Original Article

Toxicity Profile in Cervical Cancer Patients Receiving Chemoradiation with Concurrent Parametrial Boost

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Abstract

Introduction Radical surgery or chemoradiation therapy is the options for treating early stage cervical cancer. The advanced stages are treated with radiation alone or concurrent chemoradiation. Concurrent cisplatinum based chemoradiation is considered the standard of care for carcinoma of the cervix and has shown a significantly improved overall survival and progression free survival in locally advanced cancers. Despite improved survival one third of the patients with advanced cancer of cervix have failure within two years. So continued improvement in treatment of advanced cervical cancer is needed. The concurrent parametrial boost with chemoradiation helps in loco regional control. **Objective**: To determine toxicity profile in patients with cancer of cervix receiving chemo radiation with concurrent parametrial boost. **Study Design:** It is descriptive case series. **Setting and duration:** Radiotherapy Department Shaukat Khanum Memorial Cancer Hospital and Research Center Lahore from December 2008 to June 2009**. Material and methods:** Forty patients with locally advanced carcinoma of cervix were included. Concurrent parametrial boost was given along with chemoradiation. Patients were evaluated for toxicity weekly during treatment. SPSS software was used for data analysis. **Results:** 40 patients with stage II-B to IV-A of carcinoma cervix were studied. 22.5 % patients suffered from Grade 1-3 diarrhea, 27.5% had Anemia, 40 % developed neutropenia and 17.5 % suffered thrombocytopenia. **Conclusion:** Concurrent parametrial boost in locally advanced cervix carcinoma offers good results in terms of acceptable toxicity. **Key Words:** Cervix cancer, chemo radiation, concurrent parametrial boost.

INTRODUCTION

Cancer of the cervix is the second most common cancer among women after breast cancer[1]. In United States, the median age of diagnosing cervical cancer is 47 years.. The life time risk of developing cervical cancer in United States is 0.74%[2]. In Pakistan, cervical carcinoma is the most common among gynecological malignancies[3]. Chemoradiation or radical surgery is the options for treating early stage cervical cancer. More advanced stages are treated with radiation alone or combination of chemotherapy with radiotherapy[4]. According to the National Cancer Institute concurrent cisplatinum based chemoradiation is considered the standard of care for carcinoma of the cervix[4,5] and it shows significant improvement in survival when cisplatin-based chemotherapy was administered during radiation for advanced stages of cervical cancer. However, with concurrent chemoradiation in cervical cancer, the risk of gastrointestinal and hematological toxicities increase significantly, but these toxicities are acceptable giving the high response rates from combined modality treatment[1]. In Pakistan, majority of the patients present in late stages (III-IV)[6]. In view of this late presentation and poor general condition, chemoradiotherapy should be used judiciously with careful attention given to patient selection[7]. Despite improved survival with chemoradiation, one third of the patients with advanced cancer of cervix have locoregional failure within two years of treatment so continued improvement in treatment of advanced cervical cancer is desperately needed [8]. Conventionally radiation therapy is delivered to entire pelvis followed by parametrial boost and brachytherapy. This treatment should not take more than eight weeks for completion[9]. If the parametrial boost is delivered along with whole pelvic radiation, good loco regional control can be achieved in desired period of eight weeks. The

purpose of this study was to determine the toxicity profile in cervical cancer patients receiving chemoradiation and concurrent parametrial boost.

OBJECTIVE

To determine the toxicity profile in cervical cancer patients receiving chemoradiation with concurrent parametrial boost.

MATERIALS AND METHODS

Study design: Descriptive case series.

Setting: Department of Radiation Oncology, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore.

Duration of study: Six months

Sample size: The calculated sample size is 40 cases.

Sampling Technique: Purposive non probability sampling.

Sample Selection: Patients were selected according to the following criteria:

Inclusion criteria

1. Patients with histopathologically confirmed carcinoma of cervix with age between 20-60 years.
2. Patients with WHO performance status 0 and1
3. Stage IIB, IIIA, IIIB and IVA according to FIGO staging system..
4. Normal hemoglobin, blood urea /serum creatinine and liver function tests

Exclusion Criteria

1. Patients with renal failure, abnormal liver functions and Anemia
2. Already treated cases by asking previous treatment history.

