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Original Article

Effect of docetaxel combined with cisplatin chemotherapy with concurrent radiotherapy on short-term prognosis of patients with advanced cervical cancer

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Abstract: Objective: Our aim was to investigate the efficacy of docetaxel combined cisplatin chemotherapy with concurrent radiotherapy in treatment of advanced cervical cancer. Methods: Seventy-four patients with advanced cervical cancer, admitted to Linyi Cancer Hospital from January 2013 to December 2016, were selected and divided into an observation group (37 cases) and a control group (37 cases), according to a random number table. Both groups were treated with conventional radiotherapy and cisplatin chemotherapy. The observation group was given docetaxel combined with chemotherapy on the basis of the control group. Efficacy and adverse reactions of the first month after completion of treatment were compared between the two groups and one-year follow up survival rates and quality of life scores were compared. Results: The total effective rate in the observation group after treatment was higher than the control group ($P = 0.032$). Adverse reaction rates were basically the same in the two groups ($P>0.05$). At the same time, one-year follow up survival rates and quality of life scores of the observation group were higher than those of the control group (both $P<0.05$). Conclusion: Docetaxel combined cisplatin chemotherapy with concurrent radiotherapy in treatment of advanced cervical cancer had a higher one-year survival rate and quality of life score compared with cisplatin chemotherapy alone with concurrent radiotherapy. Since adverse reaction rates were not increased this treatment is worth promoting.

Keywords: Cervical cancer, docetaxel, cisplatin, recent prognosis

Introduction

Cervical cancer is one of the most common gynecological cancers and its development tends to begin at a younger age. Cervical cancer is the second most common cancer following breast cancer in females worldwide. However, in developing countries, cervical cancer has surpassed breast cancer as the number one female cancer due to lack of effective screening methods, insufficient preventive measures for health, and lack of attention to female health [1, 2]. Cervical cancer seriously affects patient quality of life and physical and mental health [3-5]. Although China has already carried out screening of two cancers, the special location of the cervix makes cervical cancer occult. Most cervical cancers have developed into advanced stage while clinically confirmed [6]. Treatment schemes for those patients are mostly radiotherapy but recurrence of the tumor will seriously affect prognosis of patients [7]. In order to increase therapeutic effect of radiotherapy, the comprehensive treatment of radiotherapy and chemotherapy are implemented clinically and the combined effect of radiotherapy and chemotherapy is superior to radiotherapy or chemotherapy alone [8-10].

Some researchers have found that small doses of chemotherapy drugs used during radiotherapy in cancer patients can increase sensitivity of radiotherapy, enhancing the radiotherapy effect [11]. The mechanism of action of chemotherapeutic drugs is different. Cisplatin is commonly

Table 1. General data of two groups of patients

Group	The observation group	The control group	t/X^2	P
Case	37	37		
Age	55.3 ± 7.1	56.1 ± 7.9	0.648	0.458
Pathology			0.506	0.477
Squamous cell carcinoma	34	31		
Non-squamous cell carcinomas	3	6		
Differentiated degree			0.260	0.878
High	12	11		
Middle	10	12		
Low	15	14		
Clinical stages			0.553	0.758
II	25	20		
III	7	10		
IV	5	7		

Table 2. The efficacy rating of two groups of patients after one year of chemotherapy (n, %)

Group	Case	Valid		Invalid*		Effective rate
		CR	PR	SD	PD	
The observation group	37	20	7	7	3	27/37 (73.0%)
The control group	37	14	4	6	6	18/37 (48.6%)
X^2		0.005				4.593
P		0.944		0.415		0.032

Note: CR, complete remission; PR, partial remission; SD, stable disease; PD, progressive disease. *Fisher exact probability method.

used in clinical practice to decompose cell DNA and disrupt cell proliferation. Therefore, cisplatin based radiotherapy and chemotherapy regimens have become the standard of treatment for all types of cancer. Docetaxel prevents mitosis of tumor cells as well as destroys proliferation of tumor cells [12, 13]. However, chemotherapy is harmful to the human body and causes some adverse reactions (bone marrow suppression and digestive track reaction) [14]. Therefore, this research compared the short-term efficacy of cisplatin and cisplatin combined docetaxel chemotherapy with concurrent radiotherapy in treatment of advanced cervical cancer. Incidence of adverse reactions was observed as well.

