

Effect of Intraperitoneal Administration of Paclitaxel Combined with Cisplatin in Treatment of Advanced Ovarian Cancer

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Abstract: Objective: To analyze the effect of intraperitoneal administration of paclitaxel combined with cisplatin in treatment of advanced ovarian cancer.

Method: Fifty-four patients with advanced ovarian cancer in our hospital were randomly selected from the beginning of July 2018 to the end of June 2019. The principle of grouping was based on double-blind randomization method. In experimental group, 27 patients were given intraperitoneal administration of paclitaxel combined with cisplatin. In control group, 27 patients were given intravenous administration of paclitaxel combined with cisplatin. Clinical data of the two groups were compared. **Results:** Short-term clinical efficacy and T lymphocyte subsets of experimental group were significantly improved when compared with control group. The difference was significant ($P < 0.05$). There was no significant difference in adverse reactions between the two groups ($P > 0.05$). **Conclusion:** The effect of intraperitoneal administration of paclitaxel combined with cisplatin is ideal for treatment of advanced ovarian cancer patients.

Keywords: Paclitaxel, Cisplatin, Intraperitoneal administration, Advanced ovarian cancer

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Clinically, the risk for women to contract ovarian cancer is higher. It belongs to malignant tumor. Its clinical onset is not apparent and its tumor is easily subjected to metastasis and spreading. Most patients are in the late stage of the cancer when diagnosis is confirmed and often miss the best time of treatment. Mortality in patient is high. Analyses showed that patients

are relatively sensitive to chemotherapy and it is an effective method for treatment of advanced ovarian cancer. Therefore, clinical researches and analyses were carried out, and treatment using paclitaxel combined with cisplatin was proposed^[1]. It has remarkable effect. However, due to poor immunity of patients, it not only kills cancer cells but also suppresses the immune function of patients during the treatment, which is not conducive to recovery of patients. Therefore, further analysis and research were carried out to investigate the application method of the drug in clinics. Analyses showed that post-operative recurrence rate of disease could be significantly reduced if patients with advanced ovarian cancer were treated with combination of surgery and chemotherapy. In this article, the effect of intraperitoneal administration of paclitaxel combined with cisplatin for treatment in 54 patients with advanced ovarian cancer was comprehensively analyzed.

1 Materials and methods

1.1 Information

Fifty-four patients with advanced ovarian cancer who were diagnosed and received treatment in our hospital were selected. Selection period was from the beginning of July 2018 to the end of June 2019. Informed consent was obtained. Randomized double-blind grouping method was used. Twenty-seven patients were grouped into control group. Age distribution was from 40 to 72 years old, median age was 56.5 years. There were 7 cases of recurrent ovarian cancer, 10 cases of stage IV cancer, and 10 cases of stage III cancer. Another twenty-seven patients were grouped into experimental group. Age

distribution was from 41 to 73 years old, median age was 56.0 years. There were 6 cases of recurrent ovarian cancer, 12 cases of stage IV cancer, and 9 cases of stage III cancer. The baseline data (age, sex, course of disease, and disease condition) of the two groups were compared, P was greater than 0.05. All the patients fulfilled the relevant inclusion criteria by the ethics committee of our hospital.

1.2 Methods

Twenty-seven experimental group patients were treated with intraperitoneal administration of paclitaxel combined with cisplatin. Patients were first given intravenous perfusion with paclitaxel of dose 135 mg/m². After 24 hours, patients were given peritoneal perfusion of cisplatin. After 7 days, peritoneal perfusion of paclitaxel was given to patients, dose 60mg/m².

Intravenous perfusion of paclitaxel combined with cisplatin was given to 27 control group patients. Routine intravenous drip was given to the patients at the same dose above.

Patients in both groups were given treatment for 3 weeks in average.

Thirty minutes before drug administration, patients in both groups were given intramuscular injection with the selected drug diphenhydramine at dose of 25mg for prevention of allergy.

