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Combinational effect of laparoscopic surgery and neoadjuvant chemotherapy on patients with colorectal cancer.

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Abstract

Objective: To investigate the combinational effect of laparoscopic surgery and neoadjuvant chemotherapy on the treatment of colorectal cancer by analyzing the serum levels of Caudal type homologous transcription factor-2 (CDX-2), Proto-oncogene (*C-erbB-2*) and Intercellular Adhesion Molecule-1 (ICAM-1) in patients before and after treatment.

Methods: 90 cases of colorectal cancer patients cheated in our hospital from April 2011 to April 2012 were selected, randomly divided into study group and control group. Each group has 90 cases. The control group was treated with laparoscopic surgery, and the study group was treated with neoadjuvant chemotherapy combined with laparoscopic surgery. The clinical efficacy, adverse reaction and survival rate, and levels of CDX-2, *C-erbB-2* and ICAM-1 before and after treatment were compared between the two groups.

Results: The total effective rate was 66.7% in the study group, which was significantly higher than that in the control group (42.2%). The levels of CDX-2, *C-erbB-2* and ICAM-1 in the study group were significantly lower than those in the control group after treatment. The incidence of adverse reactions in study group was 4.4%, and the incidence of adverse reactions in control group was 20.0%. The median overall survival time in control group was 29 months (95% CI: 19.176-36.672) and the median overall survival time in study group was 40 months (95% CI: 28.205-49.617). The 3 y and 5 y survival rates of study group were significantly higher than those of control group.

Conclusion: Combination of laparoscopic surgery combined with neoadjuvant chemotherapy has a high value for clinical treatment of colorectal cancer. It can reduce serum CDX-2, *C-erbB-2* and ICAM-1 levels and improve prognosis of patients, thus deserving further application and promotion.

Keywords: Colorectal cancer, Neoadjuvant chemotherapy, Laparoscopic surgery, CDX-2, *C-erbB-2*, ICAM-1, Prognosis.

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Introduction

Colorectal cancer is a relatively common tumor disease with relatively insidious incidence and rarely symptoms. When patient shows obvious clinical symptoms, the condition is usually in the middle and late stage, and the prognosis is poor [1]. With the rapid development of the national economy in recent years, the incidence of colorectal cancer also showed an increasing trend year by year, and the mortality of malignant tumor was also increased from fifth in 1970s to the current fourth, so more attention should be paid to the government and medical units. Surgical resection is a common method of treating colorectal cancer. However, surgical resection is easy to cause great trauma to patients, and there are some disadvantages such as tumor cell dissemination, high recurrence rate and poor overall prognosis [2,3]. In recent years, many scholars at home and abroad [4-6] have made a lot of useful exploration on how to improve the prognosis of patients with colorectal cancer, and found that neoadjuvant chemotherapy can improve the radical resection rate and prognosis. The diagnosis of colorectal cancer depends on a variety of inflammatory factors and tumor markers, which can be used to judge the development of the disease and the postoperative course [7,8]. At present, there are few reports about the effect of neoadjuvant chemotherapy on serum levels of CDX-2, *C-erbB-2* and ICAM-1 in patients with colorectal cancer. This paper mainly discussed the effect of neoadjuvant chemotherapy in the treatment of colorectal cancer, and analysed its influence on serum levels of CDX-2, *C-erbB-2* and ICAM-1 in patients before and after treatment, to provide a

valuable reference for the clinical treatment of colorectal cancer.

