

To Compare Tumor Control, Side Effects and Treatment-Related Toxicity of Two Concomitant Chemoradiation Schedules in Carcinoma of Cervix

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Abstract

Background: Currently, the standard treatment for locally advanced cervical cancer patients is concurrent chemoradiotherapy. A number of chemotherapeutic drugs have been used in a concomitant setting along with radiotherapy in the management of cervical cancer. Docetaxel and cisplatin have shown improved overall response rates with acceptable side effects. Here we aim to compare tumor control, side effects and treatment-related toxicity in two concomitant chemoradiation schedules.

Methods: The patients were divided randomly into two groups of thirty patients each. Both the groups were treated with a combination of External Beam Radiotherapy (EBRT) with 50 Gy/5 weeks/25 fractions to the whole pelvis along with concomitant chemotherapy. Group I (study group) received concomitant chemotherapy with injection docetaxel (20 mg/m²) and injection cisplatin (50 mg/m²) intravenously weekly for 5 weeks followed by HDR brachytherapy. Group II (Control Group) patients received concurrent cisplatin 40 mg/m² intravenously weekly for five weeks followed by HDR brachytherapy.

Results and Conclusion: The survival difference in the two groups was not statistically significant (p-value=0.718). Acute hematological and lower gastrointestinal toxicities were higher in the study group than the control group but these were not statistically significant. There was a trend towards better local control and better disease-free survival with doublet chemotherapy (docetaxel plus cisplatin) as compared to a single agent (cisplatin), but it was not statistically significant.

Keywords: Carcinoma cervix; Docetaxel; Chemoradiation; HDR brachytherapy

Abbreviations: KPS: Karnofsky Performance Scale; EBRT: External Beam Radiotherapy; ICBT: Intracavitary Brachytherapy; CR: Complete Response; PR: Partial Response

Introduction

Cervical cancer is the most common gynecologic malignancy. It is the fourth most common malignancy in females in both incidence and mortality, worldwide. It is being estimated that around 7.9% (527,600) new cases of cervical cancer are there worldwide and it leads to approximately 7.5% (265,700) deaths in a year [1]. Cervix cancer is more common in economically disadvantaged people and constitutes about 85% of new cases diagnosed. In India, Cervical cancer is the second most common cancer in females after breast cancer, which leads to around one lac of new cases every year [2]. In various cancer registries, the age-adjusted incidence rate varies from 4.9 to 30.2 per 100,000 women in India [3]. A most common histopathological subtype of cervical cancer is squamous cell carcinoma which accounts for around 90% cases. Histopathological grading is done as well differentiated, moderately differentiated and poorly differentiated cancer [4]. A combined modality approach is necessary for the management of patients with cervical cancer. For locoregionally advanced disease (stage IIB, III, IVA) concomitant chemoradiation is the primary treatment modality. Currently, the two main modalities of irradiation are external photon beam and brachytherapy. At the completion of treatment, the central tumor should receive approximately 8000-8500 cGy. In bulky tumors, the total dose may reach 9500 cGy [5].

Radical radiotherapy fails to control 35%-85% of patients with locally advanced cervical cancer. Simultaneous chemoradiation has demonstrated to be superior to radiotherapy alone. Some randomized trials have shown that the use of concomitant chemotherapy has

resulted in 30%-50% decrease in the risk of death as compared to RT alone [6]. A recent meta-analysis reported that chemoradiotherapy leads to a 6% improvement in 5-year survival when compared with radiotherapy alone [7]. Cisplatin is one of the most potent antitumor agents known, displaying clinical activity against a wide variety of solid tumors. However, despite the use of concurrent chemoradiation with cisplatin in locally advanced carcinoma cervix, many patients have experienced locoregional failure (20%-25%) and distant failure (10%-20%). The Cochrane meta-analysis has shown that the advantage of concomitant chemoradiation decreases as the stage increases. These facts have stimulated an interest in exploring other concurrent combinations with potentially more clinical effect [5,8,9]. Thus, though a number of chemotherapeutic drugs have been used for concomitant chemoradiation, concomitant cisplatin and docetaxel have shown improved progression-free survival and disease-free survival with acceptable side effects. Keeping these things in mind we administered concomitant cisplatin and docetaxel in our study group in a hope to improve local control by addressing the hypoxic population of tumor cells and also to keep the side effects to a tolerable level.

