RESEARCH ARTICLE

A clinical Comparison of Lobaplatin or Cisplatin with Mitomycine and Vincristine in Treating Patients with Cervical Squamous Carcinoma

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Abstract

Background: The research was to compare the efficacy and side effects of cisplatin or lobaplatin in combination with mitomycine (MMC) and vincristine in treating patients with cervical squamous carcinoma. Materials and Methods: Cervical squamous carcinoma patients who were pathologically diagnosed with stage Ib-IIb from April 2012 to May 2013 in the general hospital of Chinese People's Libration Amy were enrolled. All patients were confirmed without prior treatment and were randomly divided into two groups, Group A and B. Efficacy and side effects were evaluated after one cycle of chemotherapy. Results: Group A (n=42) were treated with Loubo® (Lobaplatin) 50mg/m^2, MMC 16mg/m^2 and Vincristine 2mg/m^2 every 21 days. Group B (n=44) were treated with Cisplatin 100mg/m^2, MMC 16mg/m^2 and Vincristine 2mg/m^2 every 21 days. All 86 patients completed one cycle of chemotherapy with cisplatin or lobaplatin in combination with MMC and vincristine. No difference was observed regardiing short-term effect between two groups. Main side effects were bone marrow suppression and gastrointestinal reactions including decrease of white blood cells, platelet and nausea/vomiting. Grade III-VI liver and kidney impairment was not reported in two groups. In group A the incidence of uterine artery spasm in the process of drug delivery was significantly lower than the group B. Conclusions: Cisplatin or lobaplatin with MMC and Vincristine in the interventional treatment of cervical squamous carcinoma were effective, especially after uterine artery perfusion chemotherapy at tumor reduction and tumor downstaging period. The adverse reactions of concurrent chemotherapy are tolerable, and low physical and mental pressure even more less stimulation of vascular in treatment with lobaplatin. However, the long-term effects of this treatment need further observation.

Keywords: Cisplatin lobaplatin side effect arterial perfusion

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Introduction

Cervical cancer was the most common female genital tract malignancy. The proportion of Chinese women suffering from cervical cancer was 15/100000. There were 46 million cervical cancer patients in China and the cervical cancer ranked first in gynecological tumors. The mortality rate of cervical cancer was 11.34% which ranking second in female cancer (Li et al., 2011). The cure rate of early stage cervical cancer was much higher while the middle and end stage were poor effect because of that removing more extensive diseased tissue was difficult and the radiation therapy effect was poor. Therefore, for patients of advanced cervical cancer, make using of the arterial infusion chemotherapy treatment and then do surgical which can effectively improve tumor resection rate and reduce tumor recurrence and metastasis (Markman, 2013).

Chemotherapy played an integral role in the treatment of advanced cervical cancer. Cisplatin and platinum-based drugs were main treatment method in the cure of middle and late stage cervical cancer which could improve free survival, overall survival and reduce the risk of recurrence and death (Waqqoner, 2012). However, cisplatin had more serious side effects and was easy to produce drug resistance. Lobaplatin is a third-generation platinum which is a platinum complex with DNA alkylating activity with broad-spectrum, low toxicity and good efficacy. It has a considerable role with cisplatin (PPD) and carboplatin (CBP) and demonstrates no cross-resistance with PPD. Lobaplatin has been used to treat chronic myelogenous leukemia, lung cancer, esophageal cancer, gastric cancer, ovarian cancer and other common tumors in the People's Republic of China. It shows obvious advantage because of the low toxicity and no cross-resistance with PPD. In the present study we investigated the efficacy and safety of the lobaplatin for the treatment of advanced cervical cancer.

