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Effects of concurrent chemoradiotherapy on immune function and tumor markers SCC−Ag and CYFRA21−1 in patients with esophageal carcinoma

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ABSTRACT

Objective: To investigate the effects of concurrent chemoradiotherapy and radiotherapy alone on immune function and tumor markers SCC-Ag and CYFRA21-1 in patients with esophageal carcinoma. **Method:** A total of 84 patients with esophageal cancer treated in our hospital from June 2015 to April 2017 were selected and randomly divided into the observation group and the control group with 42 cases each. The control group received radiotherapy only and irradiated by medical electron linear accelerator, radiotherapy for 6 weeks. The observation group was given radiotherapy and chemotherapy concurrently, 3 weeks for 1 courses, 2 cycles of chemotherapy. The fasting venous blood of patients in two groups were collected in the morning when patients were hospitalized and after chemotherapy, using flow cytometry to detect the immune function indexes of two groups of patients with esophageal cancer before and after treatment, including natural killer cells (NK), T suppressor cells (Ts), T helper cells (Th), Th/Ts and T lymphocytes (T total). The levels of serum SCC-Ag and CYFRA21-1 were detected by electrochemiluminescence assay. **Results:** There were no significant differences in the indexes of immune function between the two groups before treatment. Total T, the proportion of Th and Th/Ts in the two groups both increased significantly; the proportion of Ts decreased significantly; the difference was statistically significant. NK was higher than treatment before but not significantly. After treatment, the levels of T total, Th, Th/Ts in the observation group were significantly higher than the control group; the levels of NK and Ts were not significantly different. Before treatment, there was no significant difference in serum SCC-Ag and CYFRA21-1 between the two groups. After treatment, the serum SCC-Ag and CYFRA21-1 levels of the two groups were both significantly decreased; the serum levels of SCC-Ag and CYFRA21-1 in the observation group were significantly lower than the control group. **Conclusion:** Radiotherapy combined with chemotherapy of cisplatin and paclitaxel can improve the immune function and reduce serum SCC-Ag and CYFRA21-1 levels of esophageal cancer patients. This therapeutic schemes can be beneficial to increase the survival rate of patients with esophageal cancer.

1. Introduction

Esophageal cancer is one of the most common malignant tumor with high morbidity and mortality[1]. Studies have shown that the process of tumor genesis and development is closely related to the regulation of human immune function, and the progress and diffusion of cancer are closely related to the changes of T lymphocyte and NK cell[2]. The continuous development of molecular biology and Immunology provide more effective reference index for cancer screening, diagnosis, prognosis and curative effect evaluation and prognosis, the serum tumor markers are used more and more[3]. This study adopted cisplatin plus paclitaxel chemotherapy and radiotherapy to treat the patients with esophageal cancer, researched on immune function of patients with esophageal carcinoma and the influence of serum SCC-Ag and CYFRA21-1 levels, ang now the results are reported as follows.

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2. Data and methods

2.1. General information

A total of 84 patients with esophageal cancer treated in our hospital from June 2015 to April 2017 were selected and randomly divided into the observation group and the control group with 42 cases each. The observation group: 22 males and 20 females, aged from 42 to 65 years old; lesions were 19 cases of thoracic esophageal and 23 cases cervical esophagus; TNM stage for Ⅲ 17 cases, 25 cases Ⅳ stage; pathological types including 6 cases, 18 cases of plaque type concealed and erosive type 18 cases. Control group: 23 males and 19 females, aged from 44 to 64 years old; lesions were 19 cases of thoracic esophageal and 23 cases cervical esophagus; TNM stage for Ⅲ 18 cases, 24 cases Ⅳ stage; pathological types including 7 cases, 19 cases of plaque type concealed and erosive type 16 cases. There was no significant difference between the two groups in general data (P<0.05). Inclusion criteria: (1) by endoscopy and pathological diagnosis, pathological diagnosis of esophageal carcinoma; (2) the age range from 18 to 79 years old; (3) in an index of this study is to detect the patient did not accept other chemotherapy and immunotherapy; (4) study of informed consent. Exclusion criteria: (1) patients with previous history of radiotherapy, chemotherapy and immunotherapy; (2) patients with other site tumor diseases; (3) metastatic esophageal cancer patients.