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Methods and Subjects

Sixty treatment naive, histopathologically proven FIGO Stage IB-IVA patients of squamous cell carcinoma of cervix having Karnofsky Performance Scale (KPS) ≥ 70 and normal hematological parameters were included in the study. Patients who had prior radiation, surgery or chemotherapy, and general condition too poor with KPS <70 were excluded from the study.

The pre-treatment evaluation included history, complete systemic examination including gynecological examination, hematological and biochemistry studies, chest radiography, and ultrasonography of abdomen and pelvis. A computed tomography scan/magnetic resonant imaging scan of abdomen and pelvis performed only when clinically indicated.

The patients were divided randomly into two groups of 30 patients each. Group I (Study Group) patients were treated with EBRT with concurrent cisplatin 40 mg/m² and docetaxel 20 mg/m² intravenously weekly for 5 weeks. Group II (Control Group) patients were treated with EBRT with concurrent cisplatin 40 mg/m² intravenously weekly for five weeks.

All sixty patients were treated with EBRT 50 Gy/5 weeks/25 fractions to the whole pelvis by two-field or four-field technique, depending on pelvic girth, as required. After that, patients were assessed clinically for the feasibility of Intracavitary Brachytherapy (ICBT). If suitable for brachytherapy the patients were given intracavitary HDR brachytherapy 6 Gy to point A, weekly $\times 3$. If the patient was not found suitable for ICBT then, supplementary EBRT 16 Gy in 8-fractions over 1.5 weeks was given to the whole pelvis. Brachytherapy was delivered with microselectron HDR after loading, an intracavitary technique using Williamson Fletcher Suit applicator consisting of an intrauterine tandem and vaginal colpostats, using Iridium-192.

Disease status was evaluated according to the WHO criteria, and the reactions were graded according to the WHO and RTOG criteria. The patients were assessed for any evidence of distant metastasis during each follow-up visit.

Statistical analysis was carried out using SPSS 17 (Statistical Package for Social Sciences) software. The statistical method used was a chi-square test.

Results

The baseline characteristics of patients including demographic profiles, stages etc., are given in Table 1.

The patient and tumor parameters were closely matched in both the groups and their characteristics in Group I and II were as follows: The majority of the patients in Group I and Group II had hemoglobin (in g/dl) level in the range of ≥ 11 gm/dl i.e., 46.7% and 60% respectively. The range of Hb in Group I was 8.7 to 13.7 with a mean of 11.10 ± 1.59 while the range in Group II was 8.1 to 14.4 with a mean of 10.98 ± 1.67 .

The median age (range) at presentation: 50 (35-70) vs. 56 (38-70) years

Postmenopausal: 56.7% vs. 73.3%

Premenopausal: 43.3% vs. 26.7%

Rural background: 53.3% vs. 73.3%

Urban background: 46.7% vs. 26.7%

Smokers: 16.7% vs. 23.3%

KPS: 80 (60% vs. 80%), 90 (40% vs. 20%)

