ethics and the informed consent form was signed by each object.

Inclusion criteria: (a) Patients with advanced gastric cancer diagnosed with pathology; (b) those who received DCF chemotherapy and no other adjuvant drugs during DCF chemotherapy; (c) those with expected survival for more than 6 months; and (d) those with a history of chemotherapy.

Exclusion criteria: a) Patients who were complicated with chronic underlying diseases such as diabetes or hypertension, b) those who were complicated other diseases of the digestive system, c) those allergic to chemotherapy drugs, or d) those who were lost to follow-up halfway or dropped out of the study.

Methods

In that control group the chemical dose was measured based on the body's surface: DOCTAXEL intravenous drop for the first day (60 mg / m2), ICD for the first day (60 mg / m2) and Chemotherapy for the second day, IVD for the first day (500 mg / m2) three weeks and four consecutive cycles. ICR was calculated on the first day (60 mg / m2).

In observation group, the dosage of chemotherapy drugs was calculated in accordance with the body surface area in the first chemotherapy cycle, and the specific dosage was referred to that in control group, with three weeks as a chemotherapy cycle, for 4 consecutive chemotherapy cycles. In each chemotherapy cycle, 2 mL of venous blood was collected 12 hours after the patient was intravenously dripped with fluorouracil, and was immediately submitted for examination using the high-performance liquid chromatography. The dosage of chemotherapy drugs was adjusted in the second chemotherapy cycle according to the monitoring results of plasma fluorouracil concentration in the previous chemotherapy cycle, and the specific scheme was as follows: a) plasma fluorouracil concentration >400 ng/mL in the previous chemotherapy cycle: the dosage of fluorouracil was reduced by 30%, b) 300 ng/mL ≤ plasma fluorouracil concentration <400 ng/mL: the dosage of fluorouracil was reduced by 20%, c) 250 ng/mL ≤ plasma fluorouracil concentration <300 ng/mL: the dosage of fluorouracil was reduced by 10%, d) 200 ng/mL ≤ plasma fluorouracil concentration <250 ng/mL: the dosage of fluorouracil was not adjusted, e) 150 ng/mL ≤ plasma fluorouracil concentration <200 ng/mL: the dosage of fluorouracil was increased by 10%, f) 80 ng/mL ≤ plasma fluorouracil concentration <150 ng/mL: the dosage of fluorouracil was increased by 20%, and g) plasma fluorouracil concentration <80 ng/mL: the dosage of fluorouracil was increased by 30% [5].

Observation indices

The plasma fluorouracil concentration, short-term therapeutic efficacy, cancer-related symptom scores, serum tumor marker levels, incidence rate of adverse reactions, long-term survival, and quality of life score were compared between the two groups. Plasma fluorouracil concentration: The plasma concentration of fluorouracil of the two groups of patients was tested after treatment. Evaluation criteria for short-term therapeutic efficacy included[6]: a) complete remission (CR): tumour lesions have disappeared and no new lesions have appeared; b) partial remission (PR): at least 30 per cent decrease in the sum of the target lesions and no new lesions; c) stable disease (SD): less than 30 per cent decrease or less than 20 per cent increase in the sum of the target lesions; d) p) The disease control rate (DCR) was calculated using the following formula: CR + PR + SD = DCR.

Cancer-related symptoms included pain from cancer and symptoms of fatigue-related fatigue.

The Numeric Rating Scale (NRS) has assessed pain and the Brief Fatigue Inventory (BFI) has assessed fatigue. The score for each scale was 0-10 points and was directly proportional to the level of pain and fatigue. Sero-carcinoembryonic antigen (CEA), CA125 and CA199 were included as serum markers. The quality of life of patients with Chinese Cancer (QLQ-CCC) was evaluated before and after the treatment. The scale divided cancer patients ' quality of life into four areas: physical, mental, social and general feelings. The highest score was 100 points in each area and the score is commensurate with the quality of life.

Statistical analysis

For statistical analysis, software SPSS 26.0 was utilised. Numerical data were expressed and analysed in chi-square testing as a percentage. The default method ± was expressed as mean ± standards (above ± s) and t-test analyses. This difference, as indicated in P<0.05, was statistically significant.

RESULTS

Plasma fluorouracil concentrations

At the end of treatment, plasma fluorouracil concentration in observation group was (224.15±21.87) ng/mL, which was lower than (279.83±41.25) ng/mL in control group (P<0.05). During the treatment, the dosage of fluorouracil was adjusted for 29 out of the 45 patients in observation group according to the plasma concentration of fluorouracil.

Short-term therapeutic efficacy

The DCR of observation group was higher than that of control group (71.11% *vs.* 48.89%, P<0.05) (Table 1).

Scores of cancer-related symptoms

The cancer-related pain and fatigue score in both groups was decreased following treatment compared with previous ones (P<0.05) and lower after treatment in the observational group than in the control group (P<0.05) (Table 2).

Serum tumor marker levels

In comparison to serum CEA before treatment, CA125 and CA199 decreased in both groups after treatment (P < 0.05) and were lower in the observation group compared to P < 0.05 (Table 3).

Incidence of adverse reactions

In comparison to the control group, the incidence in the observation group of the adverse reactions such as nausea and vomiting, diarrhoea, suppression from bone marrow and mucositis was lower (Table 4)

Quality of life scores

Compared to pre-treatment, the quality of life score in both groups was increased after treatment (P<0.05) and was higher in the observation group than in the post-treatment control group (P<0.05) (Table 5).

