RESEARCH COMMUNICATION

Chemotherapeutic Effects of Different Paclitaxel plus Poldine Combination Methods for Treatment of Ovarian Carcinoma

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Abstract

The study aimed to evaluate the curative effects and toxicity of different paclitaxel (PTX) plus poldine chemotherapeutic combination methods for treatment of advanced ovarian carcinoma. A total of 27 patients with ovarian epithelial carcinoma were divided into four groups: A1, taxotere plus poldine intravenous chemotherapy (n=5); A2, taxotere intravenous chemotherapy combined with poldine intraperitoneal chemotherapy (n=7); B1, paclitaxel plus poldine intravenous chemotherapy (n=6); B2, paclitaxel intravenous chemotherapy combined with poldine intraperitoneal chemotherapy (n=9). Toxic side effects were observed after chemotherapy, and the short-term effects were assessed. Some 25 (25/27) cases completed a four-course treatment, the remaining two stopping halfway due to anaphylactic shock. The total effective rate for the A1 Group was 60% (3/5) and that of A2 group was 71.4% (5/7), Figuires for the B1 and B2 groups were 50%(3/6) and 66.7% (6/9), respectively. In comparisons of toxic side reactions, there were significant differences between taxotere groups and paclitaxel groups, and between intravenous chemotherapy alone groups and intravenous plus intraperitoneal combination chemotherapy groups ($p<0.05$). Chemotherapy of toxol plus poldine was effective in treatment of advanced ovarian cancer, the toxicities of intravenous plus intraperitoneal combination chemotherapy was lower than that of intravenous chemotherapy alone, and the heart toxicity with taxoere was lower than with paclitexal.

Keywords: Ovarian carcinoma - taxoere - paclitexal - combined chemotherapy

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Introduction

Paclitaxel (PTX) is a new type of anticancer drugs. By promoting the polymerization of microtubular proeins to stop their depolymerization, it can keep the stability of microtubular proteins and inhibit cell division (Lentini et al., 2010; Samuel et al., 2010; van de Steeg et al., 2011). As PTX has extensive antitumor activities without cross resistance with other anticancer drugs, it has been shown to be uniquely advantageous in treatment of ovarian carcinoma, breast carcinoma, etc (Akeson et al., 2008; Hornychova et al., 2008; Abaid et al., 2010; Chen et al., 2010). Between January 2000 and February 2006, a total of 25 patients with ovarian carcinoma was admitted to our hospital and treated with paclitexal or taxotere combination chemotherapy, intravenously or intravenously plus intraperitoneally, with the total number of treatment courses of 103. Based on the analyses of effectiveness and toxic side effects by different combined methods, a report was yielded as follows.

Materials and Methods

Patients

A total of 27 patients with ovarian carcinoma, agedfrom 35 to 69, were surgically and pathologically identified as cases with ovarian epithelial carcinoma at clinical stages II-III. Among 27 cases, serous cystadenoma was found in 12 cases, mucinous cystadenoma in nine cases, endometrial carcinoma in three, mixed ovarian epithelial carcinoma in two, and clear cell carcinoma in one; ascites was found in 20 cases, liver metastasis was found in three cases, lung metastasis in one case, and lymph node metastasis adjacent to the abdominal aorta in six. Five patients were given PTX -combined chemotherapy from the first course while others after no less than two courses of PC or PVB chemotherapeutic protocol. All the patients met the following requirements: A. Identified ovarian carcinoma by pathological diagnosis; B. Anticipated survival time of more than three months, generally; C. No apparent abnormality in cardiac, hepatic, or renal functions or blood constituents by detections. All patients provided written informed consent. The trial protocol was approved by the local ethics committee.

Treatment methods

Patients were randomly divided into four groups: A1 group, taxotere (135mg/m^2) plus poldine (400 mg/m^2) intravenous chemotherapy alone (five cases); A2, taxotere (135 mg/m^2) intravenous chemotherapy combined with poldine (400mg/m^2) intraperitoneal chemotherapy (seven cases); B1 group, paclitexal (135mg/m^2) plus

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poldine (400mg/m2) intravenous chemotherapy alone (six cases); and B2 group, paclitexal (135mg/m^2) intravenous chemotherapy combined with poldine (400mg/m^2) intraperitoneal chemotherapy (nine cases).