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Materials and Methods

Patient selection

86 cervical squamous carcinoma cases who were pathologically diagnosed as Ib-IIb degree in April 2012 to May 2013 in the general hospital of Chinese People's Libration Amy were enrolled. They were all initial patients and were divided randomly into two groups. Group A (the experimental group) which contained 42 patients treated with Loubo® (Lobaplatin) 50mg/m2, MMC 16mg/m^2 and Vincristine 2mg/m^2 every 21 days , and the average age were 48.2 years. Group B which contained 44 patients treated with Cisplatin 100mg/m^2, MMC 16mg/m^2 and Vincristine 2mg/m^2 every 21 days, and the average age were 45.7 years. Efficacy and side effects were evaluated after one cycle of chemotherapy. The average diameter of tumor was 2.43 cm before the treatment. Patients with measurable tumour lesions all had routine blood, liver function, kidney function and electrocardiogram (ecg). The general condition of the two group were comparable (P>0.05) (SeeTtable 1).

Methods

Loubo® (Lobaplatin) 50mg/m^2, MMC 16mg/m^2 and Vincristine 2mg/m^{2}1 for group A; Cisplatin 100mg/m^2, MMC 16mg/m2 and Vincristine 2mg/m^2 for group B were given every 21 days. The treatment repeated every 3-week. The patients underwent Interventional therapy though bilateral uterine artery. The push time was 5-10 minutes and then dealed with gelatin sponge embolism. Before chemotherapy we detected blood, heart, liver and kidney function every three weeks. After three weeks we decided to do surgery treatment or continue to the second cycle according to the condition of tumor and patients tolerance.

Table 1. Clinical Features of the 86 Cervical Cancer Patients

	Total (n=86)	Group A (n=42)	Group B (n=44)
Age (years)	47.3±3.5	48.2±2.1	45.7±2.9
Tumor size			
≤4cm	71	36	35
>4cm	15	6	9
Pathological type			
Squamous cell carcinoma	74	36	38
Adenocarcinoma	12	6	6
KPS score			
90~100	14	6	8
70~80	57	29	28
60	15	8	7
Differentiation degree			
High differentiation	19	9	10
Mid differentiation	47	25	22
Low differentiation	20	9	11
FIGO stage			
Ib1	71	36	35
Ib2	8	3	5
IIa	4	2	2
IIb	3	1	2

Table 2. Comparison of the Short-Term Effects between the two Groups

Group	n	CR	PR	SD	PD	CR+PR(%)
A	42	2	31	9	0	78.57
B	44	1	33	8	2	77.27

Criteria for evaluation of therapeutic effect

Routine blood tests for liver and kidney function were re-examined after the procedure. Reexamination of CT was performed after three weeks. The treatment responses were divided into four categories according to the Response Evaluation Criteria in Solid Tumors (RECIST): complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD), defined as follows. CR: all target lesions disappear and the diameters of all the pathological lymphnodes (including targeted nodes (with a short diameter≥15 mm by CT measurement) and non-targeted nodes) are reduced to less than 10 mm; PR: the sum of all diameters of all target lesions is reduced by 30% from the baseline level; and SD: the degree of reduction does not reach the level of PR and the degree of increase does not reach the level of PD. For PD, there must be at least a 20% increase in the sum of the shortest diameters of all the measured targeted lesions during the whole experimental study (if the value of baseline measurement is the smallest, the baseline value is used as reference). The increase of absolute value of the sum of the diameters should be >5 mm. Furthermore, the appearance of one or more new lesions is also considered as PD. The total response rate equals CR plus PR.

Statistical analysis

Significance was assessed using Chi-square test with SPASS software. Differences were considered significant at a P value of less than 0.05.

Results

Clinical activity

All 82 patients completed at least one cycles of chemotherapy, and were evaluated according to study protocol. Over all 31 patients achieved PR and 2 CR in group A. The total effective rate was 78.6%. 33 patients achieved PR and 1 CR in group B. The total effective rate was 77.3% (Table 2). Toxicity

Group A and B all had blood toxicity such as leukopenia and thrombocytopenia. Although there was no significant difference between the two groups (P>0.05), but in the gastrointestinal toxicity mainly as a vicious, vomiting and diarrhea the group A was significantly lighter than the group B (Table 1). More than grade III liver and kidney dysfunction was not happened in two groups. We

