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Effect of Docetaxel combined with Nedaplatin on serum LPA, CA199, CEA, Interleukin and immune function in patients with epithelial ovarian cancer

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ABSTRACT

Objective: To study the effect of Docetaxel combined with Nedaplatin on serum LPA, CA199, CEA, Interleukin and immune function in patients with epithelial ovarian cancer. **Methods:** A total of 78 EOC patients in our hospital from August 2012 to June 2015 were enrolled in this study. The subjects were divided into the control group (n=39) and the experiment group (n=39) randomly. The control group were treated with carboplatin, the experiment group were treated with docetaxel combined with nedaplatin. In the experimental group, 21 d for a course of treatment, in the control group, 28 d for a course of treatment, and the two groups were treated for 4 periods. The clinical efficacy after the treatment of the two groups were evaluated and compared. The changes of serum LPA, CA199, CEA and other related indexes were detected and compared between the two groups before and after chemotherapy. **Results:** There were no significantly differences of the serum LPA, CA199, CEA, IL (6,8,10) and immune function of the two groups before treatment. After treatment, two groups of patients with serum LPA, CA199, CEA and IL (6,8,10) were significantly lower in the treatment of, at the same time, the experimental group had the level of each index were significantly lower than that of the control group, the difference is statistically significant. Before treatment, two groups of patients` peripheral blood $CD3^+$, $CD4^+$ and $CD8^+$ cells accounted for ratio, the difference was not statistically significant; The peripheral blood $CD3^+$, $CD4^+$ and $CD8^+$ cells of the two groups after treatment were significantly lower than before treatment, and that of experiment were significantly higher than control group. **Conclusion:** Docetaxel combined with Nedaplatin chemotherapy can significantly reduce the serum LPA, CA199, CEA and IL (6,8,10) levels, improve peripheral blood $CD3^+$, $CD4^+$ and $CD8^+$ levels of patients with epithelial ovarian cancer, and it was worthy clinical application.

1. Introduction

Ovarian malignant tumor is the third most common malignant tumor in female reproductive organs, the incidence of which is second only to cervical cancer and cervical cancer, and it is a serious threat to the health of women[1,2]. Due to the lack of specific symptoms and early diagnostic methods, most of the patients have been diagnosed at the late stage, and epithelial ovarian cancer (EOC) mortality rate is the highest in all kinds of gynecological cancer, so it is a serious threat to the life safety of patients. With the change of social organization and people's life style, the incidence of EOC is increasing year by year. Therefore, it is urgent to choose effective treatment for EOC[3]. Most of the malignant tumor of the ovary has a high sensitivity to chemotherapy drugs, so even if the disease develops to the advanced stage, it can still get a certain therapeutic effect through chemotherapy[4]. Therefore, the current main clinical treatment regimen for EOC is cisplatin, and platinum based combination chemotherapy is the most important one. However, related research found that there are

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individual differences in the treatment of patients with EOC, EOC patients with the same pathological grading or staging after the same chemotherapy treatment shows different efficacy differences[5,6]. Therefore, it has an important clinical significance to determine the efficacy of chemotherapy in patients with EOC so as to provide the corresponding follow-up treatment. Tumor marker is a specific type of protein small molecule secreted in cancer tissues. The detection of serum tumor marker levels is of great significance for the evaluation of the efficacy of EOC chemotherapy[7,8,9]. This study was to investigate the effect of Docetaxel combined with Nedaplatin on serum LPA, CA199, CEA, Interleukin and immune function in patients with epithelial ovarian cancer.The results are as follows.

2. Informations and methods

2.1. General information

A total of 78 EOC patients in our hospital from August 2012 to June 2015 were enrolled in this study. The subjects were divided into the control group and the experiment group randomly, 39 cases in each group. In the control group, patients were aged from 31 to 66 years old, mean age (50.35±11.44) years old; Weight 39-68 kg, mean weight (49.66±11.78) kg; Tumor types: 23 cases of mucinous adenocarcinoma, 16 cases of serous adenocarcinoma; Pathological stage: 10 cases of stage I, 18 cases of stage II, 11 cases of stage III. In the experiment group, patients were aged from 32 to 63 years old, mean age (49.36±11.67) years old; Weight 40-70 kg, mean weight (51.12±12.14) kg; Tumor types: 21 cases of mucinous adenocarcinoma, 18 cases of serous adenocarcinoma; Pathological stage: 12 cases of stage I, 20 cases of stage II, 7 cases of stage III. There was no significant difference in the age, weight, tumor type, pathological stage and other general data between the two groups (P>0.05).