Materials and Methods

General information

90 patients with colorectal cancer treated in our hospital were selected from April 2011 to April 2012. Inclusion criteria: Consistent with the diagnostic criteria for colorectal cancer, confirmed by imaging and pathology [8], in line with colorectal cancer radical surgery indications [9], and patients informed consent. Exclusion criteria: patients who were not suitable for radical resection of colorectal cancer, combined with other tumor diseases, with heart, brain and other important organ diseases, with the presence of distant metastasis. Selected cases were randomly divided into study group and control group, 45 cases in each group. The study group has 27 males and 18 females. All patients in the study group aged 56-74 y, 68.5 ± 2.1 y on average. Among all patients, 26 cases have the tumor diameter<5 cm and 19 cases ≥ 5 cm. Clinical stage: 15 cases were at stage I, 18 cases of stage II and 12 cases of stage III. 29 cases have lymph node metastasis, 16 cases without lymph node metastasis. The control group has 25 males and 19 females who aged 56-75 y, 68.7 ± 2.4 y on average. Among them, 29 cases have tumor diameter<5 cm, 16 cases ≥ 5 cm. Clinical stage: 18 cases of stage I, 16 cases of stage II, and 11 cases of stage III. 28 cases have lymph node metastasis and 17 cases without lymph node metastasis. There was no significant difference in sex, age, tumor diameter and clinical stage between the two groups. Our study was approved by the ethical institute in our hospital (AN0100075).

Treatment methods

The control group received laparoscopic surgery, generally using four holes method. If the operation is difficult, a 5 mm puncture hole for the five holes method can also be added. Specific operation: patients should take low sufficient high position. The incision was made on the upper edge of umbilical ring, and the pneumoperitoneum was performed, placed the laparoscope. The tumor and surrounding tissue was examined routinely. A 12 mm main operating hole was opened on the upper right side of the pubic symphysis to open a, two 25 mm operation holes were opened on the left and right middle abdomen in turn. When using the 5-hole method, a 5 mm auxiliary operation hole can be added. The inferior mesenteric vessels were dissected and separated by ultrasound knife, and proximal part of mesentery was closed at the root to clear the fat and lymph nodes around the mesenteric blood vessels. Then, the ultrasonic knife was inserted into the fusion fascia space to expose and protect the ureter. The sigmoid colon and rectum were slightly removed, and the autonomic nerve plexus was preserved along the two layers of pelvic fascia. The operation was in accordance with the principle of total mesorectal excision. During operation, male patients should pay attention to avoid injury of seminal vesicle and prostate and female patients need to pay attention to prevention of vaginal posterior wall injury. The resected tumor and bowel can be removed by enlarging the umbilicus incision or enlarging the main operation hole on the right side of the symphysis pubis, cut outside the abdominal wall. In the abdominal wall, the stapler was used to make the colon and rectum anastomosis. Patients were given routine anti-infective therapy after surgery, followed by 12 cycles.

The treatment group was treated with XELOX regimen. XELOX regimen: intravenous infusion of 130 mg/m^2 oxaliplatin, qd, d 1: oral capecitabine 850-1000 mg/m^2, bid, d 1-14; repeated every 3 w. The observation group was treated with neoadjuvant chemotherapy combined with laparoscopic surgery. The specific operation was as follows: after routine examination, arterial infusion chemotherapy was performed, and angiography was performed after the right femoral artery was placed, to clear the blood supply of the tumor. A micro catheter was inserted into the tumor for neoadjuvant chemotherapy, injected 10 mg mitomycin, 50 mg cisplatin and 1000 mg 5-Fu. Rectal cancer patients need add 40% iodized oil more to avoid vascular embolism. Laparoscopic surgery can be performed after 4 cycles of neoadjuvant chemotherapy. The surgical procedure and the postoperative chemotherapy regimen were the same as control group.

Observe indicators

By comparing the clinical short-term efficacy of two groups, the recent study of efficacy criteria is divided into complete remission, partial remission, disease stability and disease progression. The levels of serum CDX-2, *C-erbB-2* and ICAM-1 in two groups were compared before and after treatment. The levels of serum CDX-2, *C-erbB-2* and ICAM-1 were determined by Enzyme-Linked Immunosorbent Assay (ELISA), according to the operating instructions strictly. The incidence of adverse events during the treatment of the two groups was observed and recorded. Patients were followed up for an average of 3 to 5 y, compared the survival rate between the two groups.