Materials and methods

General information

This was a prospective study. Patients with cervical cancer, confirmed by pathology in gynecologic treatment in Linyi Cancer Hospital from January 2013 to December 2016, were selected. All patients signed informed consent and this research was approved by the Ethics Committee of Linyi Cancer Hospital.

Inclusion criteria: All patients were in an advanced stage of cervical cancer (clinical stage II and above). The expected survival period was more than 3 months, they were all aged below 70 years old, but without preoperative chemotherapy treatment. All patients gave informed consent.

Exclusion criteria: Patients combined with other major organ dysfunctions in heart, brain, kidney, etc., were combined with other tissue tumors. Patients with past history of digestive tract diseases and hematological system diseases were also excluded, along with those patients who disagreed with chemotherapy treatment, were allergic to chemotherapeutic drugs, or had primary myelosuppression, or were pregnant and lactating females.

Qualified patients of 74 cases were included and divided into 37 cases each in the observation group and the control group, according to the random number table method.

Methods

The two groups were treated with conventional radiotherapy with 15MV-X ray external pelvic SAD technology of DT50Gy/25F/5W and DT30Gy/15F/3W, followed by intracavitary brachytherapy at A point (location of 2 cm above the cervix and 2 cm beside the uterine axis) DT30Gy/6F/3W. In the observation group, docetaxel (40 mg/m^2) and cisplatin (40 mg/m^2) were given intravenously once a week for a course of six weeks. In the control group, only cisplatin (40 mg/m^2) was given intravenously

Table 3. The incidence of adverse reactions in both groups during chemotherapy (n, %)

Group	The observation group	The control group	X^2	P
Number of cases	37	37		
Bone marrow suppression contrast				
Mild			0.927	0.629
0	15	13		
I	5	3		
II	4	2		
Severe			0.026	0.873
III	8	11		
IV	5	8		
Mild proportion	24/37 (64.8%)	18/37 (48.6%)	1.376	0.241
Side effect of digestive tract				
Mild			0.568	0.753
0	13	9		
I	9	8		
II	4	5		
Severe			0.010	0.921
III	8	10		
IV	3	5		
Mild proportion	26/37 (70.3%)	22/37 (59.5%)	0.534	0.465

once a week for a course of six weeks. Both groups received four courses of treatment. During the treatment period, both groups were given the same adjuvant chemotherapy as follows: hormone; proton pump inhibitors (cimetidine) to protect the gastric mucosa; necessary antiemetic measures and hydration to protect renal function.

Follow-up

Three contact phone numbers of patients and their families were recorded before patient discharge to prevent the loss of contact. Patients were followed up once a month after treatment and their one-year survival rates were recorded. Patient survival conditions and quality of life scores were evaluated after one year.

Observation index

Treatment efficacy: One month after completion of the above course of treatment, solid tumor efficacy evaluation system was used to evaluate treatment efficacy [15]. Details are as follows.

Complete remission (CR): Tumor disappears and imaging shows no new lesions. Partial remission (PR): Tumor volume decreases by more than 50% and no new lesions occurs for more than 4 weeks. Stable disease: Tumor volume decreases by less than 50% or increased less than 25% and no new lesions appear for more than 4 weeks. Progressive Disease: Tumor volume increases by 25% or a new lesion appears. PR + CR expresses as effective. Total effective rate = (CR cases + PR cases)/total number of cases * 100%.

Evaluation of side effects: Bone marrow suppression and digestive track reactions were observed one month after the start of treatment in both groups and were assessed according to the grading standards of chemotherapeutic toxicities and side effects. The results were graded as 0, I, II, III and IV.

Quality of life and survival rate: SF-36 scale was used to evaluate patient quality of life of one year after treatment (0-100 scores, the higher the score the better quality of life) and one-year survival rates of two groups were observed [16].