• Presenting complaints

Bleeding per vagina: 80% vs. 63.3%

Discharge per vagina: 50% vs. 63.3%

• Histopathology

WDSCC: 3.3% vs. nil

MDSCC: 76.7% vs. 90%

PDSCC: 20% vs. 10%

Tumor size: ≤ 4 cm vs. 36.7% vs. 40%, >4 cm-63.3% vs. 60%

Patient characteristics	Group I (Study Group) n=30	Frequency (%)	Group II (Control Group) n=30	Frequency (%)	p value
Age group (years)	≤ 45	12	40	9	30
	>45	18	60	21	70
	Range	35-70		38-70	
	Median	50		56	
Background	Rural	16	53.3	22	73.3
	Urban	14	46.7	8	26.7
Menstrual history	Post-menopausal	17	56.7	22	73.3
	Pre-menopausal	13	43.3	8	26.7
Parity	≤ 3 children	23	76.7	10	33.3
	>3 children	7	23.3	20	66.7
Duration of symptoms	Bleeding P/V	24	80	19	63.3
	Discharge P/V	15	50	19	63.3
	Pain abdomen	11	36.7	8	26.7
Duration of symptoms	≤ 1 month	3	10	1	3.3
	1-6 month	21	70	21	70
	6-12 month	3	10	5	16.7
	>12 month	3	10	3	10
Smoking history	Smoker	5	16.7	7	23.3
	Non-smoker	25	83.3	23	76.7
Karnofsky Performance Status	80	18	60	24	80
	90	12	40	6	20

Table 1: The baseline characteristics of patients including demographic profiles, stages etc.

- **Stage wise distribution**

Stage I: 10% vs. 3.3%
 Stage IIA: nil vs. 3.3%
 Stage IIB: 46.7% vs. 50%
 Stage IIIA: 10% vs. 3.3%
 Stage IIIB: 33.3% vs. 40%

Acute toxicity profile during chemoradiation

The acute side effects of concomitant chemoradiation therapy were graded as per RTOG criteria. Acute reactions and their grades in Group I and Group II were as follows:

- **Cutaneous reactions:**

Grade 1: 15/30 (50%) vs. 17/30 (56.7%)
 Grade 2: 12/30 (40%) vs. 7/30 (23.3%)
 Grade 3: 3/30 (10%) vs. 6/30 (20%)

- **Mucosal radiation reactions:**

Grade 1: 20/30 (66.7%) vs. 18/30 (60%)
 Grade 2: 8/30 (26.7%) vs. 8/30 (26.7%)
 Grade 3: 2/30 (6.7%) vs. 4/30 (13.3%)

- **Upper GI reactions:**

Grade 1: 11/30 (36.7%) vs. 12/30 (40%)
 Grade 2: 11/30 (36.7%) vs. 12/30 (40%)
 Grade 3: 3/30 (10%) vs. 2/30 (6.7%)

- **Lower GI reactions:**

Grade 1: 10/30 (33.3%) vs. 12/30 (40%)
 Grade 2: 12/30 (40%) vs. 11/30 (36.7%)
 Grade 3: 5/30 (16.7%) vs. 3/30 (10%)

- **Bladder reactions:**

Grade 1: 13/30 (43.3%) vs. 10/30 (33.3%)
 Grade 2: 2/30 (6.7%) vs. 1/30 (3.3%)

- **Haematological toxicity-haemoglobin:**

Grade 1: 13/30 (43.3%) vs. 11/30 (36.7%)
 Grade 2: 12/30 (40%) vs. 9/30 (30%)

- **Total Leucocyte Count:**

Grade 1: 9/30 (30%) vs. 7/30 (23.3%)
 Grade 2: 1/30 (3.3%) vs. 1/30 (3.3%)
 Grade 3: 1/30 (3.3%) vs. nil

- **Biochemical toxicity-blood urea:**

Grade 1: 7/30 (23.3%) vs. 5/30 (16.7%)

- **Serum creatinine:**

Grade 1: 3/30 (10%) vs. 2/30 (6.7%)

There was a trend towards higher haematological and gastrointestinal toxicity in Group I as compared to Group II but it was not statistically significant.

In Group I, 83.3% patients and in Group II, 96.7% of patients completed intended chemoradiation treatment without interruption. All patients tolerated treatment with minor morbidity. The side effects of chemoradiation were almost similar in both the groups. The acute toxicities leading to interruption of chemoradiation (>1 week) in Group I and II were Grade 3 GI toxicity (3.3% vs. nil); Grade 3 cutaneous reactions (10% vs. 3.3%); Grade 3 hematological toxicity (3.3% vs. nil) respectively.

