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Effect of laparoscopic surgery combined with neoadjuvant chemotherapy on serum CEA, VEGF, CA724, CA242, LEP and T lymphocyte subsets in patients with low rectal cancer

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ABSTRACT

Objective: To study the effect of laparoscopic surgery combined with neoadjuvant chemotherapy on serum CEA, VEGF, CA724, CA242, LEP and T lymphocyte subsets in patients with low rectal cancer. **Methods** A total of 80 patients with low rectal cancer in our hospital from June 2014 to June 2017 were enrolled in this study. The subjects were divided into the control group (n=40) and the treatment group (n=40) randomly. The control group were treated with laparoscopic surgery, the treatment group were treated with laparoscopic surgery combined with neoadjuvant chemotherapy, and both the two groups were treated for 6 periods with neoadjuvant chemotherapy after surgery. The serum CEA, VEGF, CA724, CA242, LEP levels and peripheral blood $CD3^+$, $CD4^+$, $CD8^+$, NK cells of the two groups before and after treatment were compared. **Results:** There were no significantly differences of the serum CEA, VEGF, CA724, CA242, LEP levels and peripheral blood $CD3^+$, $CD4^+$, $CD8^+$, NK cells of the two groups before treatment. The serum CEA, VEGF, CA724, CA242 and LEP levels of the two groups after treatment were significantly lower than before treatment, and that of the treatment group were significantly lower than the control group.The peripheral blood $CD3^+$, $CD4^+$, $CD8^+$, NK cells of the two groups of the two groups after treatment were significantly lower than before treatment, and that of the treatment group were significantly higher than the control group. **Conclusion:** Laparoscopic surgery combined with neoadjuvant chemotherapy can significantly reduce the serum CEA, VEGF, CA724, CA242, LEP levels, improve the immunologic function, and it was worthy clinical application.

1. Introduction

Rectal cancer is a common malignant tumor in anorectal area, the most common type is low rectal cancer, which has a high fatality rate[1]. The tumor location of low rectal cancer is about 5 cm below the dentate line, and it is usually in the late stage of pathology in clinical diagnosis. The tumor adhesion is serious and the volume is large, so it is difficult to treat[2,3]. At present, the main treatment of low rectal cancer is laparoscopic surgery, which have the advantages of small wound,preservation of pelvic autonomic plexus and ureter, promote intestinal function. However, the curative effect of laparoscopic surgery is not satisfactory[4]. In recent years, neoadjuvant chemotherapy has gradually become a hot spot for surgeons, Neoadjuvant chemotherapy combined with laparoscopic surgery can prolong the postoperative survival time, reduce the local recurrence rate, improve the prognosis and quality of life[5,6]. This study was to observe the effect of laparoscopic surgery combined with neoadjuvant chemotherapy on serum CEA, VEGF, CA724, CA242, LEP and T lymphocyte subsets in patients with low rectal cancer,the findings are presented below.

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2. Informations and methods

2.1. General information

A total of 80 patients with low rectal cancer in our hospital from June 2014 to June 2017 were enrolled in this study. Case inclusion criteria: (1) Patients diagnosed with rectal cancer by pathological sampling,and rectal examination revealed that the lower margin of the tumor was 3-6 cm from the anal verge; (2) pathological staging at stage II-III by ultrasonic examination; (3) The expected survival time > six months; (4) No chemotherapy history. Case exclusion criteria: (1) The patients with other malignant tumors; (2) Chemotherapy contraindicated patients; (3) patients with liver, lung and other distant metastas; (4) Pregnant or lactating women; (5) Patients with psychiatric disorders.