Statistical methods

Data were analyzed by SPSS 20.0 statistical software. Measurement data are expressed by mean ± standard deviation ($\bar{x}$ ± sd) and t-test of two independent samples was used to compare between the groups. Counting data was presented as the number of occurrences (percentage) and Chi-square test (X^2) or Fisher's exact probability method was used for comparison between groups. Kaplan-Meier survival analysis was adopted for survival rate analysis. $P<0.05$ was considered statistically significant.

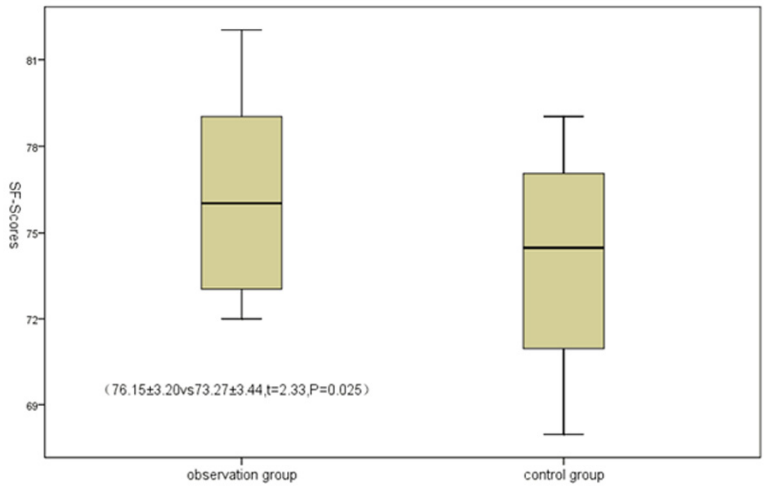

Figure 1. SF scores in two groups of patients 1 year after treatment.

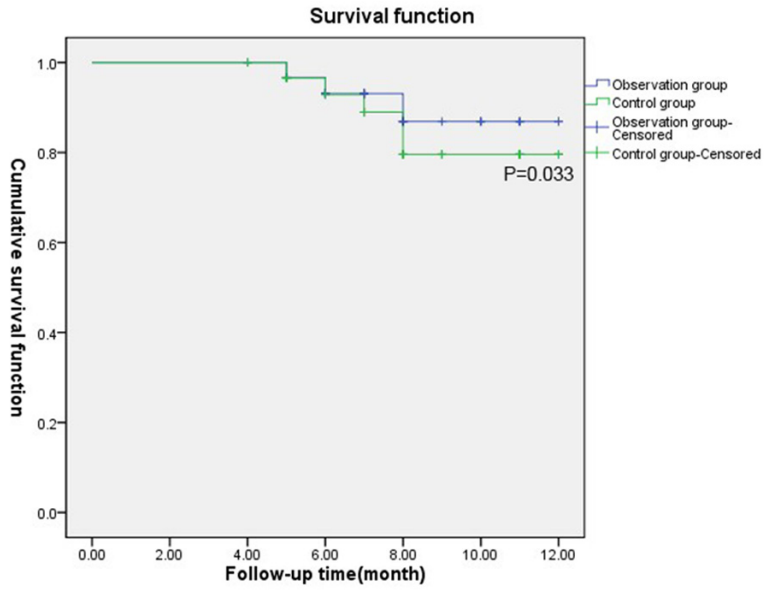

Figure 2. Kaplan-Meier table of two groups of patients.

Results

Comparison of basic data of two groups of patients

There were no statistical differences in age, pathological type, degree of tumor differentiation, and clinical stage between two groups (all P>0.05), indicating that the two groups were comparable. See **Table 1**.

Comparison of effective rate of tumor treatment between the two groups

The effective rate of tumor treatment in the observation group had a higher tendency than the control group (73.0% vs. 48.6%, P = 0.032). See **Table 2**.

Comparison of incidence of adverse reactions during chemotherapy between the two groups

Bone marrow suppression rate and incidence of digestive track adverse reactions in the observation group were lower than those in the control group (64.8% vs. 48.6%, 70.3% vs. 59.5%) but the difference was not statistically significant (all P>0.05). See **Table 3**.

Comparison of quality of life between the two groups

Healthy quality of life scores of patients in the observation group one year after treatment were significantly higher than in the control group (P = 0.025), suggesting that patients in the observation group had higher quality of life than the control group. See **Figure 1**.