Local control rate and disease-free survival rate

Local control in Group I and Group II post-EBRT (after chemoradiation) was as follows:

Complete Response (CR): 17/30 (56.7%) vs. 14/30 (46.7%)

Partial Response (PR): 11/30 (36.7%) vs. 11/30 (36.7%)

Local control (CR+PR): 28/30 (93.3%) vs. 25/30 (83.3%)

No response: 2/30 (6.7%) vs. 5/30 (16.7%)

Local control in Group I and Group II after completion of intended treatment was as follows:

CR: 29/30 (96.7%) vs. 28/30 (93.3%)

PR: 1/30 (3.3%) vs. 2/30 (6.7%)

Overall response: 30/30 (100%) in each group

The follow-up period ranged from 6-15 months (median 9 months). At last follow-up, locoregional control in Group I and II were as follows:

Stage IB: 3/3 (100%) vs. 1/1(100%)

Stage IIA: 1/1 (100%) in Group II,

Stage IIB: 14/14 (100%) vs. 13/15 (86.7%)

Stage IIIA: 3/3 (100%) vs. 1/1(100%)

Stage IIIB: 8/10 (80%) vs. 11/12 (91.7%)

All stages: 28/30 (93.3%) vs. 27/30 (90%)

At last follow-up, disease-free survival in Group I and II were as follows:

Stage IB: 2/3 (66.7%) vs. 1/1(100%)

Stage II: 1/1 (100%) in Group II

Stage IIB: 14/14 (100%) vs. 13/15 (86.7%)

Stage IIIA: 3/3 (100%) vs. 1/1 (100%)

Stage IIIB: 7/10 (70%) vs. 9/12 (75%)

All stages: 26/30 (86.7%) vs. 25/30 (83.3%)

Thus there was a trend towards better local control and better disease-free survival with doublet chemotherapy (docetaxel plus cisplatin) as compared to a single agent (cisplatin), but it was not statistically significant. The survival difference in the two groups was not statistically significant (p-value=0.718).

Late toxicity profiles

The late side effects of radiation therapy were graded as per RTOG criteria. Late effects and their grades in Group I and Group II were as follows:

Bladder toxicity-Grade 1: 4/29 (13.8%) vs. 4/29 (13.8%)
Lower GI toxicity-Grade 1: 6/29 (20.7%) vs. 6/29 (20.7%), Grade 2: 2/29 (6.9%) vs. 1/29 (3.4%)
Cutaneous reactions-Grade 1: 12/29 (41.4%) vs. 10/29 (34.5%)
Mucosal reactions-8/29 (27.6%) vs. 7/29 (24.1%)
No late reaction with Grade ≥ 3 was seen in either group.

Discussion

Cervical cancer is the most common gynecologic malignancy. It is the fourth most common malignancy in females in both incidence and mortality, worldwide. Radiotherapy alone has a failure rate of 35%-85% with locally advanced cervical cancer. The 5-year survival rate for patients treated with radiotherapy alone is 85% for stage I, 75% for stage IIA, 60-65% for stage IIB, 25-48% for stage III and 18-34% for stage IVA. Simultaneous chemoradiation has demonstrated to be superior to radiation alone [10].

Recent studies have shown a better response with the addition of newer chemotherapeutic agents like docetaxel, paclitaxel, carboplatin, gemcitabine, gefitinib, etc. [11-29].

We used low dose docetaxel (20 mg/m²) regimen in our patients in combination with cisplatin. 96.7% and 90% patients in Group I and II, were found suitable for ICBT at end of EBRT. The response rate was found better (93.3% vs. 83.3%) in Group I than Group II but was not statistically significant. Disease-free survival and locoregional control were better in Group I than Group II but not statistically significant. Grade 3/4 hematologic or GI toxicity was unusual.