2.2. Therapeutic method

The control group was treated with a medical electron linear accelerator for radiotherapy alone, with a single dose of 200 Gy, conventional fractionation and radiotherapy for 6 weeks. The total dose of radiotherapy was 60-70 Gy, which ensured that the lung volume was 20 Gy, lung volume was <20%, and spinal cord volume was <40 Gy. The observation group was given chemotherapy in the control group based on the same steps of radiotherapy, chemotherapy with paclitaxel (Haikou Pharmaceutical Factory Co. Ltd., Zhunzi H20043045) combined with cisplatin (Jiangsu Haosen pharmaceutical Limited by Share Ltd, Zhunzi H20040813) treatment. The dosage of paclitaxel was 135 mg/m^2, D1, D8, IV, GTT; cisplatin dosage was 75 mg/m^2, d1-3, IV, GTT; chemotherapy 3 weeks for 1 courses, a total of 2 courses of treatment.

2.3. Observation index

The two groups were collected fasting venous blood on admission and synchronous radiotherapy/chemotherapy after the end of the next morning respectively, using flow cytometry (Becton Dickinson) two groups of patients with esophageal cancer NK, Ts, Th, Th/Ts and T total immune function indexes. The level of serum tumor markers SCC-Ag and CYFRA21-1 was detected by Swiss Roche automatic biochemical analyzer (kit purchased from Shanghai Taikang biological science and Technology Co., Ltd.).

2.4. Statistical processing

The data was analyzed by SPSS 18.0 statistical software, and the measurement data was expressed by mean ± standard deviation (Mean ± SD), followed by normal distribution and by t test, in which P<0.05, indicating that the difference was statistically significant.

3. Result

3.1. Two groups of immune function index changes

There were no significant differences in the levels of immune function before and after treatment in the two groups (P>0.05). After treatment, the T total proportion of two groups after treatment, Th ratio and Th/Ts ratio were significantly increased compared with before treatment, while Ts decreased significantly, and the difference was significant (P<0.05); NK was higher than that before treatment, but no significant differences (P>0.05). After treatment compared the two groups, the observation group T total (67.65 ± 4.52)%, the ratio of Th (41.21 ± 4.11)%, Th/Ts (1.62 ± 0.53) were all significantly higher than the corresponding control group level T total (65.79 ± 4.45)%, the ratio of Th (38.02 ± 4.52)%, Th/Ts (1.47 ± 0.26), the difference was significant (P<0.05), two groups of NK and Ts were not significantly different, there was no significant difference (P>0.05), as shown in Table 1.

3.2. Comparison of serum SCC-Ag and CYFRA21-1 levels in two groups

Before treatment, there was no significant difference in serum SCC-Ag and CYFRA21-1 between the two groups (P>0.05). After treatment, the serum SCC-Ag and CYFRA21-1 levels of the two

Table 1.
Comparison of immune function indexes between the two groups (n=42).

Group	Time	T total (%)	Th (%)	Ts (%)	Th/Ts	NK cell (%)
Control group	Before treatment	58.73±5.34	29.43±4.12	28.46±3.77	1.09±0.39	16.47±5.41
	After treatment	65.79±4.45*	38.02±4.52*	25.14±3.28*	1.47±0.26*	18.15±3.16
Observation group	Before treatment	58.82±5.49	29.71±4.67	28.29±3.61	1.08±0.28	16.84±5.42
	After treatment	67.65±4.52$^{*\#}$	41.21±4.11$^{*\#}$	25.46±3.49*	1.62±0.53$^{*\#}$	18.32±2.89

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

Table 2.
Serum SCC-Ag and CYFRA21-1 in the two groups before and after treatment (n=42).

Group	Time	SCC-Ag (ng/mL)	CYFRA21-1 (mg/L)
Control group	Before treatment	5.42±0.41	3.38±0.67
	After treatment	4.91±0.52*	1.82±0.11*
Observation group	Before treatment	5.31±0.54	3.41±0.82
	After treatment	4.45±0.35*#	0.96±0.12*#

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

groups were significantly lower, the difference was significant (P<0.05). Comparison between groups after treatment, the serum SCC-Ag (4.45±0.35) ng/mL, CYFRA21-1 (0.96 ± 0.12) mg/L levels were significantly lower than the control group SCC-Ag (4.91 ± 0.52) ng/mL, CYFRA21-1 (1.82 ± 0.11) mg/L corresponding level, the difference was significant (P<0.05), as shown in table 2.

