EFFECT OF CAPECITABINE OR TEGAFUR GIMERACIL OTERACI COMBINED WITH OXALIPLATIN ON CLINICAL OUTCOMES AND IL-2, TNF-A, INF-Γ AND MIR-141 IN PATIENTS WITH ADVANCED COLON CANCER

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ABSTRACT

Objective: *To study the effects of capecitabine or Tegafur Gimeracil Oteraci combined with oxaliplatin on patients with advanced colon cancer and their effects on serum IL-2, TNF-α, INF-γ and miR-141 levels.*

Methods: *A total of 100 patients with advanced colon cancer admitted to our hospital were enrolled and were divided into the capecitabine group and the Tegafur Gimeracil Oteraci group according to random number table method, each 50 cases. Patients in the capecitabine group were treated with capecitabine plus oxaliplatin, and the Tegafur Gimeracil Oteraci group was treated with Tegafur Gimeracil Oteraci combined with oxaliplatin. Three weeks were a course. Two courses were performed for patients in the two groups. The clinical efficacy of the two groups with different chemotherapy regimens and the effects of serum IL-2, TNF-α, INF-γ and miR-141 levels and adverse reactions were analyzed.*

Results: *After chemotherapy, the ORR (54%) and DCR (86%) of the Tegafur Gimeracil Oteraci group were higher than those of the capecitabine group (ORR (44%) and DCR (78%), but the differences between they two were not obvious(P>0.05); Capecitabine or Tegafur Gimeracil Oteraci combined with oxaliplatin had more adverse reactions in patients with advanced colon cancer. Comparison between two groups, Capecitabine combined with oxaliplatin were more likely to cause adverse reactions such as digestive symptoms and hand-foot syndrome (P<0.05).*

Conclusion: *Capecitabine combined with oxaliplatin are more likely to cause adverse reactions than the Tegafur Gimeracil Oteraci group, but both have significant efficacy in patients with advanced colon cancer, and may effectively lower serum IL-2, TNF-α, INF-γ and miR-141 levels of patients, increase response rate after chemotherapy and thus promote life quality.*

Keywords: *Capecitabine, tegafur gimeracil oteraci, oxaliplatin, advanced colon cancer, clinical efficacy, TNF-α, miR-141.*

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Introduction

Colon cancer, as one of the most common malignant tumor worldwide, is one of the most common malignant in the digestive system[1] and has received much attention from humans. Currently, its incidence rate and mortality is increasing year by year. According to relevant literature studies[2-3], most occur between 40 and 50 years old, and the cause of the disease is unknown. It is generally believed that it may be related to some high-risk factors such as genetic environment and some intestinal chronic inflammatory lesions etc[4]. Furthermore, the onset of the disease is hidden. If life, it is mistaken as mild digestive tract symptoms, thus delaying visit time. Its atypical symptoms are easily to cause error diagnosis[5]. At advanced stage, it causes tumors cells to invade surrounding tissue even whole body, thus losing surgical chance. Therefore, some chemotherapy methods have become essential treatment methods for patients with advanced colon cancer.

This study is aimed at further exploring clinical efficacy of its regimen and adverse reactions as well as the influences on serum IL-2, TNF-α, INF-γ and miR-141 by comparing and analyzing combined chemotherapy regimens commonly used in clinic, thus better proving services for patients with advanced colon cancer.

Data and methods

General data

This study report belonged retrospective study, 100 patients with advanced colon cancer admitted into our hospital from February 2010 to March 2013 were analyzed and were randomly divided into the capecitabine group and the Tegafur Gimeracil Oteraci group, each 50 cases.

Inclusive criteria:

• Patients all met diagnosis of pathology and cell biology on advanced colon cancer;

• The selected patients were first diagnosis and not given routine chemotherapy before admission and all evaluation were tolerate to chemotherapy;

• Those without other malignant diseases or severe physical organ dysfunction;

• Patients and their families agreed the study and signed informed consent form before admission.

