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Original Research Article

Clinical efficacy of combination of oxaliplatin and vascular intervention in treatment of advanced cervical cancer and related prognostic factors

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Abstract

Purpose: *To investigate the therapeutic effect of combination of oxaliplatin and vascular intervention in patients with advanced cervical cancer (ACC), and its influence on the prognosis of patients.*
Methods: *One hundred ACC patients were selected and equally assigned to control (oxaliplatin) and combination or study (oxaliplatin plus vascular intervention) groups. The patients in control group received oxaliplatin, while those in study group were treated with oxaliplatin combined with vascular intervention. Clinical efficacy, levels of vascular endothelial growth factor (VEGF), vascular endothelial growth factor receptor-2 (VEGFR-2), fibroblast growth factor-2 (FGF-2), BFGF and platelet-derived growth factor (PDGF) before and after therapy, and survival rate at 3, 6, 12 and 18 months after therapy were determined compared between the two groups. The prognostic factors were analyzed with logistic factor analysis.*
Results: *The clinical efficacy and survival rate at 3, 6, 12 and 18 months after therapy in the combination group were higher when compared with those of the control group ($p < 0.05$). After therapy, the levels of VEGF, VEGFR-2, FGF-2, BFGF and PDGF were lower in the combination group than in control group. Age, short-term efficacy and basic diseases were identified as the influencing factors for the prognosis of patients with advanced cervical cancer ($p < 0.05$).*
Conclusion: *The combination of oxaliplatin and vascular intervention significantly improved clinical treatment efficacy and survival rate in ACC patients. Age, short-term efficacy and basic diseases affected the prognosis of patients.*

Keywords: *Oxaliplatin, Vascular intervention, Advanced cervical cancer, Prognosis*

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INTRODUCTION

Cervical cancer, a common gynecological tumor, along with breast cancer and ovarian cancer, are considered as the top three most lethal malignant tumors of the female reproductive system, with cervical cancer resulting in the highest mortality and morbidity [1-3]. Due to absence of obvious early symptoms, and the fact that only few women carry out regular gynecological

examinations, some patients with cervical cancer do not feel obvious discomfort until they are in the middle and late stages, thereby missing the optimal opportunity for treatment [4-6]. Chemotherapy is one of the main methods for preventing the development of cervical cancer. It is administered mainly *via* intravenous infusion, but it exerts strong irritating effect on patients' blood vessels.

Vascular intervention refers to targeted drug delivery through arterial infusion chemotherapy. This intervention delivers the drug to the targeted tumor tissues, and reduces the binding of drugs to plasma proteins so as to maximize the effect of drugs, kill tumor cells, shrink tumor tissues and lower tumor staging [7-9]. Oxaliplatin is a third-generation platinum anticancer drug. It is generally used in chemotherapy for patients with malignant tumors. Oxaliplatin binds to DNA and inhibits the transcription and replication of tumor cell DNA. In this study, the clinical effect of combination of oxaliplatin and vascular intervention on subjects with advanced cervical carcinoma was investigated in 100 patients chosen as the research subjects. The clinical treatment efficacy and survival of patients after the combination therapy were determined.

METHODS

General patient profile

One hundred advanced cervical cancer (ACC) patients admitted to *The First People's Hospital of Wenling* (May 2018 - November 2019) were retrospectively analyzed, and they were equally and randomly divided into control group and combination group. The age ranges of patients in the control group and combination groups were 46 - 69 and 45 – 67 years, respectively. There were no statistically significant variations in baseline data, e.g., age and courses of disease between both groups (Table 1).

Inclusion and exclusion criteria

Inclusion criteria

Patients with clinical manifestations of ACC, those who were at least 18 years of age, patients with normal liver and kidney functions, and patients without other organic diseases or allergic history, were included in this study.

This research received approval from the ethics committee of *The First People's Hospital of Wenling* (approval no. 20180340), and followed international guidelines for human studies. All patients took part in the research without coercion, and this was documented in a signed attestation.

Exclusion criteria

Those who were in coma, patients with other organic diseases, and patients with early and middle cervical cancer.

Drug administration

The control group received oxaliplatin (Manufacturer: Zhejiang Hisun Pharmaceutical Company Limited) *via* intravenous infusion at the concentration of 130 mg/m^2. The infusion time was not too fast, and the infusion was completed within 3 h [10-12]. During the infusion, patients were examined using dynamic electrocardiogram so as to regularly monitor their blood pressure, oxygen saturation and heartbeat.

