



Effect of Fuzhengyiai recipe on serum IGF-1, EGF, TK1, CRP, CA199 and CD4⁺ lymphocyte subsets in patients after traditional radical resection of colon cancer

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ABSTRACT

Objective: To study the effect of Fuzhengyiai recipe on serum IGF-1, EGF, TK1, CRP, CA199 and CD4⁺ lymphocyte subsets in patients after traditional radical resection of colon cancer. **Methods:** A total of 120 patients with colon cancer in our hospital from January 2013 to December 2015 were enrolled in this study. The subjects were divided into control group ($n=60$) and experiment group ($n=60$) randomly. The control group were treated with capecitabine and oxaliplatin on the basis of the traditional radical resection of colon cancer, the experiment group were treated with Fuzhengyiai recipe on the basis of the control group. 21 days for a period of treatment and the two groups were treated for 3 periods. The serum IGF-1, EGF, TK1, CRP, CA19-9 level and peripheral blood CD3⁺, CD4⁺, CD8⁺ and NK cells of the two groups before and after treatment were compared. **Results:** There were no significantly differences of the serum IGF-1, EGF, TK1, CRP, CA199 level and peripheral blood CD3⁺, CD4⁺, CD8⁺ and NK cells of the two groups before treatment. The serum IGF-1, EGF, TK1, CRP and CA19-9 level of the two groups after treatment were significantly lower than before treatment, and that of experiment were significantly lower than control group. The peripheral blood CD3⁺, CD4⁺, CD8⁺ and NK cells of the control group were significantly lower than before treatment, and that of experiment were significantly higher than control group. **Conclusion:** Fuzhengyiai recipe can significantly reduce the serum IGF-1, EGF, TK1, CRP and CA199 level of the patients after traditional radical resection of colon cancer, improve peripheral blood CD3⁺, CD4⁺, CD8⁺ and NK level, strengthen the immune function, and it was worthy of promotion and application in clinical practice for the future.

1. Introduction

Colon cancer is a common malignant tumor of digestive tract, accounting for third of the gastrointestinal cancer[1]. With the pace of life accelerated and diet structure change, the incidence of colon cancer in the population increased year by year, accounting for about 10% of malignant tumors, and has a younger age trend, so it seriously threatens people's physical health[2]. The pathogenesis of colon cancer is not clear, mainly related to diet, lack of physical

activity, living environment, genetic and other relevant factors[3]. There is no specific clinical symptoms in the early stage of colon cancer, so it is often difficult to detect, and the common clinical symptoms at the late stage of the disease include fever, fatigue, anemia, indigestion, nausea, vomiting, abdominal distension, abdominal pain, defecation, hematochezia and etc[4]. At present, Colon cancer is usually treated with colon cancer radical surgery combined with postoperative adjuvant chemotherapy[5]. Postoperative chemotherapy for patients with colon cancer after radical surgery often leads to low immune function, inflammatory reaction and a series of adverse reactions, therefore, it is of great clinical significance to find effective drug control patients with adverse reactions after operation. This study aims to explore the effect of Fuzhengyiai recipe on serum IGF-1, EGF, TK1, CRP,

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CA199 and CD4⁺ lymphocyte subsets in patients after traditional radical resection of colon cancer, and the results are as follows.

2. Informations and Methods

2.1. General information

A total of 120 cases of patients with colonic adenocarcinoma from January 2013 to December 2015 after surgery in our hospital were selected, with 63 male patients, 57 female patients, ages were from 42 to 76 years old, mean age (60.24 ± 15.31) years. Case inclusion criteria: (1) The diagnosis of colon cancer was confirmed by electronic colonoscopy, biopsy pathology and postoperative pathology; (2) Patients that accept surgical treatment for the first time. Case exclusion criteria: (1) Patients with other malignant diseases; (2) Emergency operation patients; (3) Colon cancer patients with IV; (4) Person whose heart, lung, liver, kidney can't functions very well; (5) Person that do not cooperate with the treatment.

