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Effect of gemcitabine chemotherapy on immune function and VEGF in patients with middle and advanced liver cancer

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ABSTRACT

Objective: To observe the effect of gemcitabine chemotherapy on the immune function and VEGF in patients with middle and advanced liver cancer. **Methods:** A total of 90 patients with middle and advanced liver cancer who were admitted in our hospital from June, 2014 to July, 2015 were included in the study and randomized into the observation group and the control group with 45 cases in each group. The patients in the control group were given adriamycin, and the patients in the observation group were given gemcitabine chemotherapy. The efficacy, immunological function indicators, VEGF level, and the occurrence of adverse reactions in the two groups were compared. **Results:** IL-6 and TNF- α levels after treatment in the two groups were significantly elevated, and the increased degree in the observation group was significantly greater than that in the control group (P<0.05). The difference of VEGF level before treatment between the two groups was not statistically significant (P>0.05). VEGF level after treatment in the two groups was significantly reduced, and the reduced degree in the observation group was significantly greater than that in the control group (P<0.05). The improvement of T cell subsets after treatment in the observation group was significantly superior to that in the control group (P<0.05). The occurrence rate of adverse reactions in the observation group was significantly lower than that in the control group (P<0.05). **Conclusions:** Gemcitabine chemotherapy on patients with middle and advanced liver cancer can effectively improve the immunological function, and enhance the efficacy, with a higher safety.

1. Introduction

Liver cancer is a common malignant tumor in the clinic whose typical symptoms and signs often occur in the middle and advanced stage, with main manifestations of hepatalgia, fatigue, emaciation, jaundice, and ascites[1]. Operation is an effective method for the treatment of liver cancer in the clinic, but the recurrence rate is high[2,3]. It is less reported that the immunological function and VEGF level are closely associated with the prognosis in patients with middle and advanced liver cancer[4]. The study is aimed to observe the effect of gemcitabine chemotherapy on the immune function and VEGF in patients with middle and advanced liver cancer.

2. Materials and methods

2.1. Clinical materials

A total of 90 patients with middle and advanced liver cancer who were admitted in our hospital from June, 2014 to July, 2015 were included in the study and randomized into the observation group and the control group with 45 cases in each group. In the observation group, 26 were male, and 19 were female; aged from 34 to 78 years old, with an average age of (54.12±5.33) years old. In the control group, 28 were male, and 17 were female; aged from 33 to 75 years old, with an average age of (56.27±4.83) years old. Inclusion criteria[5]: (1) those who were confirmed with middle and advanced cancer by the liver puncturing pathological biopsy; (2) aged from 30 to 80 years old; (3) those who had no malignant tumors. Exclusion

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criteria: (1) those who had coagulation disorders; (2) those who were allergic to gemcitabine; (3) those who had severe liver dysfunction. An informed consent was obtained from the patients. The study was approved by the Ethical Committee of our hospital. The difference of gender, age, and other general materials between the two groups was not statistically significant (P>0.05).

2.2. Methods

The patients in the observation group were given gemcitabine hydrochloride (produced by Jiangsu Hausen Pharmaceutical Company Ltd., batch no. 20080105, specification: 1.0 g/0.2 g), 1 000 mg/m^2, iv. drip, for 30 min, 1 time/week, continuously for 3 weeks, and rest for one week in the following. Four-week treatment was regarded as one course, and three courses were adopted[7]. The patients in the control group were given adriamycin (doxorubicin hydrochloride for injection) (produced by Shanxi Pude Pharmaceutical Company Ltd., batch no. 20101122, specification: 10 mg/50 mg). Usage and dosage: before administration, adriamycin was dissolved with 5 mL and 25 mL of sterile water, and then 5% glucose injection or sterile normal saline was added, 10 mg/time, 1 time/d, continuously for 1 week, and then drug withdrawal for 1 week, as one course, and a total of 3 weeks were adopted[6,8].

2.3. Observation indicators and efficacy evaluate criteria

T lymphocyte subsets, IL-6, TNF- , and VEGF levels in the two groups were observed.

2.4. Statistical analysis

SPSS 16. 5 for windows software was used for the statistical analysis. The measurement data were expressed as mean±SD, and t test was used. *Chi*-square test was used for the enumeration data. P<0.05 was regarded as statistically significant difference.

3. Results

3.1. Comparison of IL–6, TNF– α , and VEGF levels before and after treatment between two groups

The difference of IL-6 and TNF- levels before treatment between the two groups was not statistically significant (P>0.05). IL-6 and TNF- α levels after treatment in the two groups were significantly elevated, and the increased degree in the observation group was significantly greater than that in the control group (P<0.05). The difference of VEGF level before treatment between the two groups was not statistically significant (P>0.05). VEGF level after treatment in the two groups was significantly reduced, and the reduced degree in the observation group was significantly greater than that in the control group (P<0.05) (Table 1).