According to the random number table method, all the cases were randomly divided into two groups, each with 50 patients, respectively, the control group and the treatment group.The control group consisted of 29 males and 21 females, aged 45-80 years and mean age (55.38 ± 5.27) years; The body mass index (BMI) was 18-28 kg/m^2, with an average BMI (23.15 ± 1.08) kg/m^2; Pathological staging: 29 cases in stage II and 21 cases in stage III;The degree of tumor differentiation: 3 cases of high differentiation, 17 cases of differentiation and 30 cases of low/undifferentiated.The treatment group consisted of 28 males and 22 females, aged 46-79 years and mean age (56.19 ± 7.33) years;The body mass index (BMI) was 18-26 kg/m^2, with an average BMI (24.07±1.40) kg/m^2; Pathological staging: 30 cases in stage II and 20 cases in stage III;The degree of tumor differentiation: 4 cases of high differentiation, 18 cases of differentiation and 28 cases of low/undifferentiated.Statistical software was used to analyse and compare the two groups′ sex, age, BMI, pathological stage and tumor differentiation. The results showed that there was no statistical significance in the clinical data of the two groups (P>0.05). All the selected cases were informed of the study before the treatment and signed the informed consent with consent. The study was approved by the medical ethics committee of our hospital.

2.2 Experimental method

Laparoscopic surgery, in particular: The patients were under general anesthesia during tracheal intubation, and the modified lithotomy site was used to establish CO_2 pneumoperitoneum,using ultrasound knife to remove the mesorectal and sigmoid colon, we dissected the visceral and parietal layers of the pelvic fascia, and completely removed the lymph nodes.The left lower abdomen was opened with a long incision of 4-5 cm. The bowel was removed and the tumor was removed, followed by purse string suture, incision closure, and intestinal anastomosis.

Neoadjuvant chemotherapy, specifically for: Fluorouracil(purchased from Tianjin Jinyao Pharmaceutical Co. Ltd., Specifications 250 mg/branch, Chinese medicine word H12020959) was first administered intravenously at a dose of 400 mg/m^2, followed by a continuous infusion of 48 h at a dose of 1 200 mg/m^2, D1, 2; Calcium folinate (purchased from south of the Five Ridges Guangdong Pharmaceutical Co., Ltd., Specifications 100 mg/branch,Chinese medicine word H20040612) was intravenously administered intravenously at 2 h, 400 mg/m^2, d1; Oxaliplatin (purchased from Jiangsu Hengrui pharmaceutical Limited by Share Ltd, specifications 100 mg/branch, Chinese medicine word H20050962) was administered intravenously with 2 h, 85 mg/m^2, d1; 14 d for 1 course, continuous treatment for 3 courses.

Patients in the control group received laparoscopic surgery, and 6 courses of neoadjuvant chemotherapy were given after the operation. The patients in the treatment group received neoadjuvant chemotherapy combined with laparoscopic surgery. After 4-6 weeks of neoadjuvant chemotherapy, laparoscopic surgery was performed, and 6 courses of neoadjuvant chemotherapy were continued after the operation.

2.3 Detection index

10 mL venous blood of two groups before and after the morning fasting treatment were collected,the blood of 5 mL vein was centrifuged by 3 000 rpm for 10 min by centrifuge,take the supernatant as the serum and keep it in the refrigerator at 2-8 centigrade,the serum levels of CEA, VEGF, CA724, CA242 and LEP were detected and compared between the two groups before and after treatment; The other 5 mL was used to detect and compare the levels of peripheral blood cytokine levels before and after treatment in two groups, including the ratio of CD3$^+$, CD4$^+$, CD8$^+$ and NK cells.

The level of serum CEA was detected by electrochemiluminescence microparticle immunoassay (ECLI), which was detected by Elecsys1010 automatic electrochemical instrument Purchased from Switzerland Roche company;Serum levels of VEGF, CA724, CA242 and LEP were detected by double sandwich enzyme-linked immunosorbent assay (ELISA), All kits were purchased from Shanghai Ze leaf biological science and Technology Co., Ltd., and the operation process was strictly carried out according to the operating procedures in the instructions; Backman CytoFLEX flow cytometry was used to detect the levels of cytokines in peripheral blood, including the ratio of CD3$^+$, CD4$^+$, CD8$^+$ and NK cells.