The 120 cases were randomly divided into experimental group and control group, with 60 cases in each group. In the experimental group, there were 32 male patients, 28 female patients, aged 42 to 75 years old, mean age (60.24 ± 15.31) years. Lesion site: 18 cases with ascending colon, 16 cases with transverse colon, 13 cases with descending colon, 13 cases of sigmoid colon; TNM pathological stage: 28 cases in Stage II, 32 cases in III. In control group, there were 31 male patients, 29 female patients, aged 43 to 76 years old, mean age (60.81 ± 15.12) years. Lesion site: 19 cases with ascending colon, 15 cases with transverse colon, 15 cases with descending colon, 11 cases of sigmoid colon; TNM pathological stage: 27 cases in Stage II, 33 cases in III. There were no significant differences in gender, age, location of lesion, TNM pathological stage and other general data between the two groups ($P > 0.05$). All patients were informed consent and volunteered to join the study.

2.2 Experimental method

Two groups of patients were in the colon cancer after radical surgery, and were give the corresponding treatment measures. Patients in the control group were given XELOX chemotherapy, specifically for: oxaliplatin (Jiangsu Hengrui pharmaceutical Limited by Share Ltd, Specification 50 mg/branch, Chinese medicine standard word H20000337), Intravenous infusion, 130 mg/m², d1; Xeloda (Purchase from Shanghai Roche Pharmaceutical Ltd, Specification 0.5 g/film, Chinese medicine standard word H20073024), Oral administration, 1.0 g/m², 2 times/d, d1-14; Patients in the experimental group were based on the control group. The Experimental group patients was given the treatment of Fuzhengyiai recipe on the basis of control group. Fuzheng Yi'ai decoction is Decoction, specifically for: Dangshen 15 g, Radix Astragali 30 g, tuckahoe 10 g, 10 g of the rhizome of large headed Atractylodes, Lily 30 g, angelica 10 g, Danshen 15 g, 15 g of Radix Rehmanniae Preparata, Radix Paeoniae Rubra 15 g, Ligustrum lucidum 15 g, Fructus Corni 15 g, polygonatum 15 g, 10 g of placenta, Gynostemma pentaphyllum 30 g, dried tangerine peel 10 g, Fabanxia 10 g, Banzhilian 30 g, 30 g Hedyotis, licorice

6 g. Decoction is taken 2 times, 1 dose daily. 21 d for 1 cycles, two groups of patients were treated for 3 cycles.

2.3. Detection index

To evaluate the changes of immune function before and after treatment in two groups, the levels of serum IGF-1, EGF, TK1, CRP, CA19-9, CD3⁺, CD4⁺, CD8⁺ and natural killer (NK) cells were detected and compared between the two groups before and after treatment.

Serum levels of IGF-1, EGF and TK1 were detected by the corresponding double anti sandwich enzyme linked immunosorbent assay (ELISA), all of the kit are purchased from Shanghai based non Industrial Co., Ltd, and all operations were carried out strictly according to the kit instructions; Detection of serum CRP levels used a SIEMENS II BN full automatic specific protein analyzer, by using the immune turbidity transmission method; The detection of serum CA19-9 level was performed by Beckman Kurt UnicelDxI800 automatic immunoassay; CD3⁺, CD4⁺, CD8⁺ and natural killer (NK) cells were detected by FACSCalibur BD flow cytometry in peripheral blood.

2.4 Statistical method

We carry on data statistics and analysis using SPSS 19.0 software package, mean \pm standard deviation (Mean \pm SD) represents measurement data, the use of t test was to compare between groups of measurement data and count data, with $P < 0.05$ as a statistically significant.

3. Results

3.1 Comparison of serum IGF-1, EGF and TK1 levels before and after treatment for two groups' patients

Before treatment, there was no significant difference in serum IGF-1, EGF and TK1 levels between the two groups ($P > 0.05$); After treatment, for both experimental group and control group, the level of serum IGF-1 (9.25 ± 1.05 , 26.54 ± 1.76), EGF (1.38 ± 0.18 , 2.47 ± 0.22) and TK1 (1.01 ± 0.1 , 1.98 ± 0.14) levels were significantly lower than those before treatment, At the same time, the experimental group patients were significantly lower than the control group, the difference was statistically significant ($P < 0.05$). Please look at the table 1.