3.2. Comparison of T cell subsets before and after treatment between two groups

CD3$^+$, CD4$^+$, and CD4$^+$/CD8$^+$ after treatment in the observation group were significantly elevated, but CD8$^+$ was significantly reduced (P<0.05). CD3$^+$, CD4$^+$, and CD4$^+$/CD8$^+$ after treatment in the control group were significantly reduced, but CD8$^+$ was significantly elevated (P<0.05). The improvement of various indicators after treatment in the observation group was significantly superior to that in the control group (P<0.05) (Table 2).

3.3. Comparison of adverse reactions between two groups

In the observation group, during the treatment period, 1 (2.22%) had nausea and vomiting, 2 (4.44%) had skin rash, 1 (2.22%) had diarrhea, and the total occurrence rate of adverse reactions was 8.89%. In the control group, during the treatment period, 6 (13.33%) had nausea and vomiting, 4(8.89%) had alopecia, 8 (17.78%) had skin rash, 7 (15.56%) had diarrhea, and the total occurrence rate

Table 1
Comparison of IL-6, TNF- , and VEGF levels before and after treatment between two groups (ng/mL).

Groups	n		IL-6	TNF- α	VEGF
Observation group	45	Before treatment	5.83±2.10	3.02±0.67	478.35±15.11
		After treatment	14.75±7.32$^{*\#}$	11.37±3.83$^{*\#}$	325.90±17.68$^{*\#}$
Control group	45	Before treatment	5.65±1.97	3.29±0.71	474.27±12.65
		After treatment	9.02±4.12*	6.52±1.40*	409.12±13.10*

$^{*}P$<0.05, when compared with before treatment; $^{\#}P$<0.05, when compared with the control group.

Table 2
Comparison of T cell subsets before and after treatment between two groups (%).

Groups	n		CD3$^+$	CD4$^+$	CD8$^+$	CD4$^+$/CD8$^+$
Observation group	45	Before treatment	50.40±12.48	52.37±15.66	35.50±13.00	1.65±0.91
		After treatment	53.51±11.48$^{*\#}$	55.51±14.74$^{*\#}$	32.57±10.67$^{*\#}$	1.83±0.95$^{*\#}$
Control group	45	Before treatment	50.15±6.49	53.09±9.40	35.59±8.82	1.47±0.54
		After treatment	48.84±8.94	59.09±10.01*	38.03±10.51*	1.33±0.63*

$^{*}P$<0.05, when compared with before treatment; $^{\#}P$<0.05, when compared with the control group.

of adverse reactions was 55.56%. The occurrence rate of adverse reactions in the observation group was significantly lower than that in the control group (P<0.05).

4. Discussion

Liver cancer is a kind of common malignant liver cancer, which can severely threaten the human health and life[9]. The pathogenesis of primary liver cancer is complicated, among which the environment is one of the important factors. Some researches demonstrate that[10,11] HBV and HCV infection, aflatoxin, drinking water contamination, alcohol, liver cirrhosis, sex hormone, nitrosamines, and microelements are closely associated with the pathogenesis of liver cancer. The secondary liver cancer is also called the metastatic liver cancer, with blood and lymph metastasis or direct invasion on the liver. Due to the unobvious symptoms in the early stage, liver cancer is often ignored. The liver cancer can be detected until the middle and advanced stage; therefore, the best period for operation has been missed.

Chemotherapy is often adopted for the treatment of middle and advanced cancer. During the treatment period, the selection of chemotherapeutic drugs is extremely important. Adriamycin can kill the tumor cells by inhibiting the synthesis of nucleic acid which is a genetic material of liver cells. Some researches demonstrate that[12,13] adriamycin can induce alopecia and gastrointestinal adverse reactions. In the study, the occurrence rate of adverse reactions in the control group was significantly higher than that in the observation group, which is consistent with some reports. Gemcitabine, a difluoro nucleosides anti-metabolite and anticancer drug, can destroy the cell replication, and is a new type anticancer drug, with less side effects; therefore, it has been widely applied in the clinic. Some researches demonstrate that[14,15] gemcitabine inhibit the tumor angiogenesis to enhance the immune function through restraining the production of VEGF and other related angiogenic factors. The results in the study showed that the total effective rate after treatment in the observation group was significantly higher than that in the control group (P<0.05), indicating that gemcitabine in the treatment of middle and advanced liver cancer is effective. The results in the study showed that the improvement of T cell subsets after treatment in the observation group was significantly superior to that in the control group; moreover, the serum IL-6 and TNF-α levels were elevated, suggesting that gemcitabine can effectively improve the immunological function. The results in the study showed that VEGF level after treatment in the observation group was significantly lower than that in the control group (P<0.05), indicating that gemcitabine can inhibit the expression of VEGF.

In conclusion, gemcitabine chemotherapy on patients with middle and advanced liver cancer can effectively improve the immunological function, and enhance the efficacy, with a higher safety.

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