Similar results were reported by Higgins, et al. [17] where they conducted a study concurrent carboplatin and paclitaxel with pelvic radiation therapy in the primary treatment of cervical cancer. The CR rate 3 months after completion of therapy was 91%. Grade 3/4 hematologic or gastrointestinal toxicity was not found. The estimated 3-year progression-free survival is 70% and overall survival is 65%.

In another study by Duenas, et al. [20] it was concluded that gemcitabine plus cisplatin chemoradiotherapy followed by brachytherapy and adjuvant gemcitabine/cisplatin chemotherapy improves progression-free survival with clinically manageable toxicities as compared to standard treatment.

Kim, et al. [21] compared monthly 5 FU plus cisplatin and weekly cisplatin concurrently with radiotherapy in locally advanced carcinoma cervix. The two groups received 3-monthly cycles of 5 FU (1000 mg/m²/day) plus cisplatin (20 mg/m²/day) for five days and 6 cycles of weekly cisplatin (30 mg/m²) concurrently with RT respectively. The CR rate in each group was 91%.

Nagao, et al. [23] performed a pilot study for future trials to assess the efficacy and safety of combination chemotherapy with docetaxel and carboplatin in advanced or recurrent carcinoma cervix. The dosage of docetaxel was 60 mg/m² and of carboplatin was AUC=6.

The overall response rate found was 76% with no progression of the disease. It was concluded that combination chemotherapy is an effective and safe treatment of uterine cervix cancer.

Watanabe, et al. [24] conducted a study to determine taxane plus platinum treatment regimen for squamous cell carcinoma of uterine cervix. It was found that docetaxel plus nedaplatin is a tolerable regimen

for cervical squamous cell carcinoma even in patients previously treated with cisplatin-based concurrent chemoradiation.

Thus, chemoradiation with docetaxel and cisplatin showed encouraging results with acceptable toxicity. There was a trend towards better local control and better disease-free survival with doublet chemotherapy (docetaxel plus cisplatin) as compared to a single agent (cisplatin), but it was not statistically significant.

Summary and Conclusion

A prospective, open-label, parallel, randomized study has been conducted on sixty treatment naïve, squamous cell carcinoma cervix patients, treated with radical intent to compare two concomitant chemoradiation schedules (concomitant chemoradiation with docetaxel plus cisplatin versus concomitant chemoradiation with cisplatin alone). Included in the study were treatment naïve, histopathologically proven squamous cell carcinoma cervix, stage IB-IVA patients having KPS \geq 60, normal hematological and biochemical parameters who gave informed consent to participate in the study. Excluded from the study were patients who had prior radiation, surgery or chemotherapy, distant metastasis, poor general condition with KPS $<$ 60, pregnant or lactating females, history of prior malignancy, evidence of HIV/AIDS or associated significant medical or surgical illness forbidding radical chemoradiation. The patients were randomized in two groups of thirty patients each by internet service website <https://www.random.org/lists/>. All sixty patients were treated with a combination of EBRT 50 Gy/25 fractions/5 weeks to the whole pelvis along with concomitant chemotherapy. Group I patients (study group) received concomitant chemotherapy with injection docetaxel (20 mg/m²) and injection cisplatin (40 mg/m²) weekly and Group II patients (control group) with injection cisplatin (40 mg/m²) weekly along with EBRT. Subsequently, patients were assessed clinically for the feasibility of ICBT. Suitable patients were given intracavitary HDR brachytherapy 6 Gy to point A on weekly basis for 3 weeks. If the patient was not found suitable for ICBT, then supplementary EBRT 16 Gy/8 fractions/1.3 weeks was given to the whole pelvis. In both the groups, external beam radiation was delivered on a telecobalt machine. The patients were planned with two-field or four-field technique depending on pelvic 68 girths. Microselectron HDR after loading Ir-192, remote controlled brachytherapy machine was used to deliver ICBT. The patients were assessed for radiation reactions and chemotherapy-related toxicities regularly during and after chemoradiation. After completion of brachytherapy treatment, all patients were followed up regularly for at least 6 months. The patient and tumor parameters were closely matched in both the groups and their characteristics in Group I and II were as follows:

The median age (range) at presentation-50 (35-70) vs. 56 (38-70) years; postmenopausal: 56.7% vs. 73.3%; premenopausal: 43.3% vs. 26.7%; rural background: 53.3% vs. 73.3%; urban background: 46.7% vs. 26.7%; Smokers: 16.7% vs. 23.3%; KPS: 80 (60% vs. 80%), 90 (40% vs. 20%); presenting complaints- bleeding per vagina: 80% vs. 63.3%; discharge per vagina: 50% vs. 63.3%; histopathology-WDSCC: 3.3% vs. nil; MDSCC: 76.7% vs. 90%; PDSCC: 20% vs. 10%; tumor size- \leq 4 cm: 36.7% vs. 40%, $>$ 4 cm: 63.3% vs. 60%; Stage wise distribution-Stage I: 10% vs. 3.3%; Stage IIA: nil vs. 3.3%; Stage IIB: 46.7% vs. 50%; Stage IIIA: 10% vs. 3.3%, Stage IIIB: 33.3% vs. 40%. The acute side effects of concomitant chemoradiation therapy were graded as per RTOG criteria.

Acute reactions and their grades in Group I and Group II were as follows:

Cutaneous reactions-Grade 1: 15/30 (50%) vs. 17/30 (56.7%); Grade 2: 12/30 (40%) vs. 7/30 (23.3%); Grade 3: 3/30 (10%) vs. 6/30 (20%); mucosal radiation reactions-Grade 1: 20/30 (66.7%) vs. 18/30 (60%); Grade 2: 8/30 (26.7%) vs. 8/30 (26.7%) and Grade 3: 2/30 (6.7%) vs. 4/30 (13.3%); upper GI reactions-Grade 1: 11/30 (36.7%) vs. 12/30 (40%); Grade 2: 11/30 (36.7%) vs. 12/30 (40%) and Grade 3: 3/30 (10%) vs. 2/30 (6.7%); lower GI reactions-Grade 1: 10/30 (33.3%) vs. 12/30 (40%); Grade 2: 12/30 (40%) vs. 11/30 (36.7%) and Grade 3: 5/30 (16.7%) vs. 3/30 (10%); bladder reactions-Grade 1: 13/30 (43.3%) vs. 10/30 (33.3%); Grade 2: 2/30 (6.7%) vs. 1/30 (3.3%); haematological toxicity-hemoglobin, Grade 1: 13/30 (43.3%) vs. 11/30 (36.7%); Grade 2: 12/30 (40%) vs. 9/30 (30%); Total Leucocyte Count-Grade 1: 9/30 (30%) vs. 7/30 (23.3%); Grade 2: 1/30 (3.3%) vs. 1/30 (3.3%); Grade 3: 1/30 (3.3%) vs. nil, biochemical toxicity-blood urea, Grade 1: 7/30 (23.3%) vs. 5/30 (16.7%); serum creatinine-Grade 1: 69 3/30 (10%) vs. 2/30 (6.7%).

There was a trend towards higher hematological and gastrointestinal toxicity in Group I as compared to Group II but it was not statistically significant. In Group I, 83.3% patients and in Group II, 96.7% of patients completed intended chemoradiation treatment without interruption. All patients tolerated treatment with minor morbidity. The side effects of chemoradiation were almost similar in both the groups. The acute toxicities leading to interruption of chemoradiation (>1 week) in Group I and II were Grade 3 GI toxicity (3.3% vs. nil); Grade 3 cutaneous reactions (10% vs. 3.3%); Grade 3 hematological toxicity (3.3% vs. nil) respectively. Local control in Group I and Group II post-EBRT (after chemoradiation) was as follows:

CR: 17/30 (56.7%) vs. 14/30 (46.7%); PR: 11/30 (36.7%) vs. 11/30 (36.7%); local control (CR+PR): 28/30 (93.3%) vs. 25/30 (83.3%) and no response: 2/30 (6.7%) vs. 5/30 (16.7%) respectively. Local control in Group I and Group II after completion of intended treatment was as follows: CR: 29/30 (96.7%) vs. 28/30 (93.3%); PR: 1/30 (3.3%) vs. 2/30 (6.7%) respectively; overall response-30/30 (100%) in each group. The late side effects of radiation therapy were graded as per RTOG criteria. Late effects and their grades in Group I and Group II were as follows: bladder toxicity- Grade 1: 4/29 (13.8%) vs. 4/29 (13.8%); lower GI toxicity-Grade 1: 6/29 (20.7%) vs. 6/29 (20.7%); Grade 2: 2/29 (6.9%) vs. 1/29 (3.4%); cutaneous reactions-Grade 1: 12/29 (41.4%) vs. 10/29 (34.5%); mucosal reactions: 8/29 (27.6%) vs. 7/29 (24.1%). No late reaction with Grade ≥ 3 was seen in either group. One patient in Group I, who was not having any evidence of local/metastatic disease at her last follow-up in RT OPD, died after 1 month of completion of treatment due to the cardiac disease at her hometown. One patient in Group II, who was not having any evidence of local/metastatic disease at her last follow-up in RT OPD, died after 3 months of completion of treatment at her hometown. 70 The follow-up period ranged from 6-15 months (median 9 months). The follow-up is still continuing in Department of Radiation Oncology, PGIMS, Rohtak.

At last follow-up, locoregional control in Group I and II was respectively as follows:

Stage IB: 3/3 (100%) vs. 1/1(100%); Stage IIA: 1/1 (100%) in Group II, Stage IIB: 14/14 (100%) vs. 13/15 (86.7%); Stage IIIA: 3/3 (100%) vs. 1/1(100%); Stage IIIB: 8/10 (80%) vs. 11/12 (91.7%). All stages: 28/30 (93.3%) vs. 27/30 (90%).

At last follow-up, disease-free survival in Group I and II were as follows:

Stage IB: 2/3 (66.7%) vs. 1/1(100%); Stage IIA: 1/1 (100%) in Group

II, Stage IIB: 14/14 (100%) vs. 13/15 (86.7%); Stage IIIA: 3/3 (100%) vs. 1/1 (100%); Stage IIIB: 7/10 (70%) vs. 9/12 (75%). All stages: 26/30 (86.7%) vs. 25/30 (83.3%).

Thus there was a trend towards better local control and better disease-free survival with doublet chemotherapy (docetaxel plus cisplatin) as compared to a single agent (cisplatin), but it was not statistically significant. At last follow-up, one patient in Group I (stage IIIB) and two patients in Group II (stage IIB and IIIB) had residual disease. Three patients in Group I and Group II had recurrent disease. The survival difference in the two groups was not statistically significant (p -value=0.718). Survival was analyzed with multivariate analysis. The disease-free survival was not influenced by age, histopathology and tumor size. To the best of our knowledge, the present study is the first in medical literature which has assessed the toxicity and safety profile of concomitant chemoradiation with docetaxel and cisplatin in treatment naïve carcinoma cervix and comparing it with gold standard treatment in carcinoma cervix i.e., cisplatin-based chemoradiation, in terms of locoregional control, disease-free survival and toxicity. The management of patients with carcinoma cervix using weekly concomitant chemoradiation with docetaxel and cisplatin is feasible with good pelvic control and with acceptable toxicities.

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Ethical Justification

Informed written consent was taken from all the subjects. The present study is well within the ethical norms and is ethically justified.

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Nil

Conflicts of Interest

There are no conflicts of interest.

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