PACLITAXEL INTRAPERITOEAL PERFUSION CHEMOTHERAPY FOR TREATMENT OF PATIENTS WITH ADVANCED OVARIAN CANCER

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ABSTRACT
Through a relevant search of the literature our group found that paclitaxel peritoneal infusion combined with cisplatin can effectively improve the efficiency of chemotherapy. The aim of this study was to clarify the practical effect of paclitaxel hyperthermic intraperitoneal chemotherapy in treatment of advanced ovarian cancer, and to provide scientific guidance for future clinical treatment. This study of 1560 patients with advanced ovarian cancer admitted from June 2013 to June 2014, used combined chemotherapy, provides a detailed analysis of specific chemotherapy of patients during treatment, and records in detail progression-free survival, median survival time, 1 year survival rate, and adverse reactions of all 1560 patients. Compared with the clinical effect of paclitaxel hyperthermic intraperitoneal chemotherapy for advanced ovarian cancer by other medical researchers, the specific effect of this treatment is more significant. This study analysis sufficiently proves that paclitaxel has relatively high clinical value for advanced ovarian cancer. In particular, with combined chemotherapy with cisplatin, efficacy of the drug will be further brought into play, thereby effectively alleviating patient illness and effectively improving patient quality of life. This group recommends the combined use of paclitaxel and cisplatin drugs to improve the efficiency of clinical treatment of patients with advanced ovarian cancer.

Key words: Paclitaxel, Intraperitoneal Perfusion Chemotherapy, Advanced Ovarian Cancer, Clinical Effect.

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Introduction
Malignant ovarian tumor is one of common malignant tumors of the female genital organs. It ranks third place in female cancers only below cervical cancer and uterine body cancer (see Figure 1-2). However, mortality from ovarian cancer occupies the first place in all kinds of gynecological tumors, posing a serious threat to a woman’s life. Due to the complexity of embryonic development, tissue anatomy and endocrine function of the ovary, early symptoms of ovarian cancer are not obvious or typical. It is extremely difficult to identify the tissue type of ovarian tumor and judge whether it is benign or malignant before operation. The main symptoms of ovarian cancer appear in three forms.8-10

Figure 1: Cell morphology of ovarian cancer.

• Pain: due to tumor changes such as bleeding, necrosis, rapid growth, malignant ovarian tumor may cause a considerable degree of persistent pain. Patients may have intermittent tenderness during clinical examination.
- Irregular menstruation: ovarian cancer will lead to irregular uterine bleeding, or bleeding after menopause.
- Emaciation: patients with ovarian cancer may have progressive weight loss at a late stage. Meanwhile, the vital signs of ovarian cancer patients will also undergo certain changes, specifically.

![Figure 2: Clinical manifestations of ovarian cancer.](image)

(1) Lower abdominal mass: bilateral growth in malignant ovarian tumors accounts for 75%, while in benign ovarian tumor only 15%.
(2) Hydrops abdominis: although benign ovarian tumors such as fibroma or papillary cystadenoma can be complicated by hydrops abdominis, the situation is more common for malignant ovarian tumors. If malignant cells pierce through the envelop or transfer to peritoneum, hydrops abdominis may be bloody.
(3) Cachexia: if the disease delays for a long time, with long-term consumption, loss of appetite may cause progressive weight loss, fatigue, lassitude and cachexia syndrome.

At present, surgical treatment and chemotherapy are the most common treatments for patients with ovarian cancer. Nevertheless, for patients with advanced ovarian cancer, surgical treatment can not completely remove diffused cancer cells, but also make patients suffer from relatively great psychological pressure and pain, hence quality of life thus declines. Therefore, perfusion chemotherapy was adopted in this study to treat patients with a combination of paclitaxel and cisplatin. Specific methods follow.

**Method**

**General information**

We studied 1560 advanced ovarian cancer patients admitted to the hospital from June 2013 to June 2014. All patients were diagnosed with ovarian cancer by clinical diagnosis. Average age of the patients was $48.9 \pm 6.7$ years. According to FIGO staging criteria, 879 patients were in third stage while 681 patients were in fourth stage. All patients had significant cancer differentiation.

**Treatment method**

Intravenous infusion of 135mg/m2 paclitaxel was administered. Hyperthermic intraperitoneal perfusion of cisplatin was performed on patients from the second day, with dosage at 100mg/m2. After a week of continuous treatment, hyperthermic intraperitoneal perfusion of 60mg/m2 paclitaxel was administered. After clearing up ascites, chemotherapy drugs were dissolved in 1L of warm saline solution for hyperthermic intraperitoneal perfusion. In the course of treatment, a change of body position every 30 minutes was needed, so that chemotherapy drugs could be evenly distributed in the abdominal cavity. Meanwhile, symptomatic supportive treatment was provided. The treatment took three weeks for each course.

After 6 courses of treatment, the clinical treatment effect was compared and adverse reactions were recorded.

Paclitaxel, paclitaxel in English, also known as taxol, actinorhodin, tuftsin (Figure 3). Clinical studies have confirmed that paclitaxel is mainly used for ovarian cancer and breast cancer. Paclitaxel has a significant effect on radiosensitization, which may cause cell suspension in the G2 and M phase sensitive to radiotherapy.

