

Effect of Bevacizumab Combined with Neoadjuvant Chemotherapy in Advanced Ovarian Cancer and the Occurrence of Adverse Reactions

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Abstract: *Objective:* To explore the effect of bevacizumab combined with neoadjuvant chemotherapy in advanced ovarian cancer and the occurrence of adverse reactions. *Methods:* A total of 80 patients with advanced ovarian cancer, treated in Affiliated People's Hospital of Inner Mongolia Medical University from June 2019 to December 2020, were randomly divided into two groups. In the chemotherapy group, 40 patients were treated with neoadjuvant chemotherapy, while in the combined group, another 40 patients were treated with bevacizumab combined with neoadjuvant chemotherapy. The therapeutic effects were compared at the end of the treatment cycle. *Results:* There was no significant difference in the levels of CA125, CEA, and VEGF between the two groups before treatment. However, after the treatment cycle, the levels of CA125, CEA, and VEGF in the combined group were significantly better than those in the chemotherapy group ($P < 0.05$). At the same time, the incidence of adverse reactions of the chemotherapy group was 67.50%, which was significantly higher than that of the combined group (35.00%; $P < 0.05$). *Conclusion:* Bevacizumab combined with neoadjuvant chemotherapy for patients with advanced ovarian cancer has significant curative effect. The combined therapy reduces the levels of tumor markers and inflammatory factors, improves patients' quality of life, as well as reduces adverse reactions. It has high clinical promotion value.

Keywords: Bevacizumab; Neoadjuvant chemotherapy; Advanced ovarian cancer; Adverse reaction

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1. Introduction

Ovarian cancer is one of the three major gynecological tumors, which is mainly caused by the uncontrolled growth of ovarian or fallopian tube cells, mostly in menopausal women ^[1]. Although the incidence rate of ovarian cancer is not high, it is a serious condition and is not easily detected at an early stage. Until the tumor grows or deteriorates, the abdominal mass, abdominal pain, frequency of urination, and other symptoms do not draw the attention of patients, but unknowingly, cancer cells are spreading to surrounding organs and tissues. This seriously threatens the safety of women ^[2]. At present, the etiology of ovarian cancer has not been clarified, but it is generally considered that the pathogenesis may be related to immune dysfunction, endocrine disorders, excessive mental stress, and other factors. At present, the clinical treatment of advanced ovarian cancer usually focuses on chemotherapy, radiotherapy, and surgery. The commonly used chemotherapy drugs include taxol, ifosfamide, and altretamine. However, chemotherapy is a long-term process, which can cause various adverse reactions and the weakening of its efficacy, resulting in poor overall effect ^[3]. In order to improve the therapeutic effect of chemotherapy, 80 patients with advanced ovarian cancer in the Affiliated People's Hospital of Inner Mongolia Medical University

were specially selected as the research subjects to explore the clinical efficacy of bevacizumab combined with neoadjuvant chemotherapy.

2. Materials and methods

2.1. General information

A total of 80 patients with advanced ovarian cancer admitted to the Affiliated People's Hospital of Inner Mongolia Medical University from June 2019 to December 2020 were divided into two groups using the random number method. The inclusion criteria were as follows: (1) patients who met the clinical diagnostic criteria for advanced ovarian cancer; (2) patients who had not been treated with bevacizumab, and their survival time was more than half a year; (3) FIGO stage III - IV. The exclusion criteria were as follows: (1) pregnant women; (2) intolerant to the drugs used in this study; (3) presence of other malignant tumors. There was no significant difference between the two groups ($P > 0.05$) (**Table 1**).

Table 1. Comparison of the general information between the two groups

| Group (n = 40) | Age (years) | Course of disease (years) | BMI (kg/m ²) |
|-----------------|-------------|---------------------------|--------------------------|
| Reference group | 49.36±5.35 | 2.86±1.04 | 24.33±4.31 |
| Research Group | 49.72±5.21 | 2.73±1.11 | 24.29±4.35 |
| χ^2 value | 0.305 | 0.541 | 0.041 |
| <i>P</i> value | 0.761 | 0.590 | 0.967 |

2.2. Methods

Patients in the chemotherapy group were treated with taxol plus cisplatin. Diluted with 500 ml of normal saline, 135 mg/m² of taxol (Beijing Union Pharmaceutical Factory; approval number: National Medicine Standard H10980068) was given via intravenous infusion, followed by 75 mg/m² of cisplatin injection the next day (Tonghua Maoxiang Pharmaceutical Co., Ltd.; approval number: National Medicine Standard H22022966) via intraperitoneal route within 2 hours. Patients in the combination group were treated with bevacizumab (Roche Pharma Ltd.; approval number: S20120069) in combination with chemotherapy. 15 mg/kg of bevacizumab was dissolved in 250 ml of 0.9% sodium chloride, and the patients completed the intravenous infusion within 1 hour before neoadjuvant chemotherapy. Each treatment cycle was for three weeks. The efficacy of both groups was compared after four cycles of treatment.

2.3. Observation indexes

Before and after treatment, the levels of serum carbohydrate antigen 125 (CA125) and carcinoembryonic antigen (CEA) were measured, and the level of vascular endothelial growth factor (VGEF) was detected via enzyme-linked immunosorbent assay (ELISA). During the treatment, the adverse reactions of the patients in the two groups were observed. The observation indexes included hypertension, nausea and vomiting, as well as proteinuria. The total incidence of adverse reactions was regarded as the sum of the incidence of these three observation indexes.