Statistical methods

All statistical analyses were performed using SPSS 20.0 software. Categorical data was expressed as number and percentage and tested with Chi-square test. Measurement data was expressed as mean ± standard deviation and analysed by student's t-test. Kaplan-Meier analysis was used to calculate the survival rate. Comparison of survival rate was conducted with Log-Rank test. $P<0.05$ suggests that the difference is statistically significant.

Results

Comparison of recent clinical outcomes in two groups

The total effective rate was 66.7% in the study group, which was significantly higher than that in the control group (42.2%) (Table 1).

Comparison of CDX-2, C-erbB-2 and ICAM-1 levels between two groups before and after treatment

The levels of CDX-2, *C-erbB-2* and ICAM-1 in two groups were not significantly different before treatment. The levels of CDX-2, *C-erbB-2* and ICAM-1 in the study group were significantly lower than those in the control group after treatment (Table 2).

Comparison of adverse effects between two groups

The incidence of adverse reactions in study group was 4.4%, and the incidence of adverse reactions in control group was 20.0% (Table 3).

Comparison of survival rates between two groups

The median overall survival time in the control group was 29 months (95% CI: 19.176-36.672) and the median overall survival time in the study group was 40 months (95% CI: 28.205-49.617). The 3 y and 5 y survival rates of study group were significantly higher than those of control group (Table 4).

Discussion

Colorectal cancer is one of the most common abdominal tumors. With the diet problem and the improvement of people's living standard, the incidence rate of the disease is increasing year by year in China. Radical surgery, chemotherapy and radiotherapy are the main treatments. Surgical treatment has a high curative effect. With the continuous improvement of medical level in China, laparoscopic surgery has been effectively developed and applied. Laparoscopic surgery has advantages of minimal invasion, short operation time, high safety and feasibility, clear field of vision and so on [9,10]. Adjuvant chemotherapy is not only a new type of adjuvant treatment of malignant tumors, but also the hot spots in domestic and foreign clinical research. Compared to traditional chemotherapy, it has the advantages of fewer adverse reactions, greater operation effect. This has a good effect in the treatment of many tumors [11]. Preoperative arterial infusion chemotherapy has better application effect in neoadjuvant chemotherapy. It can deliver chemotherapeutic drugs from tumor blood vessels into tumor tissues with high targeting ability, reduce drug plasma protein binding to improve the effect of chemotherapy. In addition, this method can improve the concentration of drugs in tumor tissue, prolong the contact time between chemotherapy drugs and tumor, and reduce the incidence of toxic and side effects [12]. Laparoscopic radical resection of colorectal cancer is a highly effective surgical method, but the risk and difficulty of its operation are higher. Laparoscope can clearly demonstrate the intraperitoneal situation, and has the function of magnifying, allowing doctors to better observe celiac patients, and to observe many traditional open surgeries by laparoscopy cannot be observed in the anatomic space. We can observe anatomical space that many traditional open surgeries cannot be observed by laparoscopy [13]. We cannot effectively observe the lower part of rectum and peritoneum in the traditional open surgery. However, laparoscopy can clearly show the surrounding space through the probe, expose the hip space, and reduce the damage to intra-abdominal vein, which is consistent with the principle of total mesorectal excision. In addition, the use of ultrasonic knife, computer feedback control bipolar electric knife system (feedbackcontrolled bipolar) and other technology applications can make the operation more convenient, effectively reducing the amount of bleeding surgery [14].

At present, many domestic scholars and experts have applied neoadjuvant chemotherapy in the clinical treatment of colorectal cancer patients, and found that the program has good application effect [15]. At the same time, many studies have been carried out to analyse and discuss the clinical efficacy of arterial infusion chemotherapy in patients with colorectal cancer. It has been proved that perfusion chemotherapy has good application effect in the clinical treatment of colorectal cancer. It can improve the scavenging effect of chemical drugs on tumor cells, to improve the effect of chemotherapy, and can effectively reduce the adverse reactions caused by chemical drugs.