![Figure 3: Structure of paclitaxel.](image)

Procedures for general clinical use of paclitaxel are:

(1) First ask patients whether they have a history of allergy, and view data of white blood cells and platelets. It should be used with caution for patients with allergic history or with low blood cell
(2) As this drug can cause allergic reactions, take 20mg dexamethasone 12 hours and 6 hours before the administration, orally take 50mg diphenhydramine and have intravenous injection of 300mg cimetidine 30 ~ 60 minutes before the administration.

(3) Commonly applied paclitaxel dose is 135 ~ 175 mg / m2. First, add injection into saline or 5% glucose solution of 500 ~ 1000ml, glass bottle or non-polyethylene infusion apparatus are used, and adopt special tube or 0.22μm microporous membrane for filtration.

(4) Blood pressure, heart rate and respiration should be measured every 15 minutes after the start of infusion. Pay attention to allergic reactions.

(5) Normally infuse 3 hours.

(6) Blood picture should be checked at least 2 times every week after injection, repeated after 3 to 4 weeks as the case may be.

Cisplatin is heavy metal complex after combination of the center as divalent platinum with two chlorine atoms and two ammonia molecules. Similar to bifunctional alkylating agent, it can inhibit DNA replication process (Figure 4). DDP cells, which inhibit RNA and protein synthesis at high concentration, are the most sensitive. Cisplatin acts on hypoxia cells and can diffuse charged cell membranes after entering the human body. At present, it is believed that DDP mainly acts on purine and pyridine bases of DNA.

In the course of clinical therapy, paclitaxel combined with cisplatin is applied in hyperthermic intraperitoneal chemotherapy of patients with advanced ovarian cancer.

The main therapeutic principles of hyperthermic intraperitoneal chemotherapy appear in nine aspects:

(1) Tumor tissue cells and normal cells have different temperature tolerance: the tolerable temperature of normal tissue cell can reach up to 45 degrees. Tumor cells will die at 43 degrees or less;

(2) Heating can destroy the steady state of cell membrane, further improving permeability of cells;

(3) Due to cell permeability changes, cell absorption and penetration of drugs increase;

(4) Heating can increase the drug concentration and reaction rate of cells;

(5) Heating can change the metabolic mechanism of drugs;

(6) Heating increases the effect of the drug on DNA, or inhibits effective repair of DNA;

(7) Hyperthermic intraperitoneal perfusion can directly increase the intraperitoneal concentration of anticancer drugs, reduce concentration of systemic circulation drug and improve local focus toxicity, so that adverse reactions can be controlled within a reasonable range;

(8) High concentration chemotherapy is absorbed into the liver through the portal vein, which is very lethal for cancer cells in the liver;

(9) High- capacity peritoneal perfusion can have mechanical flushing effects and kill peritoneal unbound cancer cells. Based on these principles, high temperature, low permeability intraperitoneal perfusion chemotherapy is adopted for clinical treatment of patients with advanced ovarian cancer.

**Observation method**

Based on imaging examination results, we assessed the clinical therapeutic effect on patients according to the World Health Organization standard assessment method: Complete remission (CR): tumor focus tissue disappears completely, and there is no new tumor focus after 4 weeks; partial remission (PR): tumor focus tissue obviously shrinks to the size before treatment, no focus tissue volume increase appears at multifocality pathological change; stable (SD): there is no obvious change in tumor focus tissue; progress (PD): tumor focus tissue expands significantly, or new tumor focus tissue appears. Treatment efficiency = (CR+PR) / total number of people*100%.
Adverse reactions were also scored during the treatment period according to the World Health Organization criteria, mainly divided into five levels of 0-5. Meanwhile, adverse reactions were determined through routine blood examination, blood biochemical index examination, and electrocardiogram examination.

**Statistical method**

The study of the clinical treatment effect of paclitaxel hyperthermic intraperitoneal chemotherapy on patients with advanced ovarian cancer utilized statistical data package software SPSS17.0 to complete data input and output. n,% is used to express count data, while x±s mean value±mean is used to express measurement data.

**Result**

After combined use of paclitaxel and cisplatin for hyperthermic intraperitoneal therapy of patients, the total effective rate of treatment improved significantly compared with the situation before treatment, with effective rate of treatment up to 85% (1326/1560).

Average progression free survival was 25.3 + 4.7 months, average median survival time was 57.5 + 6.3 months, and average one year survival rate was 90 (1404/1560).

**Discussion**

The results of this study fully confirm that combined use of cisplatin and paclitaxel in clinical treatment of advanced ovarian cancer has a good synergistic effect. This study investigated the treatment of 1560 patients with advanced ovarian cancer. The results show that the effective rate of hyperthermic intraperitoneal chemotherapy significantly increases after combined use of paclitaxel and cisplatin. In summary, combined use of paclitaxel and cisplatin for hyperthermic intraperitoneal therapy is important for improving treatment effect and the quality of life of patients and thus is recommended to be promoted in clinical application.

**References**


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