2.2. Inclusion criteria

All patients met the inclusion criteria and were not within the exclusion criteria.Inclusion criteria: (1) The diagnosis of epithelial ovarian cancer was confirmed by pathology and cytology; (2) Not received any chemotherapy treatment; (3) Has a history of ovarian cancer cell death;(4) Full-featured Liver and kidney function. Case exclusion criteria: (1) Non epithelial ovarian cancer patients; (2) Patients with other malignant tumors; (3) Patients with contraindications to chemotherapy. All patients were informed consent and voluntarily joined in this study, and was approved by the hospital ethics committee.

2.3. Experimental methods

Patients in the control group treated with carboplatin(purchased from Kunming expensive research Pharmaceutical Co., Ltd., Chinese medicine standard word: H20053908) chemotherapy, disposable intravenous infusion, 400 mg/m^2, interval 28 d, repeated administration of one time; The experimental group were treated with docetaxel combined with nedaplatin chemotherapy, Specifically for: Docetaxel (purchased from Shanghai Pharmaceutical Co., Ltd. Chinese medicine standard word: H20103540) with disposable intravenous infusion 75 mg/m^2 and Nedaplatin (purchased from Qilu Pharmaceutical Co., Ltd.. Chinese medicine standard word: H20050563) 80 mg/m^2 ,interval 21 d, repeated administration 1 time. Two groups of patients were treated for 4 courses of treatment.

2.4. Detection index

Two groups of patients were collected before and after the treatment of fasting venous blood 5 mL, serum separation, Isolated serum in a spped of 3 000 rpm centrifuge for 15 min, then the levels of Serum LPA, CA199, CEA, interleukin- (6, 8, 10) and the ratio of CD3$^+$, CD4$^+$, CD8$^+$ were detected and compared between the two groups before and after treatment.

The detection of serum LPA was used LPA kit test, according to the instruction manual operation, The detection of serum CA199 level was used luminescence immunoassay by Cobas2000 automatic immune analyzer, operating in accordance with the instructions of the kit. The level of CEA was analyzed by chemiluminescence immunoassay with the Abbott chemiluminescence analyzer detection Architeci2000. The levels of serum IL-6, IL-8 and IL-10 were measured by enzyme-linked immunosorbent assay (ELISA). All the procedures were performed in strict accordance with the kit instructions. Peripheral blood CD3$^+$, CD4$^+$and CD8$^+$ cells were detected by Backman CytoFLEX flow cytometry. Tumor marker serum CEA and CA199 positive criteria were: CEA>5.0 ng/mL, CA199>37.0 U/mL.

2.5. Statistical method

We carry on data statistics and analysis using SPSS 19.0 software package , mean ± standard deviation (mean ± 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 LPA, CEA and CA199 levels before and after treatment between the two groups′ patients

Before treatment, there was no significant difference in the serum levels of LPA, CEA and CA199 between the two groups (P>0.05); After treatment, the serum LPA, CEA and CA199 levels in the two groups were significantly lower than before treatment, the difference was statistically significant (P<0.05). At the same time, the serum levels of LPA, CEA and CA199 in the experimental group were significantly lower than those in the control group, the difference

Table 1.
Comparison of serum LPA, CEA and CA199 levels before and after treatment between the two groups' patients.

Group	*n*	Time	LPA (μmol/L)	CEA (ng/mL)	CA199 (U/mL)
Experimental	39	Before treatment	11.46±1.67	25.42±6.31	67.56±13.44
		After treatment	2.65±1.46*#	5.03±1.31*#	15.46±9.20*#
Control	39	Before treatment	12.37±1.82	25.19±5.83	68.01±13.44
		After treatment	5.28±1.58*	14.54±3.41*	34.37±14.27*

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

was statistically significant (P<0.05). Please look at the table 1.

3.2. Comparison of the level of interleukin in the two groups before and after treatment

Before treatment, there was no significant difference in the serum levels of IL-6, IL-8 and IL-10 between the two groups (P>0.05); After treatment, the serum IL-6, IL-8 and IL-10 levels in the two groups were significantly lower than before treatment, the difference was statistically significant (P<0.05). At the same time, the serum levels of IL-6 (27.65±0.46), IL-8 (35.03±0.31) and IL-10 (12.34±2.20) in the experimental group were significantly lower than those in the control group, which the levels were correspondingly (37.28±1.52), (38.54±1.41) and (15.21±2.27)，and the difference was statistically significant (P<0.05). Please look at the table 2.