Electrocardiogram, blood routine and liver function examinations were carried out during the week before treatment, blood routine, and liver functions were rechecked during treatment (more times when necessary). After each treatment course (four weeks for a course), all indexes and the tumor marker CA125 were rechecked to evaluate the curative effects of different combined methods, with the total number of courses 103 (two cases in paclitexal groups had to be stopped halfway due to anaphylactic shock in courses two and three, respectively), and toxic effects were evaluated after each course of chemotherapy, and the curative effects were evaluated and compared after four courses.

Dexamethasone (10 mg) was orally administered 12 h before chemotherapy and 6h before treatment, respectively. 30 m before treatment, Benadryl 20 mg was intramuscularly injected, ondansetron 3mg was intravenously injected, and meanwhile diuretic and hematopoietic were used.

Evaluation criteria

The evaluation criteria for curative effects were based on WHO standards, and the unified criteria for the objective assessment of curative effects on tumor were: CR: ascites disappeared and the state lasted for more than four weeks, no mass was found by pelvic and Type-B ultrasonic detection, and CA125 in serum was decreased to a normal level; PR: ascites was obviously decreased by more than 50% and the state lasted for more than four weeks; SD: ascites was decreased by no more than 50% or increased by less than 25%; PD: ascites was increased by more than 25%. The total effective rate was figured out according to CR+PR, and the statistic data were tested by $\chi 2$.

Results

Short-term efficacy

Of 27 patients with ovarian carcinoma, except for 2 who were stopped halfway due to anaphylactic shock caused by paclitaxel(PTX), other 25 successfully completed 4-course treatment. In A1 group, there was one case of CR and two cases of PR, with the total effective rate of 60% (3/5); in A2 group, there was one case of CR and four cases of PR, with the total effective rate of 71.4% (5/7); in B1 group, one case of CR and two cases of PR, and the total effective rate of 50% (3/6); and in B2 group, one case of CR and four cases of PR, with the total effective rate of 55.6% (5/9).

Table 1. Comparisons of Therapeutic Effects among the Different Groups

	n	CR	PR	Effective* (%)	Total rate (%)
A1	5	1	2	60.0	
A2	7	2	4	71.4	75.0 (9/12)
B1	6	1	2	50.0	
B2	9	1	4	55.6	53.3 (8/15)

CR, complete response; PR, partial response; * p<0.05

Toxic side reactions

Toxic side reactions in four groups mainly took the forms of neutrocytopenia, alopecia, thrombocytopenia, arthralgia, gastrointestinal reaction, cardiotoxicity, allergic response, etc. After symptomatic treatment, these symptoms could subside and their degrees could be tolerable. In paclitexal groups, anaphylactic shock occurred in two cases during Course 2 and 3, respectively. After emergency treatment, anaphylactic shock was resolved. In taxotere groups, no anaphylactic shock occurred. The incidence rate of cardiotoxicity in taxotere groups was 10.4% (5/48), lower than that in paclitaxel groups; and the incidence rate of toxic side reactions (such as cardiotoxicity, allergic response, gastrointestinal reaction, etc.) in combined chemotherapy groups was lower than that in intravenous chemotherapy alone groups (p<0.05) (Tables 1 and 2).

Discussion

Nowadays, chemotherapy occupies an important place in treatment of malignant cancers. Being a general therapeutic measure, chemotherapy can effectively inhibit the growth, diffusion and metastasis of tumor cells. The emergence of drugs of PTX and the change in medical mode have also seen recent years. All these have provided an effective method for treatment of ovarian carcinoma, especially for ovarian epithelial carcinoma, which can even be successfully cured because of its hypersensitivity to chemotherapeutic drugs.

Taxotere is one type of new and highly-efficient PTX antitumor drugs. Though it has a similar mechanism to paclitaxel, both belonging to anti-microtubular drugs,

Table 1. Comparisons of Incidence Rates of Toxic Side Reactions among Different Groups Caused by Paclitaxel (PTX) plus Poldine Combination Chemotherapies

	A1	A2	B1	B2
Neutrocytopenia	16/20 (80.0%)	23/28 (82.1%)	17/21 (81.0%)	26/34 (76.5%)
Alopecia	18/20 (90.0%)	25/28 (89.3%)	18/21 (85.7%)	30/34 (88.2%)
Thrombocytopenia	6/20 (30.0%)	6/28 (21.4%)	5/21 (23.8%)	8/34 (23.5%)
Arthralgia	8/20 (40.0%)	10/28 (35.7%)	9/21 (42.9%)	14/34 (41.2%)
Gastrointestinal reaction*	17/20 (85.0%)	12/28 (42.9%)	20/21 (95.2%)	26/34 (76.5%)
Cardiotoxicity*	4/20 (20.0%)	1/28 (3.6%)	8/21 (38.1%)	3/34 (8.8%)
Allergic reaction*	0 (0%)	0 (0%)	6/21 (28.6%)	1/34 (3.0%)
Anaphylactic shock*	0 (0%)	0 (0%)	1/21 (4.8%)	1/34 (3.0%)