Table 1: General profile of the patients

Parameter		Combination	Control	χ^2/t	*P*-value
Age (years)		54.07±6.80	55.01±6.39	0.71	0.48
Height (cm)		167.72±9.42	168.24±9.76	0.27	0.79
Weight (kg)		70.45±4.30	70.38±4.64	0.08	0.94
Courses of disease (months)		5.68±1.69	5.72±1.73	0.12	0.91
Smoking history (cases)		22	20	0.16	0.69
Drinking history (cases)		30	34	0.69	0.41
Hypertension (cases)		12	10	0.23	0.63
Diabetes mellitus (cases)		8	7	0.08	0.78
Hyperlipidemia (cases)		4	6	0.44	0.51
Education levels	*Primary school education and below (cases)*	5	4	0.12	0.73
	Junior middle school education (cases)	29	32	0.38	0.54
	High school education and above (cases)	16	14	0.19	0.67

If any of the patients had abnormalities during infusion, the infusion was stopped immediately. The combination group received combination of oxaliplatin and vascular intervention. The patients had percutaneous puncture of the right femoral artery. The catheter was inserted into the femoral artery through the puncture point, right to the opening of uterine artery along the femoral artery. After the catheter position was determined, oxaliplatin was injected into the catheter at the concentration of 130 mg/m^2. The puncture was done under local anaesthesia, and the chemotherapy was performed once every 3 weeks, and 6 times in all.

Indexes measured

The clinical efficacy, concentrations of VEGF, VEGFR-2, FGF-2, BFGF and platelet-derived growth factor (PDGF) [13-15] before and after therapy, and percentage survival at 3, 6, 12 and 18 months after therapy were compared between the two groups. The prognostic factors were identified using logistic factor analysis.

The evaluation criteria for clinical efficacy included complete remission (CR), partial remission (PR), progressive disease (PD) and stable disease (SD). Complete remission referred to complete absence of target lesions. Partial remission referred to lesion width reduction ≥ 30 %, PD referred to lesion width increase ≥ 20 %, or the emergence of fresh lesions, while SD meant that the range of changes in lesion sizes was between PR and PD.

ORR = CR + PR .....(1)

DCR = CR + PR + SD .....(2)

where *ORR* = objective remission rate; *DCR* = disease control rate; *CR* = complete remission; *PR* = progressive disease, and *SD* = stable disease

Statistics

The SPSS 20.0 was applied for analysis of research results, while graphics was done with GraphPad Prism 7. Measured data are presented as mean ± SD, and were analyzed with t-test, while results involving enumerations are expressed as n (%), and were compared using χ^2 test and expressed as [n (%)]. Values of$p$ < 0.05 indicated that the differences had statistical significance.

RESULTS

Comparison of clinical treatment efficacy

Table 2 shows that values of DCR and ORR were markedly higher in combination group than in control patients.

Table 2: Values of DCR and ORR in both groups

Group	*CR*	*PR*	*SD*	*PD*	*DCR (%)*	*ORR (%)*
Study	*13*	*25*	*7*	*5*	*90*	*76*
Control	*7*	*18*	*10*	*15*	*70*	*50*
χ^2					*6.25*	*7.25*
P-value					*0.01*	*0.007*

Levels of VEGF, VEGFR-2, FGF-2, BFGF and PDGF before and after therapy

Table 3 shows that after therapy, the levels of these indicators in the combination group were markedly lower, when compared with the control. Before therapy, the levels of these indicators in the two groups were comparable.

Table 3: Levels of VEGF, VEGFR-2, FGF-2, BFGF and PDGF prior to, and post-therapy (mean ± SD, pg/mL)

Parameter	Combination group	Control group	*t*	*P*-value
VEGF				
Before therapy	395.62±61.35	396.88±61.20	0.10	0.92
After therapy	127.80±25.44	233.57±32.00	18.30	<0.001
VEGFR-2				
Before therapy	374.10±52.88	374.71±53.06	0.06	0.95
After therapy	159.82±24.69	247.89±35.71	14.34	<0.001
FGF-2				
Before therapy	22.50±5.62	22.73±5.84	0.20	0.84
After therapy	8.85±0.39	12.88±2.40	11.72	<0.001
BFGF				
Before therapy	17.02±3.67	17.31±3.58	0.15	0.88
After therapy	5.59±1.60	11.07±2.54	12.91	<0.001
PDGF				
Before therapy	621.00±100.24	623.08±99.43	0.10	0.92
After therapy	322.58±27.81	396.15±30.37	12.63	<0.001

Table 4: Analysis of factors affecting prognosis

Parameter	Estimated value	Wald	*P*-value	OR value	95 % confidence interval of OR value
Age	0.376	10.456	<0.001	1.275	1.045, 1.787
Short-term efficacy	0.061	20.524	<0.001	1.062	1.028, 1.075
Basic diseases	0.158	14.572	<0.001	1.104	1.049, 1.768

Comparison of the percentage survival at 3, 6, 12 and 18 months after therapy

The percentage survival values in the combination group at 3, 6, 12 and 18 months after therapy were significantly higher than the corresponding values for the control group (p < 0.05; Figure 1).