DATA COLLECTION PROCEDURE

Forty patients with good WHO performance status were enrolled for the study.

TREATMENT

After selection of patients and written informed consent complete medical history was taken. Radiation dose 46-50 Gy in five weeks to entire pelvis with conventional fractionation @ 200 cGy / day five days a week through four field technique and along with it 0.4 Gy with anteroposterior (AP) and posteroanterior (PA) portals as parametrial boost dose with 4 cm central rectal shield was delivered. Chemotherapy was cisplatin 40 mg/m^2 of body surface area weekly with radiation for first five weeks. Brachytherapy boost (LDR) was done after one week of above treatment for two sessions with one week gap to complete the dose at point A up to 80-90 Gy. All patients were examined for grade of toxicities during the treatment for first five weeks, weekly and six weeks after completion of treatment. The maximum grade for all toxicities during any time of treatment considered significant and data was entered in specified proforma.

PATIENT MONITORING AND FOLLOW-UP

During therapy, patients were evaluated for toxicity at weekly intervals. After completion of therapy, patients were followed up in the outpatient clinic with clinical examination at 6 weeks. Common toxicity criteria (CTC version 2.0) were used.

DATA ANALYSIS

Data collected on proforma was entered in statistical package of social sciences (SPSS), version 10, software. Toxicities as diarrhea, anemia, neutropenia and thrombocytopenia were allotted a grade from 0-4 according to common toxicity criteria. Toxicity frequency, percentage was determined as diarrhea, anemia, neutropenia and thrombocytopenia.

RESULTS

Patients

Forty patients were enrolled in the study. The mean age of the patients was 46 years (range 26-60), median age was 47 years. All patients were of good performance status and they completed the treatment without modification.

Histology and stage of disease

All the patients were having the histology of squamous cell carcinoma Grade I-III.28 (70 %) patients were in stage IIB, 11 (27.5%) patients in stage III and only 01 (2.5 %) patient was in stage IVA.

Toxicity evaluation

Diarrhea: During first five weeks of treatment, 4 (10.0 %) patients were having grade I diarrhea while grade II diarrhea was observed in 5 (12.5 %) patients and only one patient had grade III diarrhea. Remaining 30 (75 %) patients were having no diarrhea. At 6 weeks post treatment follow up, no grade III diarrhea was observed. Only 5 (10.0 %) were having grade I

diarrhea and in the remaining patients no diarrhea was seen. Grade II anemia was seen in 6 (15 %) patients, grade I and III was 4 (10 %) and 2 (5 %) patients respectively. Neutropenia grade I seen in 11 (27.5 %) patients and grade III neutropenia was present in only two patients. Grade I thrombocytopenia was seen in 7(17.5 %).

DISCUSSION

Cervical cancer is the second most common cause of cancer-related mortality among women globally Most of these deaths occur in women with bulky or locally advanced cervical cancer, when lesions are not amenable to high cure rates with surgery or radiation therapy. It is believed that 94-100% of cervical cancers are associated with sexually transmitted genital infection by the human papilloma virus[10]. In our country lack of effective screening programme and awareness of patients lead to the delay in diagnosis [11]. Mean age was 46 years and median age was 47 years which is equal to internationally stated [2] and two patients were less than 30 years. The age of patients is very important regarding the complications. There is no treatment modification nor dropping of patient from study because the maximum age taken was sixty and dose and schedule of therapy was modified. Most of the patients were in stage IIB. Regarding parametrium side, maximum patients were with right side involvement. The over all treatment time in cancer of cervix treatment is very important as it must be completed in eight weeks (9). It has been seen that the unscheduled gap in treatment decreases the overall survival. The concurrent parametrial boost helps in completion of treatment in time and it is very useful technique for busy and low resource radiation centres.The gastrointestinal toxicity in this study is 22.5 % which is significantly less than previous studies. Very few patients were in grade 3 and there is no grade 4 toxicity observed in this study in contrast to 70 % seen in other studies [12]. Neutropenia collectively is 37.5 % which was less than international study (50 %) [12]. Anemia and thrombocytopenia was 27.5 % and 17.5 % which was also comparatively less than international studies. No patient needed indoor treatment for complications. Parametrial radiation boost along with midline block improves dose to high risk clinical target volume at the expense of pelvic toxicity[13]. Concurrent parametrial boost in management of locally advanced carcinoma cervix is somewhat controversial in some literature due to its toxicity. We found it very helpful regarding locoregional control and acceptable toxicity because low dose parametrial boost (40 cGy daily) was delivered along with whole pelvic radiation for five weeks and total boost dose was 10 Gy instead of higher doses [14]. There is strong recommendation in favour of concurrent parametrial boost in patients with locally advanced cancer of cervix receiving chemoradiation in terms of good locoregional control and acceptable toxicity.