* p<0.05 among different groups; others p>0.05 among different groups

it has the double capability in inhibiting microtubular depolymerizationm, and its efficacy against tumors has been verified (Kovács and Csaba, 2006; Jin et al., 2007). In our study, the total effective rate of paclitaxel combined with poldine was 53.3% which was similar to those reported (Wang et al., 2000; Kumar et al., 2010), but that of taxotere groups was 75.0%, which was much higher compared to paclitaxel groups. Of 17 effective patients, 16 had presented ascites, two complicated with liver metastasis, one with lung metastasis, and four with lymph node metastasis next to the abdominal aorta, which suggested all chemotherapeutic methods conducted in this study are effective in treatment of pathological changes of peritoneum and lymph node, liver and lung metastasis. Of all the patients, only five underwent PTX -combined chemotherapy from the first course, indicating that PTX displayed no cross resistance with cyclophosphamide, adriamycin, etc., indicating that it can be used when there is resistance against cyclophosphamide, adriamycin, etc. Thus, paclitaxel plus drug combined chemotherapy can be applied as the first-line in treatment of ovarian epithelial carcinoma. Though PTX can improve the short-term survival rate of patients with ovarian epithelial carcinoma, but whether it can improve the long-term survival rate still need lots of follow-up data to testify.

The anatomic and physiological features of abdominal cavity and the bionomics of ovarian epithelial carcinoma have determined the possibility of employment of intraperitoneal chemotherapy for treatment of ovarian epithelial carcinoma. Early clinical trials of intraperitoneal chemotherapy have demonstrated the safety of chemotherapeutic drugs and intraperitoneal chemotherapy and the advantages of intraperitoneal chemotherapy in pharmacokinetics. Our study proved intravenous and intraperitoneal combination chemotherapy could reach the same clinical effective level as intravenous chemotherapy alone but with fewer toxic side effects, which can provide the basis for the selection of an effective and safe chemotherapeutic method. However, there are controversies in this respect. Some scholars had suggested that fewer cisplatins or carboplatin instead should be used in order to weaken toxic side effects caused by intraperitoneal chemotherapy. As poldine was used in our study, compared to intravenous chemotherapy, whether less poldine should be used in intraperitoneal chemotherapy still needs further researches to justify.

All PTX drugs can cause toxic side reactions. In our study, toxic side reactions in four groups mainly took the forms of neutrocytopenia, alopecia, thrombocytopenia, arthralgia and gastrointestinal reaction, with the low incidence of cardiotoxicity and allergic response. With regards allergic response, two patients suffered from anaphylactic shock within 10 minutes after intravenous injection of paclitexal in Course 2 and 3, respectively, and chemotherapy had to be stopped halfway. For others, allergic responses included slight skin itching, macular eruption, etc., and after antiallergic treatment, these reactions became tolerable without other responses being caused. Thus, in order to prevent the occurrence of such allergic responses, we think that the use of PTX in batches at the divided time is advisable to decrease drug concentration. However, further study is needed to observe whether the effect is satisfactory in so doing. Neutrocytopenia is the main form of dose-limiting toxic side reactions caused by PTX chemotherapeutic drugs. In our study, in order to prevent the occurrence of neutrocytopenia, patients in four groups were orally administrated or intramuscularly injected with hematopoietic. Though the ratio of decreased neutrophil of four groups in our study showed no difference compared to what was reported (Yacoub et al., 2010), such decrease returned to normal after symptomatic treatment without affecting the on-going chemotherapy.

The incidence of cardiotoxicity caused by PTX is low. However, once it occurred, the consequence will be serious. Our study showed the incidence rate of cardioxicity in taxotere groups was lower than that of paclitexal and that of intravenous and intraperitoneal combination groups was lower than that of intravenous chemotherapy alone groups. These indicated that taxotere is safer to heart compared to paclitexal and intravenous and intraperitoneal combination chemotherapy brings about less toxicity than intravenous chemotherapy alone. However, in order to prevent serious consequences, careful observation and active prevention should be implemented during treatment as well as follow-up period.

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