

Efficacy of internal Supplementation and External Attack Anti-cancer Combination with FOLFIRI Chemotherapy in Advanced Colorectal Cancer

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Abstract

Objective: To investigate the efficacy of internal supplementation and external attack anti-cancer combination with FOLFIRI in advanced colorectal cancer. **Methods:** A total of 70 patients with advanced colorectal cancer who were treated in the Affiliated Hospital of Shaanxi University of Chinese Medicine from February 2019 to February 2022 were randomly divided into observation group and control group, with 35 cases in each group. The control group was given FOLFIRI chemotherapy, and the observation group was given internal supplementation and external attack anti-cancer combination with FOLFIRI chemotherapy, both with 14 days as a cycle, and both groups were treated for 8 cycles. The immune function, serum tumor marker level, TCM syndrome score, clinical efficacy and adverse reactions of the two groups were observed and compared. **Results:** After treatment, the immunoglobulin A (IgA), immunoglobulin G (IgG) and immunoglobulin M (IgM) of the two groups were higher than those before treatment, the carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), carbohydrate antigen 724 (CA724), and TCM syndrome scores were lower than those before treatment, and the clinical efficacy rates of IgA, IgG, IgM and IgM in the observation group were higher than those in the control group, and the incidence of CEA, CA199, CA724, TCM syndrome scores and adverse reactions were lower than those in the control group, the difference was statistically significant ($P < 0.05$). **Conclusion:** The combination of internal supplementation and external attack anti-cancer regimen combined with FOLFIRI chemotherapy has a good effect on advanced colorectal cancer, improves immune function, reduces adverse reactions and improves quality of life.

Keywords

Colorectal Cancer; Internal Supplementation and External Attack Anti-Cancer; FOLFIRI Chemotherapy Regimen; Immunoglobulin; Carcinoembryonic Antigen; Carbohydrate Antigen 199.

1. Introduction

Colorectal cancer (CRC) is the third most common cancer in the world and the second most common among tumor-related mortality, and new data show that the incidence and mortality of CRC in China is gradually increasing [1]. CRC is not obvious in the early stage, and it is mostly advanced when it is found, and the treatment method for early colorectal cancer is mostly surgical radical resection, and the advanced stage is mainly chemotherapy [2]. However, the current single chemotherapy regimen is not satisfactory for patients, so it is necessary to find a safer and more effective treatment regimen [3]. With the development of the modernization of traditional Chinese medicine, more and more researchers related to colorectal cancer have

turned their attention to traditional Chinese medicine. Patients with advanced colorectal cancer are mainly positive and declining, with positive qi dissipation, a wide range of evil qi invasion, or distant metastasis, showing a large virtual and real state. Luo Tianyi proposed in the "Health Treasure Guide" that "nourishing the right accumulation and self-elimination", so for patients with middle and advanced cancer diseases, positive qi is depleted, and the treatment is aimed at supporting the righteousness and taking into account the elimination of evil. Fuzheng can adjust the physiological function of the internal organs, improve the immune function and disease resistance, improve symptoms, and can use methods such as strengthening the spleen and invigorating qi, warming the kidney and aphrodisiac, nourishing the yin and nourishing the blood, and benefiting the yin and vitality. Chinese medicine can be applied externally to dispel evil spirits, which not only does not consume healthy qi, but also dissolves stasis and detoxification to eliminate cancer and improve the treatment effect. This study aims to investigate the efficacy of internal supplementation and external attack anti-cancer regimens combined with FOLFIRI regimen in advanced colorectal cancer, which is reported as follows [4].

2. Data and Methods

2.1. General information

A total of 70 patients with advanced colorectal cancer treated in the Affiliated Hospital of Shaanxi University of Chinese Medicine from February 2019 to February 2022 were randomly divided into observation group and control group, with 35 cases in each group. There were 18 males and 17 females in the observation group. There were 19 cases of TNM stage III and 16 cases of stage IV. There were 20 cases of colon cancer and 15 cases of rectal cancer. In the control group, there were 16 males and 19 females; there were 18 cases of TNM stage III and 17 cases of stage IV. There were 22 cases of colon cancer and 13 cases of rectal cancer. The general data of the two groups were statistically analyzed, and the difference was not statistically significant ($P > 0.05$), which was comparable. All patients signed informed consent.