2.4 Data processing

We Used SPSS 19.0 software package to process the test result data, The data representation of the results of this study are both mean ± standard deviation (x±s), all of which belong to measurement data, the use of t test was to compare the difference between groups,with P<0.05 as a statistically significant.

3. Results

3.1 Comparison of serum CEA, VEGF, CA724, CA242 and LEP levels before and after treatment in two groups

Before treatment, the levels of serum CEA, VEGF, CA724, CA242 and LEP in the control group were (7.21±2.53) ng/mL, (301.52±41.52) μg/L, (6.15±2.24) IU/mL, (24.38±8.40) IU/mL and (3.11±1.86) ng/mL, that in the treatment group were (7.19±2.47) ng/mL, (299.60±43.47) μg/L, (6.19±2.31) IU/mL, (24.50±8.62) IU/mL and (3.09±1.93) ng/mL, there was no significant difference between the two groups (P>0.05); After treatment,the levels of erum CEA,VEGF,CA724,CA242 and LEP in the control group were (5.06±1.24) ng/mL, (221.68±25.39) μg/L, (4.77±1.10) IU/mL, (16.94±6.13) IU/mL and (5.85±2.14) ng/mL, that in the treatment group were (3.95±1.03) ng/mL, (172.38±19.51) μg/L, (4.05±1.01) IU/mL, (11.18±4.64) IU/mL and (7.46±3.11) ng/mL. The above serum levels of the two groups were significantly lower than those before treatment, and the serum levels of the patients in the treatment group were significantly lower than those in the control group, the difference was statistically significant(P<0.05). Please look at the Table 1.

3.2 Comparison of immune function indexes before and after treatment in two groups

Before treatment, the ratio of CD3+, CD4+, CD8+ and NK cells in peripheral blood in the control group were (66.08±7.15)%, (54.27±6.08)%, (37.45±4.62)% and (24.26±5.02)%, that in the treatment group were (65.74±7.27)%, (55.03±5.67)%, (38.06±4.25)% and (24.55±5.12)%, there was no significant difference between the two groups (P>0.05); After treatment,the ratio of CD3+, CD4+, CD8+and NK cells in peripheral blood in the control group were (41.21±4.36)%, (28.15±3.43)%, (20.14±2.89)% and (12.38±2.11)%, that in the treatment group were (54.62±5.08)%, (35.28±4.12)%, (30.48±3.17)% and (18.75±2.26)%. The above ratio of $CD3^+$, $CD4^+$, $CD8^+$and NK cells in peripheral blood of the two groups were significantly lower than those before treatment, and that in the treatment group were significantly higher than those in the control group, the difference was statistically significant (P<0.05). Please look at the Table 2.

4. Discussion

The clinical treatment of low rectal cancer is difficult because of the anatomical position of rectum, the biological characteristics of tumor cells and the particularity of lymph drainage,Laparoscopic surgery is the most important treatment for low rectal cancer, however, there is still the possibility of recurrence after operation, and the 5 year survival rate of the patients is only about 50%[7,8]. In recent years, neoadjuvant chemotherapy has gradually attracted the attention of surgeons in order to further improve the postoperative survival rate of patients. Neoadjuvant chemotherapy has many advantages, such as: (1) It can obviously improve the anal sphincter preservation rate of the patients; (2) It can obviously reduce the volume of primary tumor and improve the rate of radical resection; (3) It can inhibit the foci of primary and peripheral lymph node metastasis; (4) It can cause necrosis, fibrosis and other changes of tumor cells; (5) It can obviously reduce the tumor cells during operation, such as traction, extrusion and so on[9-11]; This study was to observe the effect of laparoscopic surgery combined with neoadjuvant chemotherapy on serum CEA, VEGF, CA724, CA242, LEP and T lymphocyte subsets in patients with low rectal cance,so as to provide some ideas for the clinical treatment of low rectal cancer.