Table 3. Gastrointestinal Toxicity: Number of Courses Associated with who Toxicity Grade

Drug	WHO toxicity							
	I	II	III	VI	I	II	III	VI
	Nausea and vomiting				Diarrhea			
Lobaplatin								
	2	23	11	5	4	28	7	3
Cisplatin								
	3	10	19	12	6	18	15	3

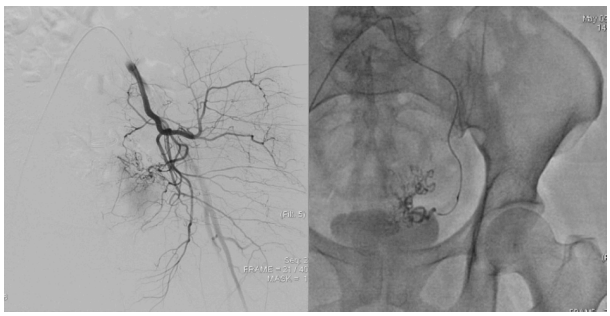

Figure 1. The Artery Situation of the Lobaplatin and Cisplatin. A Uterine artery developing well after applying lobaplatin, B Uterine artery shrink and spasm after applying cisplatin

also found that the arterial spasm of experimental group was significantly lower than the control group ($P<0.05$) (Table 3). (Figure 1) It is beneficial to inject.

Discussion

Large amounts of data showed that in the treatment of cervical cancer, cisplatin-based chemotherapy had a higher efficiency (Ali et al., 2013). The recommended treatment is BOMP. The BOMP treatment can reduce symptoms, improve quality of life and prolong survival. Chemotherapy combined with surgery and radiotherapy played a very important role in the treatment of cervical cancer (Leath CA 3rd et al., 2013).

However, treatment with cisplatin brings tremendous pressure to patients because of its serious side effects such as nephrotoxicity, gastrointestinal toxicity, ototoxicity and neurotoxicity (Waissbluth et al., 2013; Tsang et al., 2009), and even because of it is easy to produce drug resistance.

Lobaplatin is the third generation platinum anti-tumor compounds, with broad-spectrum, low toxicity and good efficacy (McKeage, 2001; Liu et al., 2006). This study shows that in the treatment of advanced cervical cancer, lobaplatin have a good short-term clinical efficacy as cisplatin, especially they combined with mitomycin and vincristine. In the treatment of arterial infusion chemotherapy advanced cytoreductive surgery for cervical cancer before descending on to play a good effect. Cisplatin or lobaplatin with MMC and Vincristine in the interventional treatment of cervical squamous carcinoma were effective especially after uterine artery perfusion chemotherapy at tumor reduction and tumor downstaging period. The patients had low adverse drug reaction, low physical and mental pressure even more less stimulation of vascular in treatment with lobaplatin, so the lobaplatin was better in this treatment.

GFR is a sensitive indicator of the reaction of glomerular filtration function, GFR in patients treated with chemotherapy in the early stage of chemotherapy appeared obvious changes, but this time with BUN and SCR in the index has not significantly change that GFR in judging early renal damage in more reliable (Wen Z et al., 2008). In order to detect renal damage earlier, the renal toxicity of two chemotherapy was evaluated by renal dynamic detection of glomerular filtration rate, and the renal toxicity of the experimental group was significantly lighter than that of the control group. This is because cisplatin Containing Heavy Metals Platinum, after entering the body through the kidney excretion, and therefore its renal toxicity is obvious (Yan et al., 2003). The combination rate of the protein was low, and it did not need a lot of transfusion and forced diuretic can be excreted from the kidney, so the renal toxicity is small.

This study is the first to explore the efficacy of lobaplatin with mitomycin and vincristine through the intra-arterial chemotherapy treatment, and compare the effectiveness and toxicity of cisplatin and lobaplatin with MMC, Vincristine in advanced cervical arterial infusion chemotherapy. Its long-term effects need to be further tracked and analyzed.

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