DISCUSSION

Stomach cancer is a common malignancy in the digestive system with a high rate of incidence. In China, the incidence and death rates of gastric cancer are second to malignant tumours, seriously endangering the lives and health of humans [7,8]. There are a large number of people with gastric cancer. Gastric cancer is not characteristic of early clinical symptoms and is diagnosed in some patients at an advanced stage. Early gastric cancer is relatively small in patients, with roughly 50 per cent losing the chance of radical surgery due to advanced stage progression of tumours, resulting in shortened survival time [9]. The way this type of gastric cancer is treated has become an awkward problem in gastric cancer treatment.

Chemotherapy drugs are often administered to patients with gastric cancer who have lost the opportunity for radical surgery in clinical practise to prolong their survival [10]. DCF (docetaxel + cisplatin + fluorouracil) is the first-line chemotherapy regimen for advanced gastric cancer that can effectively control the progression of the tumour and therefore have a good anti-tumor effect. Some patients, however, are prone to adverse reactions such as nausea and vomiting, diarrhoea, and suppression of the bone marrow during chemotherapy, which will adversely affect the chemotherapy effect and even lead to a cessation of chemotherapy.

Clinically, the dosage of chemotherapy drugs is usually calculated on the patient's body surface area, which mainly takes into account the height and weight of the patient but ignores the effects of individual absorption and clearance efficiency on the effect and safety of chemotherapy [11]. The concentration of plasma drugs in most patients with malignant tumours cannot be controlled within the optimal range during chemotherapy [12]. In addition, fluorouracil is one of the basic chemotherapy drugs used to treat malignant tumours, and the toxic and side effects caused by the drug may be relieved when the plasma concentration is in a steady state, which is

conducive to the benefit of chemotherapy [13]. In this study we examined whether the plasma concentration monitoring fluorouracil could provide more reasonable guidelines for the chemotherapy of advanced gastric cancer patients. In this study, the plasma fluorouracil level was lower in the observational group than that in the control group (71.11% vs. 48.89%). The observation group also showed lower cancer pain and fatigue-related fatigue values and serum tumour markers, higher quality of life and less adverse reactions after therapy, suggesting a pl-monitoring result for the adjustment of chemical treatments for patients with advanced gastric cancer. There are also lower results in the observation group. These findings are partly in line with the Gong [14] study report comparing the effect on advanced gastric cancer patients with various fluororouracil plasma levels, with results showing a higher rate of adverse fluorouracil reactions than in mid-plasma and lower plasma plasma levels in the high plasma plasma concentration group.

Finally, the monitoring of plasma fluorouracil concentrations has a good chemotherapy effect in patients with advanced gastric cancer that enhances efficacy and reduces chemical adverse effects, thus improving patients ' quality of life.

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Tables

Table 1. **Short-term therapeutic efficacy [n (%)]**

Group	n	CR	PR	SD	PD	DCR
Control	45	0 (0)	7 (15.56)	15 (33.33)	23 (51.11)	22 (48.89)
Observation	45	0 (0)	12 (26.67)	20 (22.22)	13 (28.89)	32 (71.11) *

*P<0.05 *vs.* control group.

Table 2. **Scores of cancer-related symptoms ($\bar{\chi}$ ± s, point)**

Group	Time	Cancer-related pain score	Cancer-related fatigue score
Control (n=45)	Before treatment	7.58±1.82	7.35±2.07
	After treatment	5.77±1.36#	5.28±1.32#
Observation (n=45)	Before treatment	7.41±1.85	7.19±2.10
	After treatment	4.49±1.08#*	3.95±1.13#*

P<0.05 *vs.* before treatment. *P<0.05 *vs.* control group.

Table 3. **Serum tumor marker levels ($\bar{\chi}$ ± s)**

Group	Time	CEA (ng/mL)	CA125 (U/mL)	CA199 (U/mL)
Control (n=45)	Before treatment	22.45±4.23	35.06±6.94	46.76±9.37
	After treatment	18.19±3.51#	27.48±5.13#	36.53±7.24#
Observation (n=45)	Before treatment	22.27±4.29	34.81±6.87	46.42±9.43
	After treatment	14.68±3.04#*	21.15±4.56#*	29.27±6.05#*

P<0.05 *vs.* before treatment. *P<0.05 *vs.* control group.

Table 4. **Incidence rates of adverse reactions [n (%)]**

Group	n	Nausea and vomiting	Diarrhea	Bone marrow suppression	Mucositis
Control	45	17 (37.78)	16 (35.56)	11 (24.44)	13 (28.89)
Observation	45	8 (17.78) *	7 (15.56) *	4 (8.89) *	5 (11.11) *

*P<0.05 *vs.* control group.

Table 5. **Quality of life scores ($\bar{\chi}$ ± s, point)**

Group	Time	Physical health	Mental health	Social function	General feeling
Control (n=45)	Before treatment	69.56±5.09	70.38±5.20	69.27±4.81	70.09±5.18
	After treatment	75.09±6.53#	76.12±6.17#	74.35±5.03#	75.94±5.23#
Observation (n=45)	Before treatment	69.68±5.04	70.52±5.13	69.38±4.75	70.20±5.04
	After treatment	81.45±6.37#*	81.39±6.28#*	80.46±5.14#*	81.57±5.69#*

P<0.05 *vs.* before treatment. *P<0.05 *vs.* control group.