3.2 Comparison of serum levels of CRP and CA19-9 before and after treatment in two groups

Before treatment, there was no significant difference in the serum levels of CA19-9 and CRP between the two groups ($P > 0.05$); After treatment, for both experimental group and control group, the level of serum CRP (8.35 ± 1.21 , 14.36 ± 2.11), CA19-9 (19.69 ± 2.71 , 29.42 ± 3.15) levels were significantly lower than those of before treatment, with CRP (35.16 ± 5.04 , 35.21 ± 4.72), CA19-9 (43.45 ± 5.19 , 43.51 ± 5.23), and the difference was statistically

significant ($P<0.05$). At the same time, the experimental group of patients with CRP, CA19-9 water was significantly lower than the control group, the difference was statistically significant ($P<0.05$). Please look at the table 2.

3.3 The level of peripheral blood lymphocyte subsets before and after treatment in two groups of patients

Before treatment, peripheral blood NK, two groups of patients

Table 1

Comparison of serum IGF-1, EGF and TK1 levels before and after treatment in two groups.

Group	n		IGF-1 (ng/mL)	EGF (ug/L)	TK1 (pmol/L)
Control	60	Before treatment	49.18±2.04	3.52±0.26	3.04±0.31
		After treatment	26.54±1.76 [*]	2.47±0.22 [*]	1.98±0.14 [*]
Experimental	60	Before treatment	48.96±2.10	3.49±0.21	2.99±0.28
		After treatment	9.25±1.05 ^{**}	1.38±0.18 ^{**}	1.01±0.11 ^{**}

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, ^{**} $P<0.05$

Table 2

Comparison of serum levels of CRP and CA19-9 before and after treatment in two groups.

Group	n		CRP (mg/L)	CA19-9 (KU/L)
Control	60	Before treatment	35.21±4.72	43.51±5.23
		After treatment	14.36±2.11 [*]	29.42±3.15 [*]
Experimental	60	Before treatment	35.16±5.04	43.45±5.19
		After treatment	8.35±1.21 ^{**}	19.69±2.71 ^{**}

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, ^{**} $P<0.05$.

Table 3

The level of peripheral blood lymphocyte subsets before and after treatment in two groups.

Group	n		NK	CD3 ⁺	CD4 ⁺	CD8 ⁺
Control	60	Before treatment	45.18±5.11	67.38±8.42	37.29±4.05	31.25±7.21
		After treatment	29.48±4.25 [*]	52.19±7.25 [*]	24.36±3.01 [*]	22.35±6.42 [*]
Experimental	60	Before treatment	45.28±4.96	67.52±8.33	37.18±4.12	30.98±7.35
		After treatment	46.35±5.13 [#]	69.18±8.62 [#]	38.31±3.94 [#]	33.17±6.33 [#]

Note: compared with before treatment, ^{*} $P<0.05$; compared with the control group, [#] $P<0.05$.

4. Discussion

Colon cancer radical surgery combined with postoperative adjuvant chemotherapy is a common clinical treatment of colon cancer. Research shows: The vast majority of tumors will cause immune dysfunction in patients during the development and transfer process, especially for patients with advanced cancer, its immune function decline more obvious[6,7]. Postoperative adjuvant chemotherapy combined with adjuvant chemotherapy for colon cancer patients often leads to the decrease of immune function, inflammatory reaction and adverse drug reaction, which are factors that influence the prognosis of patients. At present, the application of traditional Chinese medicine in colon cancer after radical surgery has gradually become the focus of attention of researchers. Traditional Chinese medicine believes that the colon cancer is caused by deficiency of vital qi, spleen and stomach lost our, viscera function disorder, humidity, evil poison damp heat accumulation caused by intestinal blood runs sluggish[9]. Fuzheng suppressor recipe is one decoction which is made by Codonopsis, astragalus, Poria, Atractylodes, lily, angelica, radix salviae miltiorrhizae, Radix Rehmanniae Preparata, radix paeoniae rubra, glossy privet fruit, dogwood, polygonatum, placenta, gynostemma pentaphylla, dried tangerine peel, pinellia

