Concurrent Chemoradiotherapy for Locally Advance Cervical Cancer

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Abstract **Purpose** To observe the effect and side effects of concurrent chemoradiotherapy for advanced cervical cancer. **Methods** 87 patients with advanced cervical cancer were randomly allocated into 2 group as radiotherapy group and concurrent chemoradiotherapy group. The radiotherapy group received routine radiotherapy. When total dose reach 46Gy, the middle field is shielded by plumbum, continuous radiotherapy, total dose reach 70Gy in point A, 56Gy in point B. Patients in concurrent chemoradiotherapy group were treated with the same radiotherapy method and use chemotherapy at the same time. **Results** All patients were followed-up for more than five years. The follow-up rate was 93.0%. In concurrent chemoradiotherapy group, 3-year survival rate and 5-year survival rate were 86.4% and 65.9%. In radiotherapy group, the 3-year survival rate and the 5-year survival rate were 55.8% and 39.5%. There is significant difference in two groups ($P<0.05$, $\chi^2=4.144$; 5.09). **Conclusion** Concurrent chemoradiotherapy for advanced cervical cancer can significantly improve the 3-year and 5-year survival rate and concurrent chemoradiotherapy is safe and reasonable.

Key Words Advanced cervical cancer; Concurrent chemoradiotherapy; Radiotherapy

Cervical cancer is one of the most popular gynecological tumors. The incidence of cervical cancer is about 371×10^3 patients per year in the world and about 190×10^3 patients die pre year.[1] Therapy on cervical cancer in earlier period is mainly relying on radical surgery and mainly relying on radiotherapy in advanced stage. However, effect of simple conventional radiotheraphy is poor and five-year survival rate of patients is barely 40%~50%.[2,3] Our department treated 87 cases of cervical cancer patients in Ⅱb to Ⅳa stages from December 1997 to June 1999. Now we summary the results of our therapy on advanced cervical cancer by concurrent chemoradiotherapy.

MATERIALS AND METHODS

Clinical data

All 87 patients are final diagnosis by pathological diagnosis and KPS score more than 70 points. There are 79 cases of squamous carcinoma, 3 cases of adencarcinoma and 5 cases of adenosquamous. The ages of patients are 25 to 71 years old with 51.5 as median age. The cancers are Ⅱb to Ⅳa stages according to FIGO staging standard. Divide 87 patients into two groups randomly with 44 cases in combination group (5 cases in Ⅱb stage, 33 cases in Ⅲ stage, 6 cases in Ⅳa stage) and 43 cases in radiotherapy group (6 cases in Ⅱb period, 31 cases in Ⅲ stage, 6 cases in Ⅳa stagd). Combination group was treated by concurrent chemoradiotherapy.

Therapeutic method

All 43 patients in radiotherapy group were treated by intracavitary therapy and external irradiation with ^{60}Co teletherapy machine. Irradiated field include the whole uterus, the paracervical, parametrial and uterosacral regions as well as the external iliac, hypogastric, and obturator lymph nodes. The radiotherapy group received routine radiotherapy 2Gy per day, 5 times a week to total dose of 30Gy with ^{192}Ir brachytherapy, 8Gy per week. When total dose reach 46Gy, shielded middle of the filed by plumbum, and continuous radiotherapy, total dose reach 70Gy in point-A and 56Gy in point-B.

Patients in combination group were treated with the same radiotherapy method. But in the process of radiotherapy, 20mg DDP and 750mg 5-FU were added by intervenous drop for 5 days and retreated every 28 days. These patients were treated 4 timing

with chemotherapy.During the process of chemotherapy routinely use 5-HT receptor antagonist and Dexamethasone to prevent gastrointestinal response and ensure the carry out of chemotherapy.

Statistics analysis

Kaplan-Meier Method calculates the survival rate and Log Rank Test calculates significance of difference. The rest data are analyzed by chi-square test.

RESULTS

Follow-up

All the patients were followed-up more than 5 years, 6 cases who can´t be followed up were calculated as died cases and the rate of follow-up is 93.0%

Therapeutic effects

According to the standard of WHO on solid tumor therapeutic effect, the effect can be CR, PR, NC or PD. We consider CR and PR as effective. The effective rate is 100% (44/44) in combination group and or is 93.0% (40/43) in radiotherapy group. There is no significant difference between two groups in short term therapeutic effect (P>0.05, x^2=1.43). 3-year survival rate and 5-year survival rate were 86.4% and 65.9% in combination group, and which were 55.8% and 39.5% in radiotherapy group, Survival rates have significant difference between two groups (P<0.05, x^2=4.14; 5.09). Survival curves have significant difference between two groups (P<0.05, x^2=4.92).