In this study, age in the capecitabine group was 51.3±4.6 consisting of 26 males and 24 females. For TNM staging, there were 23 cases in III stage, 27 cases in IV stage; that in the Tegafur Gimeracil Oteraci group was 50.2±4.2 years, consisting of 28 males and 22 females. For TNM staging, there were 26 cases in III stage and 24 cases in IV stage. There were statistical differences between two groups with respect to age, sex and pathological staging of patients (P>0.05). Detail data are shown in table 1.

Group	Age (years)	Male (cases)	Female (cases)	TNM staging
The capecitabine group	51.3±4.6	26	24	23 cases in III stage, 27 cases in IV stage
The Tegafur Gimeracil Oteraci group	50.2±4.2	28	22	26 cases in III stage, 24 cases in IV stage

Table. 1: General data.

Methods

First, half an hour before chemotherapy, patients in two groups were intravenously injected with 5mg of dexamethasone for pretreatment; patients in the Tegafur Gimeracil Oteraci group were given capecitabine plus oxaliplatin, namely, 130mg/m2 of oxaliplatin was injected into 5% glucose solution by intravenous drip for 2 h, and 2000mg/m2 of capecitabine was orally administered after meal twice daily. The Tegafur Gimeracil Oteraci group was given Tegafur Gimeracil Oteraci combined with oxaliplatin, and oxaliplatin administration was same to the capecitabine group, 50mg/m2 of Tegafur Gimeracil Oteraci was combined and orally administered after meal twice daily. The average three-week was a course. Patients in two groups were given two-course treatment. Physiological indexes were reexamined and relevant complications were treated in ime during chemotherapy period.

Observation

The clinical efficacy, adverse reactions, and changes of serum IL-2, TNF-α, INF-γ and miR-141 levels before and after chemotherapy in two chemotherapy regimens were observed: Drug clinical efficacy was divided into complete (CR), partial response (PR), Stable disease (SD) and progressive disease referring to relevant literature evaluation criteria. Objective response rate (ORR) = (CR+PR)/total cases. Disease control rate DCR = (CR+PR+SD)/total cases. Adverse reactions referred to grading criteria of adverse reactions of anti-tumor drugs, all were 0-IV grade[6]. For measurement of serum IL-2, TNF-α, INF-γ and miR-141 in patients, blood of patients was extracted at fasting state in the morning using ELISA method[7]. Detail procedures referred to instruction of kits.

Statistical methods

Statistical analysis was done using SPSS 19.0 software. The enumeration data including CR PR SD were compared using χ^2 test. P<0.05, it was considered as statistically significance.

Results

Comparison of clinical efficacy of chemotherapy regimens in two groups

In this study, the clinical efficacy of capecitabine combined with oxaliplatin and Tegafur Gimeracil Oteraci combined with oxaliplatin on chemotherapy in patients with advanced colon cancer showed that the ORR (54%) and DCR (86%) were higher in The ORR (44%) and DCR (78%) in the capecitabine group. Two groups were not significantly different. The difference between the two was not statistically significant tested by χ^2 (P>0.05). It is shown in table 2.

Group	N (case)	CR (case)	PR (case)	SD (case)	PD (case)	ORR (%)	DCR (%)
The capecitabine group	50	1	21	17	12	44.0 (22/50)	78.0 (39/50)
The Tegafur Gimeracil Oteraci group	50	0	27	16	7	54.0 (27/50)	86.0 (43/50)
χ^2						1.003	1.082
P						0.322	0.301

Table. 2: Comparison of clinical efficacy of chemotherapy regimens in two groups.

Comparison of serum IL-2, TNF-α, INF-γ and miR-141 levels of patients in two groups

In this study, the changes of serum IL-2, TNF-α, INF-γ and miR-141 levels in the two groups before and after chemotherapy were compared, it was concluded that serum IL-2, TNF-α, INF-γ and miR-141 levels in the two groups before chemotherapy had no significant differences(P>0.05)and those in the capecitabine group and the Tegafur Gimeracil Oteraci group all significantly decreased, there were no obvious differences between two groups. There were no statistical significance tested by t test (P>0.05). It is shown in table 3.