2.2. Diagnostic criteria

In line with the diagnostic criteria of colorectal cancer in ' practical oncology ', and confirmed by pathological examination for stage III-IV colorectal cancer; in line with the ' guiding principles of clinical research of new drugs of traditional Chinese medicine ' TCM qi and blood deficiency syndrome differentiation diagnostic criteria [5].

2.3. Inclusion criteria

1) without other malignant tumors; 2) The estimated survival time was more than 3 months, and the whole course of treatment was accepted with complete clinical data. 3) no immune system defect disease; 4) no mental illness, can cooperate with treatment, can understand the questionnaire content; 5) without severe infection and other diseases affecting serological indicators [6].

2.4. Exclusion criteria

1) Patients who received other forms of treatment other than this study; 2) Patients with a history of intestinal surgery; 3) patients with abnormal liver and kidney function, intestinal perforation, gastrointestinal bleeding obstruction and other malignant tumors; 4) patients without clear tumor lesions; 5) with abnormal coagulation and hematopoietic function; 6) Drug allergy in this study [7].

2.5. Dropout and elimination criteria

1) Patients withdrew from the study for their own reasons; 2) Patients with severe adverse reactions who could not tolerate treatment; 3) severe medical diseases can not be controlled.

2.6. Treatment methods

The control group was treated with FOLFIRI regimen chemotherapy: irinotecan hydrochloride (CPT-11, Jiangsu Hengrui Pharmaceutical Co., Ltd., Chinese medicine approval H20020687, specification: 40 mg), 180 mg/m² intravenous infusion on the first day; cF (Shanghai Saikerui Biotechnology Co., Ltd., Batch No.: SCS-301734, Specification: 1 mg), 200 mg / m² intravenous infusion on the first day; 5-fluorouracil (5-Fu, Shanxi Pude Pharmaceutical Co., Ltd., Sinopharm H2005113, specification: 0.25 g), 400 mg/m² intravenous drip, 2400 mg/m² micropump continuous intravenous push 46 h[8]. On the basis of the control group, the observation group was treated with internal supplementation and external attack anti-cancer prescription: 1) Fuzheng Tiaoqi Decoction (oral): roasted Astragalus 15 g, raw Paeonia 15 g, Codonopsis 15 g, Angelica 12 g, Corydalis 12 g, Toosendan 9 g, Pinellia 9 g, Pericarpium Citri Reticulatae 9 g, roasted Glycyrrhiza 6 g, Jiangxiang 3 g. (2) Resolving Stasis and Removing Tumor Powder: Radix Paeoniae Rubra 12g, Semen Persicae 12g, Rhizoma Cyperi 12g, Radix Linderae 12g, Frankincense 6g, Flos Carthami 6g, Ferula 4.5g. The decoction was soaked in water for 30 minutes, and then decocted for 30 minutes. Each dose was decocted twice. A total of 450 ml was decocted, one dose per day, taken twice. Resolving Stasis and Removing Tumor Powder: All drugs were studied together, adjusted into a paste with vinegar, applied to the affected area or the skin corresponding to the visceral tumor, fixed with gauze, changed once a day, and applied to the skin with a little vaseline. If the skin blisters, it can be suspended for a few days and then applied. Two weeks was a cycle, and both groups were treated with 12 cycles [9].

2.7. Observation indicators

2.7.1. Levels of humoral immune indexes and serum tumor markers

On the first day of admission and the second day after treatment, 7 ml of fasting venous blood was taken from the patient in the morning, centrifuged at 2 500 r / min for 15 min, and the centrifugal radius was 5 cm. The serum was separated, and the supernatant was taken. The levels of humoral immune indexes including immunoglobulin A (IgA), immunoglobulin G (IgG) and immunoglobulin M (IgM) were determined by double antibody sandwich enzyme-linked immunosorbent assay. The levels of tumor markers carbohydrate antigen-199 (CA199) and carbohydrate antigen-724 (CA724) were detected. The level of carcinoembryonic antigen (CEA) was detected by electrochemiluminescence microparticle immunoassay. All steps were carried out in strict accordance with the instructions [10].