Side effects

Side effects of both combination group and radiotherapy group in the process of treatment are mainly bone marrow depression and gastrointestinal tract response. In combination group, 30 cases have gastrointestinal tract response below Ⅲ degree and mainly showed as nausea and vomiting, 4 cases have bone marrow depression below Ⅱ degree, which were mainly showed as the descend of white cell. In radiotherapy group, 24 cases have gastrointestinal tract response below Ⅲ degree, and mainly showed as nausea and vomiting, 2 cases have bone marrow depression below Ⅱ degree and. None of the side effects influenced treatment in both groups.

DISCUSSION

Prognosis of advanced cervical cancer is poor for its character as the local gross tumor volume is large, the areas of infiltrate is wide and deep, lymphatic and blood vessel are infiltrated, a great deal of anoxic cells and insensitivity to radiotherapy.[4] In recent years, many researchers treated advanced cervical cancer with concurrent chemoradiotherapy. Clinical research on advanced cervical cancer show concurrent chemoradiotherapy with DDP can elevate the survival rate of cervical cancer and decrease death rate.[5] So National Cancer Institute introduce cervical cancer patients should be given chemotherapy with DDP when receiving radiotherapy.[6]

Drugs used on cervical cancer chemotherapy including CTX, 5-FU, DDP, ADM and so on. Among these drugs, main target of DDP is DNA on cells generation. DDP binding with basic group intracellular and made DNA can´t reproduce. DDP can also influence anoxic cells. So DDP both act as chemotherapeutics and act as radiosensitizer.[7] 5-FU act on cell in S period and has postpone effect on cell between G_1 and S period. At the same time, 5-FU inhibit the repair of radiation damaged DNA. Radiotherapy also depends on cell cycle and resist often on S and G_1 period. There is complementary action between drug and ray.[7,8] So DDP and 5-FU are most popularly used in concurrent chemoradiotherapy, they have the function as follow:

1) Inhibit the repair of radiation damage cells thereby degrade the repopulation of tumor cells.

2) Diminish the gross tumor volume and improve the sensibility of tumor to radiotherapy.

3) Make more G_0 cells into cell cycle and increase the therapeutic effect of radiotherapy.

4) 5-FU and DDP can sensitization radiotherapy and do not extend radiotherapy time.[9,10]

Our research treated 44 cases of advanced cervical cancer by concurrent chemoradiotherapy and utility rate is 100%(44/44) with 3-year and 5-year survival rate were 86.4% and 65.9%. In 43 cases of radiotherapy group, utility rate is 93.0% (40/43) with 3-year and 5-year survival rate were 55.8% and 39.5%. There is no significant difference between two groups in short term therapeutic effect (P>0.05, x^2=1.43). However, survival rates have significant difference between two groups (P<0.05, x^2= 4.14; 5.09). Side effects of both combination group and radiotherapy group in the process of treatment are mainly show as bone marrow depression and

gastrointestinal tract response.

Although there is no significant difference between two groups in short term therapeutic effect, concurrent chemoradiotherapy elevated 3-year and 5-year survival rate. Therapeutic effects of DDP and 5-FU were utility and with light side effects which can be tolerance by patients. So we get to the conclusion that concurrent chemoradiotherapy is safe and reasonable.

REFERENCES

1. Li Helian, He Jin. Dissimilarity method therapy for patients with cervical cancer influence survival quality. Chinese journal of practical gynecology and obstetrics, 2003, 19:142–144.
2. Zhang Wenhua. Chemotherapy headway of the cervical cancer. Journal practical oncology, 2003, 18:172–174.
3. Li Qun. Concurrent chemoradiotherapy for advance cervical cancer and recrudescence cervical cancer. Chinese journal of clinical oncology, 2003, 30:715–717.
4. Wang Yixun. Study actuality of the prognosis factor for patients with cervical cancer. Chinese journal of practical gynecology and obstetrics, 2003, 19:148–149.
5. Song Lei. Chemotherapy for the cervical cancer. Chinese journal of practical gynecology and obstetrics, 2003, 19: 144–146.
6. Shen Keng, Lian Jinghe.Challenges and controversiesa in gynecologic oncology, Beijing: People´s health publishing company, 2002, 50–54.
7. Sun Yang. Medical oncology, Beijing: People´s health publishing company, 2001, 388–447.
8. Zhou You zheng. Chemotherapy headway of the cervical cancer. Chinese journal of clinical oncology, 2005, 32: 117–119.
9. Yin Weibai, Gu Xianzhi. Radiation therapy oncology. Beijing: Publishing company of China Medical University, 2002, 373–376.
10. Ma Wu, Zhan Sulian, Lin Yang. Clinic study of the concurrent chemoradiotherapy for cervical cancer. Modern Oncology, 2005, 13: 84–85.