Group	cases	IL-2 (ng/L)		TNF-α (ng/L)		INF-γ (ng/L)		miR-141	
		BC	AC	BC	AC	BC	AC	BC	AC
The capecitabine group	50	133.45 ±6.87	40.77 ±5.37	50.22 ±5.41	22.18 ±4.22	64.35 ±4.77	25.34 ±3.66	19.44 ±2.88	4.88 ±2.11
The Tegafur Gimeracil Oteraci group	50	134.25 ±5.88	42.98 ±6.11	48.35 ±4.69	20.79 ±4.53	64.78 ±5.12	24.27 ±4.13	18.36 ±3.52	4.21 ±1.23
t		0.706	1.921	1.847	1.588	0.435	1.371	1.679	1.94
P		0.482	0.058	0.068	0.116	0.665	0.174	0.096	0.055

Table. 3: Comparison of serum IL-2, TNF-α, INF-γ and miR-141 levels of patients in two groups ($\bar{x}\pm s$).
Notes: BC, Before chemotherapy; AC, After chemotherapy.

Comparison of adverse reactions in two groups

This study compared the adverse reactions of chemotherapy in the capecitabine group and the Tegafur Gimeracil Oteraci group. It can be concluded that both groups have adverse reactions such as myelosuppression, nausea and vomiting, hand-foot syndrome, liver dysfunction, and anemia, etc. After χ^2 test, it was believed that adverse reactions including myelosuppression, liver dysfunction, anemia had no statistical significance (P>0.05); it was believed that nausea, vomiting, hand-foot syndromes had statistical significance (P<0.05), and the capecitabine group higher than the Tegafur Gimeracil Oteraci group. Positive symptomatic treatment was given for adverse reactions of patients during chemotherapy period, which not caused adverse outcomes for patients. It is shown in table 4.

Group	Cases	M (%)	N (%)	H (%)	L (%)	A (%)
The capecitabine group	50	9 (9/50)	31 (31/50)	28 (28/50)	18 (18/50)	17 (17/50)
The Tegafur Gimeracil Oteraci group	50	11 (11/50)	21 (21/50)	15 (15/50)	15 (15/50)	14 (14/50)
χ^2		0.254	5.763	6.902	0.413	0.421
P		>0.05	<0.05	<0.05	>0.05	>0.05

Table. 4: Comparison of adverse reactions in two groups.
Notes: M, Myelosuppression; N, Nausea and vomiting; H, Hand-foot syndrome; L, Liver dysfunction; A, Anemia.

Discussion

Colon cancer is the common malignant tumor in digestive system in medicine. According to relevant reports, it is second only to gastric cancer and esophageal cancer, ranking the third place in malignant tumors of the digestive tract, and the mortality rate is extremely high[8]. In china, the incidence rate and mortality rate of colon cancer are increasing year by year. Its hidden onset enables chemotherapy to become essential method for the treatment of advanced colon cancer. At present, the first-line chemotherapy for patients with advanced colon cancer is oxaliplatin + calcium leucovorin + 5-fluorouracil, oxaliplatin + capecitabine, oxaliplatin + Tegafur Gimeracil Oteraci, etc[9], thus exploring clinical efficacy, adverse reactions, safety and tolerance of chemotherapy medication on patients with advanced colon cancer has become the study hotsopt.

Capecitabine, as a 5-fluorouracil prodrug, can accurately identify tumor cells and inhibit tumor proliferation by inhibiting synthesis of RNA and protein in tumor cells[10]; Oxaliplatin, a novel platinum anti-tumor drugs, further inhibits growth of tumor cells by enabling denaturation of DNA in tumor cells and strengthen its anti-tumor function combined with capecitabine, which can play synergy effects; Tegafur Gimeracil Oteraci, as a compound drug, its metabolites of 5-fluorouracil has anti-tumor killing function and its internal component of gempyrimidine can inhibit killing tumor of degradation of 5-fluorouracil, thus prolonging the time of drug action and its internal component of ottilasi promotes tolerance of digestive tract to drugs by inhibiting phosphorylation of 5-fluorouracil[11]. Results of this study are in accordance with drug pharmacology, digestive symptoms in the Tegafur Gimeracil Oteraci are better than those of the capecitabine group and differences have statistical significance(P<0.05).