1.3 Observation of indicators^[2]

Clinical efficacy, T lymphocyte subsets and adverse reactions of the two groups were compared and analyzed.

1.4 Analysis of effect

After treatment, those patients with all tumors disappeared, CA125 value decreased to normal value and symptom maintenance time greater than 4 weeks, were determined as complete remission. Those with the maximum vertical diameter of tumor reduced by more than 50%, CA125 value decreased by more than 50% and symptom maintenance time greater than 4 weeks, were determined as partial remission. Those with maximum vertical diameter of tumor reduced by 50% or less, CA125 value decreased by 25% or less and symptom maintenance time greater than 4 weeks, were determined as stable. Those did not fulfill the above requirements were determined as progress. Total effective rate = 100.00% - rate of progress^[3].

1.5 Statistical calculation

In this study, measurement data and count data of two groups of patients were analyzed using t test and X² test respectively. SPSS19.0 software was used for calculation of data. The data was represented in the forms of (mean±standard deviation) and rate respectively. Statistical significance existed when $P < 0.05$.

2 Results

Short-term clinical efficacy and T lymphocyte subsets of experimental group were significantly improved. When compared to control group, the difference was statistically significant ($P < 0.05$). Adverse reaction was compared between the two groups, the difference was not statistically significant, $P > 0.05$.

Table 1 Comparison of short-term clinical efficacy between two groups of patients

Group	Number of corresponding cases in each group	Number of cases of complete remission	Number of cases of partial remission	Number of cases of stable	Number of cases of progress	Total effective rate
Experimental	27	10	10	6	1	96.29%
Control	27	5	8	8	6	77.77%
X ²						4.1033
P						< 0.05

Table 2 Comparison of T lymphocyte subsets and adverse reactions in 2 groups of patients

Group	Number of corresponding cases in each group	CD4+CD25+ (%)	CD4+CD8+ (%)	Adverse reaction (%)
Experimental	27	1.45±0.11	1.85±0.23	2 (7.40)
Control	27	1.98±0.29	1.45±0.11	1 (3.70)
t/X ²		9.2021	8.4489	0.3529
P		< 0.05	< 0.05	> 0.05

3 Discussions

Clinically, incidence of advanced ovarian cancer is high. Its tumor is located deep in pelvic cavity of patient. If the patient is in the early stage, signs and clinical manifestations are usually not apparent and diagnosis method is not effective enough for confirmation. Therefore, patient is usually in the advanced stage upon confirmation of diagnosis. There are certain characteristics in patients with advanced ovarian cancer. For example, pelvic diffuse implantable metastasis and peritoneal diffuse implantable metastasis may occur in patients. Cytoreductive surgery alone can not effectively treat the disease contracted by patients. The efficiency is about 30%, and relapse prone to occur after surgery. Therefore, patients should be given chemotherapy after surgery, which can significantly improve the treatment efficiency in patients. Analysis shows that the effect of single-agent chemotherapy is not ideal and it cannot effectively control the recurrence rate in patients. Its clinical approbation is not high.

Clinical characteristics of patients with advanced ovarian cancer were analyzed. It was found that for patients with biological characteristic of peritoneal implant metastasis, treatment of intraperitoneal perfusion of chemotherapy resulted in higher drug concentration in localized parts of patient. Drug could maintain for a longer period of time and systemic toxicity in patient was lower. Concentration of anticancer drugs in abdominal cavity was 12 to 15 times higher than that in plasma. Intraperitoneal tumor of patient was situated in a higher concentration of drug, this could enhance the chemotherapy effect. Therefore, clinical research and related experiments were carried out to investigate for effective treatment for patients, selection of chemotherapy drug, and path of chemotherapy.

Analysis showed that combination of paclitaxel and cisplatin drugs had significant effect for treatment of patients with advanced ovarian cancer. It was proposed that intraperitoneal administration of paclitaxel combined with cisplatin is able to effectively alleviate patient's condition. Follow-up showed that patients were not prone to disease recurrence and there was no drug resistance^[4]. The two drugs can be synergistic and cisplatin resistance could be overcome. Survival of patients could be prolonged.