CD3⁺, CD4⁺ and CD8⁺ cell percentage had no significant difference ($P>0.05$); After treatment, the ratio of NK, CD3⁺, CD4⁺ and CD8⁺ cells in peripheral blood of patients in control group was significantly lower than that before treatment, at the same time, the experimental group was significantly higher than the control group, the difference was statistically significant ($P<0.05$). Please look at the table 3.

tuber, Scutellaria barbata, Hedyotis diffusa and licorice and ect, having the function of invigorating spleen and promoting blood circulation and removing toxin[10]. Preclinical pharmacology research shows that Fuzheng suppressor recipe was able to inhibit the growth and metastasis of transplanted tumor in mice, and can also block the blood supply of tumor microcirculation[11]. Literatures have been reported that Fuzheng Yi'ai decoction can not only enhance the immune function of patients with colon cancer, but also can reduce the adverse effects, prolong the survival time of patients, improve the curative effect[12]. This study was to investigate the effect of the treatment of the cancer of the colon on the levels of serum IGF-1, EGF, TK1, CRP, CA19-9 and CD4⁺ lymphocyte subsets in patients with colon cancer after radical resection of colon cancer, so that we can provide a certain clinical basis for the treatment of colon cancer patients using the method of Fuzheng suppressor recipe.

The results of this study showed that: Before treatment, there was no significant difference in the serum levels of IGF-1, EGF, TK1, CRP and CA199 between the two groups ($P>0.05$); After treatment, the serum levels of IGF-1, EGF, TK1, CRP and CA19-9 in the two groups were significantly lower than that before treatment, and the experimental group patients were significantly lower than the control group, the difference was statistically significant ($P<0.05$). It prompts Fuzheng suppressor recipe can not only inhibit node activity

of tumor cells in patients with colorectal cancer, inhibit tumor cell proliferation and differentiation, but also can reduce postoperative inflammatory response, protect the surgical wound. GF-1 is a cell factor with a variety of functions, which can increase glucose and protein synthesis, reduce protein degradation and increase RNA synthesis, detect the level of serum, so it has important significance for evaluating the prognosis of colorectal cancer[13]. EGF is a polypeptide composed of 53 amino acid residues, can regulate cell factor phosphorylation, glycolytic pathway enhanced activation of DNA synthesis, promote cell proliferation and differentiation, and the level of EGF in serum can reflect the degree of tumor cell proliferation, so as to reflect the treatment effect of colon cancer[14]. TK1 is a cytoplasmic thymidine kinase in human cells. It is a key marker to characterize the degree of tumor cell proliferation, so it can reflect the occurrence and development of colon cancer and its therapeutic effect in the serum[15]. CRP is an acute phase reaction protein, when the body is stimulated, the liver cells can synthesize and secrete CRP, which can reflect the body's stress on inflammatory response in the serum[16,17]. CA19-9 is an antigen molecule which is capable of specifically recognizing tumor cells, and the increasing level of serum has a certain correlation with the colon cancer. so CA19-9 is an important tumor marker of colon cancer, and the higher the level of CA19-9 in serum, the better the activity of tumor cells[18]. In addition, the results of this study show that: Before treatment, there was no significant difference in the ratio of peripheral blood NK, CD3⁺, CD4⁺ and CD8⁺ cells in the two groups ($P>0.05$); After treatment, the ratio of NK, CD3⁺, CD4⁺ and CD8⁺ cells in peripheral blood of patients in control group was significantly lower than that before treatment, and the experimental group was significantly higher than the control group, the difference was statistically significant ($P<0.05$). The results suggested that the body's immune function of patients with colon cancer after radical operation could be regulated by the anti tumor suppressor. Colon cancer radical surgery combined with postoperative chemotherapy can decrease the immune function of the patients, while all the ingredients of Chinese medicine in Fuzheng suppressor recipe have the function of clearing away heat and toxic materials, Dissipating Dampness, invigorating spleen and kidney, so as to enhance the immune function of patients[19,20].

In summary, Fuzheng suppressor recipe can significantly reduce the level of serum IGF-1, EGF, TK1, CRP and CA19-9, improve the level of lymphocyte subsets such as CD4⁺, improve the immune function of the body in patients with colon cancer after radical resection of colorectal cancer, So this method is worthy of promotion and application in clinical practice for the future.

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