CONCLUSION

Good locoregional control in locally advanced carcinoma cervix can be achieved with concurrent parametrial boost along with chemoradiation with acceptable and comparable toxicity.

REFERENCES

1. Haie-Meder C, De Crevoisier R, Bruna A. Concomitant chemoradiation in patients with cervix cancer. Bull Cancer 2005; 92: 1032-8.
2. Ries LAG, Eisner MP, Kosary CL. SEER cancer statistics review, National Cancer Institute. [online] 2005. Available from: http://seer.cancer.gov/csr/1975_2002/. Table 1-11(http:11 seer.cancer.gov/csr/1975 2002/results single/sect 01 table.11 2 pqs. pdf)
3. Liaqat NF, Noorani K. Causes of post-menopausal bleeding-a study of 328 cases. J Coll Physicians Surg Pak 2000; 10: 134-7.
4. Tambaro R, Scambia G, Di Maio M, Pisano C, Barletta E, Iaffaioli VR, et al. The role of chemotherapy in locally advanced, metastatic and recurrent cervical cancer. Crit Rev Oncol Hematol 2004; 52: 33-4.
5. Green J, Kirwan J, Tierney J. Concomitant chemotherapy and radiation therapy for cancer of the uterine cervix. Cochrane Database Syst Rev.2005 ; (3) : CD002225
6. Aman, K. Z. Presentation of cervical cancer in a teaching hospital of Lahore. Mother Child 2000; 38: 52-5.
7. Saibishkumar EP, Patel FD, Sharma SC. Results of a phase II trial of concurrent chemoradiation in the treatment of locally advanced carcinoma of

uterine cervix: an experience from India. Bull Cancer 2005; 92:7-12.
8. David KG, Kathryn W, Adam PD, Brigitte M, Patricia JE, Janice R, et al. A phase II study of cute toxicity for celebrex (celecoxib) and chemoradiation in patients with locally advanced cervical cancer: primary endpoint analysis of RTOG 0128. Int J Radiation Oncol Boil. Phys 2007; 67:104-9.
9. Stehman FB, Ali S, Keys HM, Muderspach LI, Chafe WE, Gallup DG, et al. Radiation therapy with or without weekly cisplatin for bulky stage 1B cervical carcinoma: follow-up of a Gynecologic Oncology Group trial. Am J Obstet Gynecol 2007; 197: 443-4
10. Malik A I. The role of Human Papilloma Virus (HPV) in the aetiology of cervical cancer. J Pak Med Assoc 2005; 55: 553-8.
11. Ikram M, Talib W, Chatha S, Saeed R, Saeed M. Carcinoma of cervix. Prof Med J 2005; 12: 392-6.
12. Huang GS, Einstein MH, Semenyuk N, Tabibian P, Fields AL, Anderson PS, et al Acute toxicity of weekly outpatient cisplatin and radiation therapy including high-dose-rate brachytherapy in patients with cervix cancer , 2003 ASCO Annual Meeting.
13. Fenkell L, Assenholt M, Nielsen SK, Haie-Meder C, Pötter R, Lindegaard J, Tanderup K. Parametrial boost using midline shielding results in an unpredictable dose to tumor and organs at risk in combined external beam radiotherapy and brachytherapy for locally advanced cervical cancer. Int J Radiat Oncol Biol Phys. 2011; 79:1572-9
14. Carlos A. Perez Brian D. Kavanagh Principal and practice of radiation oncology. 5th ed. 1555.Philadelphia: Lippincott Williams; 2008.

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