2.7.2. TCM syndromes

The evaluation was carried out according to the relevant standards of the ' Guiding Principles for Clinical Research of New Drugs of Traditional Chinese Medicine ', mainly from the evaluation of chest tightness, night sweats, tongue and pulse and other syndromes. Each severe was 2 points, moderate was 1 points, and mild was 0 points.

2.7.3. Clinical efficacy

According to WHO solid tumor efficacy evaluation criteria, markedly effective: complete remission; effective: partial remission, stable condition; ineffective: the condition did not change, still in progress. The effective rate of treatment (%) = (markedly effective cases + effective cases) / total cases × 100 %.

2.7.4. Adverse reactions

The adverse reactions during treatment were observed and compared between the two groups, including blood toxicity, nausea and vomiting, diarrhea, dermatitis, alopecia and neurotoxicity [11].

2.8. Statistical analysis

SPSS 26.0 statistical software was used for data analysis. The measurement data were expressed as $x \pm s$. The independent sample t test was used for comparison between groups, and the paired t test was used for comparison within groups. The enumeration data were expressed as percentage, and the χ^2 test was used for comparison between groups. $P < 0.05$ was considered statistically significant.

3. Results

3.1. Immune function indicators

There was no significant difference in immune function indexes between the two groups before treatment ($P > 0.05$). After treatment, IgG, IgA and IgM in the two groups were higher than those before treatment ($P < 0.05$), and IgG, IgA and IgM in the observation group were higher than those in the control group ($P < 0.05$). See Table 1.

Table 1: Comparison of immune function indexes between the two groups before and after treatment (g/L, $x \pm s$)

Group	Cases	IgG		IgA		IgM	
		Treatment before	Treatment after	Treatment before	Treatment after	Treatment before	Treatment after
Control group	35	8.23±0.78	11.23±1.45	1.42±0.56	2.35±0.36	0.56±0.28	1.23±0.48
Observation group	35	8.35±0.81	14.65±1.62	1.25±0.63	3.57±0.78	0.48±0.35	2.59±0.56
t		0.423	9.874	0.236	6.873	0.652	7.256
p		0.726	0.001	0.652	0.001	0.825	0.001

3.2. Tumor markers

There was no significant difference in CEA, CA199 and CA724 between the two groups before treatment ($P > 0.05$), and after treatment, CEA, CA199 and CA724 were lower than those before treatment ($P < 0.05$), and CEA, CA199 and CA724 in the observation group were lower than those in the control group ($P < 0.05$). See table 2.

Table 2: Comparison of tumor markers before and after treatment ($x \pm s$) between the two groups

Group	Cases	CEA (ng/ml)		CA199(U/ml)		CA724(U/ml)	
		Treatment before	Treatment after	Treatment before	Treatment after	Treatment before	Treatment after
Control group	35	44.85±5.69	35.38±5.87	85.63±8.56	56.39±7.14	63.58±9.18	45.62±6.45
Observation group	35	45.63±6.32	26.65±6.86	82.75±7.89	46.92±6.35	61.98±8.76	39.35±6.96
t		0.469	5.692	0.568	4.382	0.657	6.895
p		0.578	0.001	0.784	0.001	0.635	0.001

3.3. TCM syndrome score

There was no significant difference in TCM syndrome scores between the two groups before treatment ($P > 0.05$). After treatment, the scores of TCM syndromes in the two groups were lower than those before treatment ($P < 0.05$), and the scores of TCM syndromes in the observation group were lower than those in the control group ($P < 0.05$). See Table 3.

Table 3: Comparison of TCM syndrome scores between the two groups before and after treatment (points, $x \pm s$)

Group	Cases	Treatment before	Treatment after
Control group	35	8.96±2.37	6.57±1.46
Observation group	35	8.68±2.54	5.35±1.23
t		0.459	2.365
p		0.826	0.001

3.4. Effectiveness of treatment

The effective rate of treatment in the observation group was higher than that in the control group ($P < 0.05$). See Table 4.