4. Discussion

Esophageal cancer is a malignant lesion of the digestive tract caused by abnormal hyperplasia of squamous epithelium or glandular epithelium. In recent years, the incidence of cancer in our country has been increasing and it is a common malignant tumor. The initial symptoms of the disease are not obvious, and there is a tendency of early spread and metastasis, and the patient often arrives in the middle and late stage[4,5] .At present, esophageal cancer is mainly treated by surgery, radiotherapy and so on. However, the single treatment of these methods is often limited, and radiotherapy will cause some patients with local lesions recurrence or even distant metastasis[6,7]. As a result, current clinical studies are increasingly focused on combined therapy, where concurrent chemoradiotherapy is often used in combination therapy for esophageal cancer and in the treatment of advanced esophageal cancer without surgery[8]. Research data show that the commonly used chemotherapy for esophageal cancer with paclitaxel, cisplatin and paclitaxel[9-12], which is a new type of anti-microtubule drugs can promote tubulin polymerization and prevent microtubule depolymerization, so that microtubule function losing and influence tumor cell division, induced tumor cell death[13-15] .Cisplatin is a heavy metal complex, which can inhibit the replication of cancer cell DNA, thereby achieving anti-cancer effect[16,17]. Studies have shown[18-20] that cisplatin and paclitaxel combination chemotherapy can be effective in the treatment of esophageal cancer, and can even make esophageal cancer patients with a 3 year survival rate as high as 30%. Therefore, this study combined with cisplatin and paclitaxel chemotherapy on the basis of radiotherapy, to observe and compare the immune function and tumor markers before and after treatment in patients with esophageal cancer.

The formation and development of tumor are closely related to human immune function. Studies have shown that T cell-mediated immune cells play an important role in the anti-tumor mechanism of the body[21]. T cells can be divided into many subgroups according to different functions, including delayed allergic reactions, T cells, Th, Ts, T cells, cytotoxic T cells, etc. Among them, Ts cells can inhibit the cellular immune and humoral immune function, Th cells can play in helping the cellular and humoral immune function; NK cells are involved in anti-tumor, antiviral and it is one of the important immune cells[21]. Studies have shown[22] that Th cells in peripheral blood of patients with esophageal cancer are significantly lower than those of healthy people, and Ts cells are significantly higher than healthy people, thus leading to imbalance of Th /Ts levels, thus reducing the cellular immune function of patients. The results of this study were also consistent with the results: after treatment, the immune function of the two groups had a certain change compared with before treatment, the T total, Th and Th/Ts were significantly higher, while the Ts decreased significantly. At the same time, take concurrent chemoradiotherapy in observation group T total, Th and Th /Ts were significantly higher than that of the control group (P<0.05), the delivery of treatment was not statistically significant compared with the two groups of Ts, NK cell ratio (P>0.05). The results showed that the two groups can promote the immune function of the patients, and the effect of concurrent radiotherapy and chemotherapy on the immune function of the patients was more significant than that of radiotherapy alone. The reason may be that concurrent chemoradiotherapy can improve cellular immune dysfunction, increase the total T, Th cell content, and Th and /Ts levels, while the patient can also improve the immune function after remission. The rise in the study of two groups after treatment compared with before treatment, the level of NK cells to a certain extent, but no significant difference between groups after treatment of NK cells has no obvious difference compared to the level, further expand the sample size for further research.

Tumor markers are produced by tumor cell metabolism and play an important role in the diagnosis of tumor[23]. SCC-Ag and CYFRA21-1 are the tumor factors associated with esophageal cancer, in which SCC-Ag is a glycoprotein and has a higher concentration in squamous cell carcinoma[24,25]. Studies have shown that the level of SCC-Ag is closely related to the degree of tumor burden, which can be used as a reference for judging the prognosis of esophageal cancer[26]. CYFRA21-1, a major component of the epithelial matrix, is a cytokeratin 19 (CK19) fragment in the epithelial cell cytoplasm, which is highly expressed in lymph nodes and peripheral blood of patients with esophageal cancer. When certain parts of the body become cancerous, the protease in the body degrades CK19 rapidly and releases CYFRA21-1 into the blood, which has important reference value for the diagnosis of esophageal cancer[27]. This study shows that, compared with before treatment, after treatment, two

groups of serum SCC-Ag, CYFRA21-1 levels were significantly decreased (P<0.05); observation group after treatment serum SCC-Ag and CYFRA21-1 levels were significantly lower than the control group (P<0.05). It is indicated that concurrent chemoradiotherapy can decrease the level of serum SCC-Ag and CYFRA21-1 and improve the therapeutic efficacy of esophageal carcinoma. The reason may be that the esophageal cancer cells are suppressed after treatment and the surface release of SCC-Ag and CYFRA21-1 is reduced, leading to a decrease in serum related markers. The effect of concurrent chemoradiotherapy on esophageal cancer cells was better than that of radiotherapy alone, so the decrease of serum SCC-Ag and CYFRA21-1 was more obvious.

To sum up, concurrent chemoradiotherapy and radiotherapy alone can improve the immune function of the patients and can improve T total, Th and Th /Ts levels of the patient, decrease the level of Ts, reduce the tumor markers SCC-Ag, CYFRA21-1 level, and the improvement of concurrent chemoradiotherapy is better. It is worthy popularizing.

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