Comparison of survival rate between the two groups

One-year specific survival rate of two groups of patients are shown in **Figure 2**. The survival rate of the observation group after one year had a higher tendency (P = 0.033). See **Table 4**.

Discussion

At present, radiotherapy is the first choice for treatment of middle and advanced stage cervical cancer due to missing the opportunity of surgical treatment. However, for patients with large tumors or advanced cervical cancer, it is generally recommended to take concurrent radiotherapy and chemotherapy to improve therapeutic effect and reduce metastasis and recurrence rate [17-20]. Chemotherapy mainly destructs genetic material of tumor cells and inhibits proliferation of tumor cells so as to

Table 4. Clinical efficacy in both groups after one year (n, %)

Group	Case	Death count	Survival rate
The observation group	37	3	34/37 (91.9%)
The control group	37	10	27/37 (73.0%)
X^2			4.573
P value			0.033

achieve the purpose of treatment. Radiotherapy, by exerting effect in killing and inhibiting cancer cells, ultimately prevents occurrence and development of tumors. However, the efficiency of chemotherapy and radiotherapy on tumor treatment has often benefited from the sensibilization effect of some chemotherapeutic drugs.

Cisplatin is currently the most widely used radiosensitizer drug. Its main mechanism is to collaborate with radiotherapy for destruction of the DNA production of tumor cells. In addition, cisplatin also inhibits recovery of damaged cancer cells during radiotherapy, to a certain extent. At the same time, cisplatin could effectively control the further transfer of existing micro-metastases in the body so as to improve the clinical curative effect of cervical cancer [21]. The mechanism of docetaxel in chemotherapy is mainly through interference of tumor cell mitosis to prevent tumor growth. The specific mechanism is through the combination of tubulin β subunit and forming microtubules that are not easily disaggregated and deactivate the microtubules, thus preventing tumor cells from further mitosis and remaining in G2/M phase. Cells at this time are the most sensitive to radiation, so as to achieve the radiosensitization effect and ultimately maximize the killing function of radiotherapy on cancer cells.

The current evaluation of tumor treatment effects mainly includes clinical efficacy, patient survival, quality of life score, and survival rate of adverse reactions. The latest meta-analysis of cervical cancer concurrent chemotherapy program (total 12 types) showed that patients treated with cisplatin combined with docetaxel had the highest chemosensitivity and lowest incidence of adverse reactions. This is recommended as the best treatment for patients with cervical cancer. Our research results also showed that tumor remission rate of patients in the observation group treated with cisplatin combined with docetaxel had an increased trend compared with group of patients treated with cisplatin alone. This was consistent with previous studies [10, 22].

Bone marrow suppression, nausea, vomiting, and other digestive track adverse reactions are the main side effects of chemoradiotherapy, affecting patient quality of life. Studies have shown that 90% of patients treated with chemoradiotherapy had gastrointestinal function changes and the life impact rate is close to 50%. Bone marrow suppression is also a major adverse reaction of chemoradiotherapy [14, 23]. This research showed that incidence of adverse reactions of two groups of patients was basically the same, indicating that the addition of docetaxel did not aggravate adverse reactions of chemoradiotherapy in patients with cancer. It suggests that docetaxel could increase the effect of chemotherapy without increasing side effects. This is consistent with the literature [10].

Short-term survival rate and quality of life are important indicators in evaluating clinical efficacy [24]. Cisplatin combined with docetaxel is the best treatment for cervical cancer [10]. Our study shows that the addition of docetaxel improves quality of life in patients compared with use of cisplatin alone and survival rates tend to increase within one year.

Limitations to our study include a short follow up period and the relatively small sample size. Cooperation with more centers to increase sample size is necessary to verify our results in future research.

In conclusion, compared with cisplatin alone with radiotherapy, docetaxel combined with cisplatin adjuvant radiotherapy enhances clinical efficacy of patients without increasing toxic side effects of drugs. It improves patient quality of life and increases one-year survival rate. Therefore, its clinical practice is recommended.

Disclosure of conflict of interest

None.

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