Meanwhile, study results show that ORR (54%) and DCR (86%) in the Tegafur Gimeracil Oteraci group all higher than ORR (44%) and DCR (78%) of the capecitabine group after combination medication treating patients with advanced colon cancer, but differences between them are not obvious and have not statistical significance (P>0.05), showing they two have good clinical efficacy in treating patients with advanced colon cancer; In addition, adverse reactions such as myelosuppression, digestive symptoms, anemia, hand-foot syndromes, liver dysfunction all increase, and there are

no statistical significance between the capecitabine group and the Tegafur Gimeracil Oteraci group with respect to myelosuppression, anemia and liver dysfunction (P>0.05); there are statistical significance between two groups with respect to digestive symptoms and hand-foot syndromes (P<0.05), and adverse reactions in the capecitabine group are more significant.

In recent years, reports on the treatment of patients with advanced colon cancer with capecitabine or tegafur Gimeracil Oteraci combined with oxaliplatin at home and abroad have emerged constantly, but their reports on the effects of IL-2, TNF-α, INF-γ and miR-141 are still rare. IL-2, TNF-α and INF-γ act as cell biological factors, which are inseparable from the occurrence, development and prognosis of colon cancer. Relevant scientists believe that[12], higher levels of serum IL-2, TNF-α, INF-γ may indicate the deterioration of the patient's condition[13]. TNF-α can be produced by tumor cells themselves, which is not only one of the promoters of chronic inflammation, but low dose sustained role in tumor invasion and metastasis of colon cancer patients has played an important role[14]. Human microRNA-141 (miR-141) has the function of regulating cell growth, participating in cell differentiation and apoptosis in human body. After gene mutation or abnormal expression, its function is similar to that of oncogene, which causes the loss of regulation and becomes one of reasons in tumor infinite proliferation[15]. It can be seen that serum IL-2, TNF-α, INF-γ and miR-141 levels are higher in colon cancer patients, which is an important indicator for clinical monitoring of patients' prognosis after chemotherapy.

The results of this study showed that serum IL-2, TNF-α, INF-γ, and miR-141 levels significantly decrease after chemotherapy in both groups, and the difference between the two groups was not significant. The difference was not statistically significant after calculation (P>0.05), indicating capecitabine or Tegafur Gimeracil Oteraci combined with oxaliplatin all can significantly lower IL-2, TNF-α, INF-γ and miR-141 levels; furthermore, after comparing clinical efficacy of chemotherapy in two groups, the Tegafur Gimeracil Oteraci group were ORR (54%) and DCR (86%), and the capecitabine group were ORR (44%) and DCR (78%, both groups can improve ORR and DCR, but differences between them have no statistical significance (P>0.05), presenting capecitabine or Tegafur Gimeracil Oteraci combined with oxaliplatin have accurate efficacy and similar efficacy on patients with advanced colon cancer.

According to this study, it can be concluded that capecitabine or Tegafur Gimeracil Oteraci combined with oxaliplatin is effective in the treatment of patients with advanced colon cancer, and the effect is equivalent, which can effectively reduce serum IL-2, TNF-α, INF-γ. And miR-141 levels, and differences between them are not obvious. Two chemotherapy regimens all have relevant adverse reactions, but capecitabine combined with oxaliplatin have better efficacy in the treatment of hand-foot syndromes compare to the Tegafur Gimeracil Oteraci group. However, due to the small number of people included in this study, the sample size is limited and defective. In order to make the results more accurate, large sample data is still needed for further research.

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