3.3. The level of T lymphocyte subsets before and after treatment in all patients

Before treatment, there was no significant difference in the ratio of CD3+, CD4+ and CD8+ cells in peripheral blood of the two groups (P>0.05). After treatment, the ratio of CD3+, CD4+ and CD8+ cells in peripheral blood were significantly lower than before treatment, the difference was statistically significant (P<0.05). After treatment, the ratio of CD3+ (30.79±4.41), CD4+ (25.12±1.59) and CD8+ (27.69±4.32) cells in peripheral blood in the experimental group were significantly higher than those in the control group, which the ratio were correspondingly (14.37±3.33), (14.71±1.33) and (12.22±1.12), and the difference was statistically significant (P<0.05). Please look at the table 3.

4. Discussion

Epithelial ovarian cancer is a malignant tumor of the female reproductive system, and the incidence rate showed an upward trend, epithelial ovarian cancer was hidden, and Most of the patients were diagnosed as late, athough ovarian epithelial ovarian cancer is sensitive to chemotherapy, due to the heterogeneity of the tumor,there was a great difference in the effect of chemotherapy in different patients[10]. Therefore, the selection of effective specific serum tumor markers to judge the efficacy of chemotherapy in patients can provide more targeted treatment for patients. LPA is a kind of small lipid molecules, with the help of G protein receptor mediated partial signal transduction pathway, it has the function of signal transmission[11,12]. CA199 is a kind of glucose and lipid, which is produced by adenocarcinoma cells, which is mainly used in the diagnosis of malignant tumors of digestive system[13,14]. CEA is a common tumor marker in digestive tract cancer, but it also has a certain diagnostic value in the female reproductive system tumors[15–17].This study examines the effect of docetaxel combined with nedaplatin chemotherapy on epithelial ovarian cancer serum LPA, CA199, CEA, Interleukin and T cell subsets，so that we can provide a suitable tumor marker for the treatment of epithelial ovarian cancer. Docetaxel is the second generation Taxoids semi synthesis of antitumor drugs, produced in paclitaxel based, because the solubility is higher than paclitaxel, its anti-tumor effect is good, and the anticancer spectrum is wide[18]. Nedaplatin is a cisplatin analogues,

Table 2.
Comparison of serum IL-6, IL-8 and IL-10 levels in the two groups before and after treatment.

Group	*n*	Time	IL-6 (pg/mL)	IL-8 (pg/mL)	IL-10 (ng/L)
Experimental	39	Before treatment	60.46±12.67	66.42±16.31	16.16±3.44
		After treatment	27.65±0.46*#	35.03±0.31*#	12.34±2.20*#
Control	39	Before treatment	59.37±11.82	65.19±15.83	17.01±3.14
		After treatment	37.28±1.52*	38.54±1.41*	15.21±2.27*

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

Table 3.
The level of T lymphocyte subsets before and after treatment in all patients (%).

Group	*n*	Time	$CD3^+$	$CD4^+$	$CD8^+$
Experimental	39	Before treatment	46.19±7.31	46.86±2.96	43.68±6.84
		After treatment	30.79±4.41*#	25.12±1.59*#	27.69±4.32*#
Control	39	Before treatment	47.49±8.52	47.02±4.66	44.35±5.73
		After treatment	14.37±3.33*	14.71±1.33*	12.22±1.12*

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

the mechanism is similar to that of cisplatin. The results of this study showed that before treatment, the serum levels of LPA, CA199, CEA,, interleukin and T lymphocyte subsets were not significantly different between the two groups (P>0.05); After treatment, the serum levels of LPA, CA199, CEA, interleukin and T lymphocyte subsets were significantly lower than those before treatment in two groups, and the level of each index of the experimental group were significantly lower than the control group, the difference was statistically significant (P<0.05). This suggests that docetaxel and Nedaplatin Combined with chemotherapy can significantly reduce the epithelial ovarian cancer serum LPA, CA199, CEA, IL-6 and T lymphocyte subsets level. The proliferation of tumor cells was inhibited by the proliferation of the tumor cells, and the platinum group had a good effect on killing the tumor cells.,the combination of them has a good effect, so the indicators have been reduced in this study[19–21]. In addition, there were no significant differences in the levels of T lymphocyte subsets between the two groups before and after treatment (P>0.05), while after different treatment, the two groups of patients were significantly lower than before treatment, and the immune function indexes in the experimental group were significantly higher than those of the control group (P<0.05). This suggests that docetaxel combination with nedaplatin have a certain role in promoting the cellular immune function of patients with ovarian cancer. Its mechanism may be that, Docetaxel can inhibit tumor cell division and proliferation, thus providing protection for the patient's immune system and ultimately improving the immune function of the patient[22,23].

In summary, docetaxel combined with nedaplatin chemotherapy can significantly reduce the epithelial ovarian cancer patient′ serum LPA, CA199, CEA, white cell dielectric hormone (6,8,10) level, promote the upgrading of the level of T cell subsets, improve the cellular immune function, so it is worthy clinical application.

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