As a natural anti-tumor plant drug, paclitaxel originates from short-leaf yew tree. This drug can promote

polymerization of tubulin, inhibit de-polymerization of tubulin, and prevent proliferation and division of cancer cells. Its effect can be synergistic when combined with cisplatin. In addition, paclitaxel can inhibit cell division and cell kinetic abnormalities. It has inhibitory effects for various tumor cells^[5].

Analysis showed that peritoneal administration allows direct contact of drug with cancer cells in advanced ovarian cancer patients with tumor located in pelvic or abdominal cavity. Drug can directly reach the tumor and efficacy exerted is stronger. Drug enters liver through portal vein of patient and is processed by hepatic enzymatic metabolism, thus efficacy of drug is reduced and thereby the systemic adverse reaction in patients is significantly reduced^[6]. Clinical practice confirmed that the application of intraperitoneal administration of paclitaxel combined with cisplatin for treatment of advanced ovarian cancer patients has significant effect. When compared with intravenous drip therapy, its efficacy can be increased by 20-fold.

Relevant literature reported that there is large amount of ascites in peritoneal cavity of patient with stage II or higher ovarian cancer. Direct surgical treatment will greatly increase the difficulty of treatment and ideal therapeutic effect cannot be obtained. Chemotherapy treatment before surgery can relieve the ascites symptom in patient, and spreading of cancer cells in patient can be controlled. Studies have shown that CD4+CD25+ can immunosuppress regulatory T cells, inhibit the immune response due to exogenous antigen or autoantigens, and prevent body from immunizing its own homologous cells. To a certain extent, ovarian cancer cells belong to immune cells^[7]. For dysregulated autologous cell division, positive rate of CD4+CD25+ cells indirectly reflect the effect of drug in treatment of cancer. During monitoring of chemotherapy, decreased number of peripheral blood CD4+CD25+T cells indicates that negative regulation of body's immune system weakens in the patient. Immune response to tumor cells is enhanced and proliferation of cancer cells in patients is effectively controlled. On the contrary, increased number of CD4+CD25+T cells in peripheral blood can pose a positive effect for immune escape of cancerous cells^[8], which can lead to increased proliferation of cancer cells in patients and aggravation of patient's condition.

Related literature concluded that intraperitoneal administration of paclitaxel combined with cisplatin gives rise to limited penetration ability of drug. If it

is applied for treatment of advanced ovarian cancer patients, surface layer of 1–3 mm tumor can acquire higher concentration of drug. If patient has multiple metastases or tumor with large diameter, the effect of intraperitoneal drug administration is not ideal. If patient has extensive intra-granular metastasis, ideal therapeutic effect can be acquired^[9]. Drug that enters abdominal cavity can quickly pass through the patient's peritoneum into blood circulation and undergo first pass metabolism by liver. Compared with intravenous administration, its bone marrow suppression and digestive tract reaction are more similar. Therefore, intraperitoneal drug perfusion treatment uses higher dose of drug when compared with intravenous administration, thus adverse reactions are more serious^[10].

Results of this study showed that: short-term clinical efficacy and T lymphocyte subsets of the experimental group were significantly improved. This result suggested that application of intraperitoneal administration of paclitaxel combined with cisplatin in treatment of patients with advanced ovarian cancer has higher feasibility, higher reference value and higher clinical value.

Based on the above data, intraperitoneal administration of paclitaxel combined with cisplatin had ideal effect in treatment of advanced ovarian cancer patients. It could significantly improve short-term clinical efficacy and T lymphocyte subsets. Its application can be promoted in clinics. In post-mortem discussion of the clinical study, the number of sample selections should be appropriately increased, and relevant treatment plans should be further analyzed to increase the clinical significance of the study.

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