The results showed that the total effective rate was 66.7% in the study group, which was significantly higher than that in the control group (42.2%). This indicates that laparoscopic surgery combined with neoadjuvant chemotherapy is more effective in the treatment of colorectal cancer than laparoscopic surgery. We hypothesized that the reason may be that neoadjuvant chemotherapy can reduce tumor volume and reduce clinical stage, and then achieve the purpose of controlling tumor progression. In addition, we found that the incidence of adverse reactions in study group was 4.4%, and the incidence of adverse reactions in control group was 20%. It shows that laparoscopic surgery combined with neoadjuvant chemotherapy is safe and reliable without adverse reactions.

CDX-2, *C-erbB-2* is the important oncogenes of cell source, and actively participates in the process of regulating cell growth and reproduction. Once the gene structure of CDX-2 and *C-erbB-2* changes or over expression, some abnormal cells will gradually be transformed into tumor cells [16]. High expression of ICAM-1 can promote the invasion and metastasis of tumor, and can reduce the adhesion between cancer cells, so that the cancer cells can migrate into human blood circulation with the migration of human lymphocytes [17]. The expression of CDX-2, *C-erbB-2* and ICAM-1 in colorectal tissues and serum can be used to judge the degree of malignancy and clinical prognosis of colorectal cancer [18]. The results showed that there was no significant difference in the levels of CDX-2, *C-erbB-2* and ICAM-1 between the two groups before treatment. The study groups of CDX-2, *C-erbB-2* and ICAM-1 were significantly lower than control group after treatment. It shows that laparoscopic surgery combined with neoadjuvant chemotherapy can effectively reduce the serum levels of CDX-2, *C-erbB-2* and ICAM-1. This may be the pathology and physiological basis of laparoscopic surgery combined with neoadjuvant chemotherapy in the treatment of colorectal cancer [19].

The 3 y and 5 y survival rates of the study group were significantly higher than those of the control group. This indicates that the 3 y and 5 y survival time of laparoscopic surgery combined with neoadjuvant chemotherapy is significantly higher than that of simple surgery. The limitations of this study are that the chemotherapy program is single, and the number of cases is not enough. There is no screening and optimization of the length of chemotherapy, which may affect the accuracy of the results of this study.

In summary, laparoscopic surgery combined with neoadjuvant chemotherapy can significantly improve the survival and prognosis of colorectal cancer patients can reduce the serum CDX-2, *C-erbB-2* and ICAM-1 levels, which is worthy of application and promotion.

Table 1. *Comparison of recent clinical outcomes in two groups.*

Group	N	Complete remission	Partial remission	Disease stability	Disease progression	The total effective rate of treatment (%)
Control group	45	10	20	11	4	66.7
Study group	45	5	14	17	9	42.2
χ^2						7.89
P						0.027

Table 2. *Comparison of CDX-2, C-erbB-2 and ICAM-1 levels between two groups before and after treatment.*

Group	N	CDX-2 (ng/ml)		*C-erbB-2* (ng/ml)		ICAM-1 (ng/ml)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	45	57.3 ± 9.4	33.9 ± 5.4	23.6 ± 5.3	11.9 ± 2.1	203.7 ± 39.6	126.2 ± 9.3
Study group	45	57.5 ± 10.6	47.5 ± 6.5	23.8 ± 5.2	17.3 ± 2.8	203.9 ± 38.4	172.6 ± 11.5
t		0.17	6.5	0.13	6.95	0.17	6.53
P		0.378	0.031	0.335	0.027	0.378	0.028

Table 3. *Comparison of adverse effects between two groups.*

Group	N	Anastomotic bleeding	Lung infection	Intestinal obstruction	Adverse reaction rate (%)
Control group	45	1	0	1	4.4
Study group	45	2	4	3	20
χ^2					1.45
P					0.04

Table 4. *Comparison of survival rates between two groups.*

Group	1 y survival rate (%)	3 y survival rate (%)	5 y survival rate (%)
Control group	88.9	77.8	51.1
Study group	82.2	48.9	33.3
χ^2	0.24	7.12	6.07
P	0.411	0.019	0.035

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