2.4. Statistical analysis

The data collected were analyzed by SPSS 24.0 statistical software. The counting data were expressed in (n/%), tested by χ^2 ; the measurement data were expressed in ($\bar{x} \pm s$), tested by t-test. $P < 0.05$ indicates a statistically significant difference.

3. Results

3.1. Comparison of CA125, CEA, and VEGF levels before and after treatment

There was no significant difference in the CA125, CEA, and VEGF levels between the two groups before treatment. After the treatment cycle, the CA125, CEA, and VEGF levels of the combined group were 41.13 ± 9.14 U/mL, 5.42 ± 1.36 U/mL, and 80.17 ± 9.45 pg/mL, respectively, which were significantly better than those of the chemotherapy group (54.32 ± 9.36 U/mL, 10.73 ± 2.11 U/mL, and 103.56 ± 12.49 pg/mL, respectively; $P < 0.05$) as shown in **Table 2**.

Table 2. Comparison of CA125, CEA, and VEGF levels between the two groups before and after treatment ($\bar{x} \pm S$)

| Group (n = 40) | CA125 (U/mL) | | CEA (U/mL) | | VEGF (pg/mL) | |
|--------------------|------------------|-----------------|------------------|-----------------|------------------|-----------------|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Chemotherapy group | 86.33±9.65 | 54.32±9.36 | 36.56±4.35 | 10.73±2.11 | 244.68±28.16 | 103.56±12.49 |
| Combined group | 86.25±9.67 | 41.13±9.14 | 36.61±4.29 | 5.42±1.36 | 244.28±27.93 | 80.17±9.45 |
| t value | 0.037 | 6.377 | 0.052 | 13.378 | 0.064 | 9.445 |
| P value | 0.971 | 0.000 | 0.959 | 0.000 | 0.949 | 0.000 |

3.2. Comparison of the incidence of adverse reactions between the two groups

A total of 27 patients in the chemotherapy group developed adverse reactions, accounting for 67.50% of the whole group, which was significantly higher than that of the combined group (35.00%; $P < 0.05$) as shown in **Table 3**.

Table 3. Comparison of the incidence of adverse reactions between the two groups (n/%)

| Group (n = 40) | Hypertension | Nausea and vomiting | Proteinuria | Adverse reaction rate |
|--------------------|--------------|---------------------|-------------|-----------------------|
| Chemotherapy group | 5 (12.50) | 18 (45.00) | 4 (10.00) | 27 (67.50) |
| Combined group | 2 (5.00) | 11 (27.50) | 1 (2.50) | 14 (35.00) |
| χ^2 value | | | 8.455 | |
| P value | | | 0.003 | |

4. Discussion

Ovarian cancer is uncommon in clinical practice, but its incidence rate has increased significantly in recent years. Currently, surgery is the main treatment for this condition. The cancer cells that have not been removed through surgery would be cleared via chemotherapy. However, this treatment has a certain failure rate and negative impact on patients, affecting their quality of life [5]. Neoadjuvant chemotherapy is when a patient receives chemotherapy treatment before surgery to control and reduce the spread of cancer cells as much as possible. This treatment can effectively reduce the difficulty of surgery and improve the effect of surgical clearance [6]. Taxol plus cisplatin is usually used in clinical practice, but its long-term use can lead to drug resistance and the gradual attenuation of its treatment effect [7]. In recent years, bevacizumab, a chemotherapy drug targeting VEGF, has gradually shown its advantages. It specifically binds to VEGF, inhibits the biological activity on the surface of endothelial cells, so as to inhibit angiogenesis, effectively reduces tumor blood supply, as well as slows down tumor growth and cancer cell metastasis, thus delaying

and killing tumor cells [8]. At the same time, bevacizumab improves the hemodynamics in the tumor area, accelerates the effectiveness of certain drugs, promotes drugs to act faster and better on tumor tissues, as well as reduces the impact of those drugs on other normal tissues.

This study showed that there was no significant difference in the levels of CA125, CEA, and VEGF between the two groups before treatment. However, after the treatment cycle, the levels of CA125, CEA, and VEGF of the combined group (41.13 ± 9.14 U/mL, 5.42 ± 1.36 U/mL, and 80.17 ± 9.45 pg/mL, respectively) were significantly better than those of the chemotherapy group ($P < 0.05$). At the same time, the incidence of adverse reactions of the chemotherapy group was 67.50%, which was significantly higher than that of the combined group (35.00%; $P < 0.05$). It is suggested that bevacizumab combined with neoadjuvant chemotherapy can effectively reduce the expression of oncogenes in patients, inhibit the angiogenesis of tumor cells, slow down the development and metastasis of ovarian cancer, promote a more obvious targeted therapeutic effect, improve the therapeutic effect, reduce the adverse reactions of patients, as well as improve their quality of life.

In conclusion, bevacizumab combined with neoadjuvant chemotherapy for patients with advanced ovarian cancer has achieved more significant clinical effect compared to conventional chemotherapy, which is conducive to reducing adverse reactions, improving prognosis, and creating favorable conditions for follow-up treatment; thus, it is worthy of further research and promotion.

Disclosure statement

The author declares that there is no conflict of interest.

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