The results of the study showed that there was no significant difference in serum CEA, VEGF, CA724, CA242 and LEP levels between the two groups (P>0.05); The serum levels of CEA, VEGF, CA724, CA242 and LEP in the two groups were lower than those before treatment, and the serum indexes in the treatment group were

Table 1

Comparison of serum CEA, VEGF, CA724, CA242 and LEP levels before and after treatment in two groups.

Group	n	Time	CEA (ng/mL)	VEGF (μg/L)	CA724 (IU/mL)	CA242 (IU/mL)	LEP (ng/mL)
Control group	50	Before treatment	7.21±2.53	301.52±41.52	6.15±2.24	24.38±8.40	3.11±1.86
		After treatment	5.06±1.24*	221.68±25.39*	4.77±1.10*	16.94±6.13*	5.85±2.14*
Treatment group	50	Before treatment	7.19±2.47	299.60±43.47	6.19±2.31	24.50±8.62	3.09±1.93
		After treatment	3.95±1.03*#	172.38±19.51*#	4.05±1.01*#	11.18±4.64*#	7.46±3.11*#

Note: compared with before treatment, *P<0.05; compared with the control group, #P<0.05.

Table 2

Comparison of immune function indexes before and after treatment in two groups (%).

Group	n	Time	$CD3^+$	$CD4^+$	$CD8^+$	NK
Control group	50	Before treatment	66.08±7.15	54.27±6.08	37.45±4.62	24.26±5.02
		After treatment	41.21±4.36*	28.15±3.43*	20.14±2.89*	12.38±2.11*
Treatment group	50	Before treatment	65.74±7.27	55.03±5.67	38.06±4.25	24.55±5.12
		After treatment	54.62±5.08*#	35.28±4.12*#	30.48±3.17*#	18.75±2.26*#

Note: compared with before treatment, *P<0.05; compared with the control group, #P<0.05.

lower than those in the control group, and there was a significant difference (P<0.05). The results suggest that laparoscopic surgery combined with neoadjuvant chemotherapy can significantly reduce the serum levels of CEA, VEGF, CA724, CA242 and LEP in patients with low rectal cancer. CEA is a specific tumor associated antigen, and its serum level can be used to evaluate the recurrence and metastasis of rectal cancer[12]. VEGF is one of the most potent permeability factors in angiogenic factors. It can affect the invasion and metastasis of rectal cancer cells by assisting and promoting the formation of blood vessels, and is highly expressed in rectal cancer[13]. CA724 is a tumor associated glycoprotein, and its serum levels increase markedly with tumor progression[14]. CA242 is a carbohydrate antigen with low content in human serum, and its serum level is closely related to the pathological changes of digestive tract[15].Studies have reported that LEP is associated with the development of low rectal cancer and its serum levels increase significantly with the progression of cancer[16]. Laparoscopic surgery combined with neoadjuvant chemotherapy is effective in the treatment of low rectal cancer, so it can significantly reduce the serum levels of CEA, VEGF, CA724, CA242 and LEP[17]. In addition, the results showed that the ratio of $CD3^+$, $CD4^+$, $CD8^+$ and NK cells in the peripheral blood of the two groups was significantly lower than that before the treatment, and the treatment group was higher than the control group, and there was a significant difference (P<0.05). It suggests that laparoscopic surgery combined with neoadjuvant chemotherapy can obviously improve the immune function of patients with low rectal cancer.This may be due to the fact that laparoscopic surgery combined with neoadjuvant chemotherapy has little effect on the immune function of the patients, and the complete removal of the tumor cells is beneficial to the recovery of immune function[18,19].

In conclusion, laparoscopic surgery combined with neoadjuvant chemotherapy can significantly reduce the levels of serum CEA, VEGF, CA724, CA242 and LEP in patients with low rectal cancer, and improve the immune function of patients, so it is worthy of clinical application.

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