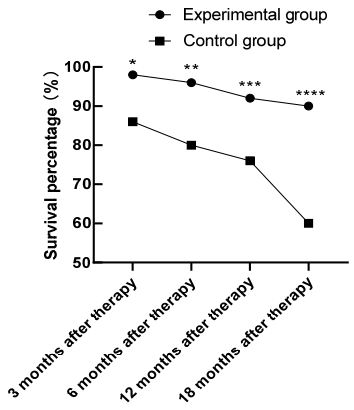

Figure 1: Comparison of survival rates at 3, 6, 12 and 18 months after therapy. *P < 0.05, percentage survival in the experimental group at 3 months post-therapy *vs*. the percentage survival in the control group at 3 months after therapy; **p < 0.05, survival percentage in the experimental group at 6 months after therapy vs % survival in controls at 6 months after therapy; ***p < 0.05, percentage survival in combination group at 12 months post-therapy vs % survival in controls at 12 months after therapy; ****p < 0.05, percentage survival in combination group at 18 months post-therapy vs % survival in controls at 18 months after therapy

Analysis of factors affecting prognosis

Logistic factor analysis showed that age, short-term efficacy and basic diseases were factors that influenced prognosis of ACC subjects' post-therapy (p < 0.05; Table 4).

DISCUSSION

Cervical cancer, the leading malignant tumor that affects women's health, has very high morbidity and mortality, with annual death toll in tens of thousands. Since the early symptoms of cervical cancer are not usually obvious, they are easily missed or ignored. Therefore, many patients with cervical cancer are already in middle and late stages when they are diagnosed, thereby missing the optimal opportunity for treatment. At this time, such patients are unlikely to be cured by radical surgery. Symptoms such as recurrence occur easily because part of the tumor may be left out during resection due to the large tumor size [16-18]. Chemotherapy is a common therapy for patients with advanced cervical cancer. Oxaliplatin is a drug regularly used for chemotherapy, and it exerts anticancer and antitumor effects. However, the drugs used in chemotherapy for cervical cancer patients have strong irritative effects which may cause adverse reactions such as nausea, vomiting and hair loss. In severe cases, other complications may occur in patients.

Vascular intervention refers to targeted chemotherapy drugs that directly act on tumor tissues. Through arterial puncture, the irritation of drugs on patients' blood vessels can be reduced, and the reduction of drug efficacy caused by the unwanted combination of drugs and plasma can be avoided [19-21]. This study investigated the curative effect and prognosis of combination of oxaliplatin and vascular intervention in subjects with advanced cervical cancer. The results showed that the clinical efficacy, levels of BFGF, PDGF, VEGF, VEGFR-2 and FGF-2 after therapy, and percentage survival at 3, 6, 12 and 18 months after therapy in the combination group were better than those in the control group. Logistic factor analysis showed that age, short-term efficacy and basic diseases were factors that influenced prognosis of advanced cervical cancer patients after therapy. Both VEGF and VEGFR-2 indicate the levels of vascular growth, development and regeneration. Higher levels of VEGF and VEGFR-2 indicate faster growth of tumor cells. Therefore, the growth of tumor cells can be evaluated by measuring the expression levels of VEGF and VEGFR-2 [22-24]. It has been reported that FGF-2, BFGF and PDGF are associated with the pathogenesis of cervical cancer. The study showed that the levels of BFGF, PDGF, VEGF, VEGFR-2 and FGF-2 in the combination group post-therapy were lower than the control values, indicating that the combination therapy effectively and significantly suppressed tumor growth and development, and improved prognosis.

Cervical cancer occurs mostly in middle-aged and elderly women older than 45 years old. This study has confirmed that the older the patient, the worse the prognosis of cervical cancer. In addition, the prognosis of patients with poor short-term efficacy and basic diseases is worse than that of patients in general. It has been reported that combination of oxaliplatin and arterial intervention significantly improved clinical efficacy and prognosis, and promoted recovery of ACC subjects [25]. This is similar to the results of the study, which proves the reliability of our study results.

CONCLUSION

The combination of oxaliplatin and vascular intervention significantly improves the clinical efficacy and survival of patients with advanced cervical cancer. In addition, age, short-term efficacy and basic diseases affect the prognosis of patients.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Xinlong Huang and Xinqin Zhang conceived and designed the study, and drafted the manuscript. Xinlong Huang, Haiyan Yan, Zhenqing Su, Junsong Wang and Jianxun Zhang collected, analyzed and interpreted the experimental data. Haiyan Yan and Xinqin Zhang revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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