Table 4: Comparison of treatment efficiency between the two groups [case (%)]

Group	Cases	markedly effective (cases)	effective (cases)	ineffective (cases)	effective rate of treatment [cases (%)]
Control group	35	21	5	9	26(74.29)
Observation group	35	25	8	2	33(94.26)
χ^2					9.326
p					0.001

3.5. Adverse reactions

The incidence of adverse reactions in the observation group was lower than that in the control group ($P < 0.05$). See Table 5.

Table 5: Comparison of adverse reactions between the two groups [cases (%)]

Group	Cases	Haematological toxicity	Nausea and vomiting	Diarrhea	Dermatitis	Alopecia	Neurotoxicity
Control group	35	5(14.29)	20(57.14)	10(28.57)	17(48.57)	7(20.00)	15(42.86)
Observation group	35	9(25.71)	12(34.29)	5(14.29)	7(20.00)	3(8.57)	8(22.86)
χ^2		1.863	7.569	0.683	2.023	1.635	4.562
p		0.263	0.128	0.367	0.238	0.795	0.153

4. Discussions

At present, the pathogenesis of colorectal cancer is not clear, and chemotherapy is still the most important treatment for patients with advanced colorectal cancer. However, there are many

adverse reactions in the FOLFIRI chemotherapy regimen, so it is necessary to find a combination of drugs to reduce adverse reactions and improve the quality of life of patients [12]. The FOLFIRI chemotherapy regimen prolongs the survival time of patients by killing cancer cells and reducing cancer tissue lesions. Studies have shown that FOLFIRI chemotherapy can prolong the survival time and improve the quality of life of patients with advanced colorectal cancer [13]. However, the adverse reactions of this method are large, so it is necessary to combine other drugs to improve the therapeutic effect [14]. The TCM syndromes of patients with advanced colorectal cancer are manifested as 'deficiency in origin and excess in superficiality'. 'Deficiency in origin' refers to the essence of deficiency, that is, deficiency of five zang-organs and deficiency of qi, blood, yin and yang. 'Excess in superficiality' refers to the tangible things formed in the local (colorectal) by long-term stagnation of pathogenic qi such as 'phlegm, blood stasis, heat, dampness and toxin'. The fundamental pathogenesis is deficiency of healthy qi. Therefore, strengthening healthy qi is the most important treatment for patients with advanced colorectal cancer. The internal supplementation and external attack anti-cancer prescription is to take internal service to support the right and regulate qi dispersion, strengthen the spleen and invigorate qi, and nourish yin and vitality [15]. External application to dissolve stasis, break tumor, disperse blood circulation and dissolve stasis, eliminate stagnation. Therefore, internal and external anti-cancer treatment has outstanding effect on adjuvant chemotherapy in patients with advanced colorectal cancer and improves its safety [16].

IgG, IgA and IgM are all indicators to determine whether the immune function is normal. When the index is reduced, the immune function of the body is inhibited. CA-199 is a tumor marker of glycolipids, mainly in pancreatic cancer, gallbladder cancer, colorectal cancer and gastrointestinal malignancies. CEA is a blood tumor marker, which is a strong evidence for the diagnosis, efficacy, prognosis and selection of gastrointestinal cancer. CA724 is one of the important laboratory markers of digestive tract cancer. It is mainly used in the clinical observation and preliminary screening of digestive tract malignant tumors. The results of this study show that the combined treatment of advanced colorectal cancer patients with internal supplementation and external attack anti-cancer prescription and FOLFIRI chemotherapy can improve the levels of IgG, IgA and IgM, reduce the levels of CA-199, CA724 and CEA, and prolong the survival time of patients. The main reason is that the combination of the two drugs has a good effect on inhibiting the growth of tumor cells. At the same time, the traditional Chinese medicine in this study has the effect of regulating immune function. Therefore, the combination of the two drugs can improve the immune function of patients with advanced colorectal cancer. In summary, the combination of internal and external anti-cancer prescription and FOLFIRI chemotherapy regimen has a prominent therapeutic effect on advanced colorectal cancer, and has high safety and can reduce the adverse reactions of patients. However, the sample size of this study is small, and further research is needed [17].

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