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Original Article

Toxicity Profile of Double-agent Adjuvant Chemotherapy after Concurrent Chemoradiation and Brachytherapy in Locally Advanced Cervical Cancer: Comparison with Standard Chemoradiation Protocol

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Abstract

Introduction: Carcinoma cervix is the most common gynecological malignancy in India and a major cause of cancer mortality and morbidity in the females despite Concurrent chemoradiotherapy (CCRT). Attempts are on to improved overall survival by addition of adjuvant chemotherapy (ACT) to CCRT. **Aim:** The aim of this study is to establish toxicity profile of double-agent ACT after CCRT and ICRT in locally advanced cervical cancer (LACC) and to compare it with standard chemoradiation protocol. **Materials and Methods:** Patients were randomized into two arms: in conventional arm (Arm 1, n = 23), patients received a standard protocol of weekly injection cisplatin 40 mg/m^2 concurrently with pelvic external beam radiotherapy (5040cGy/28 fractions) followed by ICRT (03 fractions of 7 Gy each). In interventional arm (Arm 2, n = 24), patients received CCRT/ICRT protocol; and were further offered ACT with three cycles of consolidation chemotherapy using injection paclitaxel and injection carboplatin every 3 weeks after CCRT and ICRT. **Results:** The incidence of anemia was 14/23 (50% Grade 1) in Arm 1 and 12/24 in Arm 2 (17% Grade 1, rest higher grade). In Arm 2, 37% of patients had ≥Grade 2 neuropathy and 16% of patients had Grade 1 alopecia, whereas nil incidence was reported in Arm 1 (P = 0.005 and 0.04, respectively). Grade 3 neutropenia was observed in 4/23 (17%) patients of Arm 1 and 8/24 patients (33%) of Arm 2. None of the patients in Arm 1 required indoor supportive care while 4/24 patients (17%) were managed as an indoor patient. Among late toxicities, in Arm 2, the incidence of Grade 2 and Grade 3 anemia was 42%, whereas in Arm 1, its incidence was 22%. In Arm 1, no patient exhibited features of neuropathy, whereas, in Arm 2, 12/24 (50%) of the patients had neuropathy (P value for these two late events was <0.05 statistically significant). No therapy-induced mortality was noted. **Conclusion:** Exhibition of ACT with injection Paclitaxel and injection carboplatin in locally advanced carcinoma cervix is a technically viable option with manageable toxicity.

Keywords: *Acute toxicities, adjuvant chemotherapy, concurrent chemoradiation therapy, delayed toxicities, locally advanced cancer cervix*

Introduction

Cervical carcinoma is the second most frequent cancer among women worldwide and most common gynecological cancer in Indian women.[1-3] It is the fourth leading cause of global cancer death among women with an estimated 528,000 new cases (accounting for around 12% of all cancers) and 266,000 deaths in 2012.[4] In India, 122,844 women are annually diagnosed with cervical cancer and 67,477 die from the disease. It is estimated that cervical cancer will occur in approximately 1 in 53 Indian women during their lifetime compared with 1 in 100 women in more developed regions of the world.[5-8] In addition to a higher incidence of cervical cancer in less developed regions, patients in these areas have a higher proportion of locally advanced stages, including stage IIB to IVA of the International Federation of Gynecology and Obstetrics (FIGO) staging classification, or advanced stage IVB cancers.[9] Overall, 80%–90% of patients present with advanced stage with the bulky central disease.[5]

Since 1999, the mainstay of treatment for locally advanced cervical cancer (LACC) has been injectio cisplatin-based concurrent chemoradiation therapy (CCRT), following a National Cancer Institute clinical announcement.[10] Radiotherapy (RT) and concurrent chemotherapy were shown to

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improve the control of pelvic disease and significantly increased overall survival (OS) rates in various randomized trials and is considered as the standard of care for patients with bulky stage IB disease, stage IIB through IVA and high-risk cervical cancer cases.[11-12] However, outcomes in this disease remained suboptimal, with long-term progression-free survival (PFS) and OS rates of approximately 60%.[1,13-14] Local and distant failures of 17% and 18%, respectively, in LACC after CCRT were still encountered.[15] Interventions provided to improve treatment outcomes include chemotherapy administered before CCRT (neoadjuvant chemotherapy [NACT]) and additional chemotherapy given after the standard treatment, which is referred to as "consolidation chemotherapy" or "ACT".[16-18]

The objective of ACT after completion of RT or CCRT is to eradicate the residual disease in the pelvis and treating occult disease outside the pelvic radiation field.[1] The results of the ACT after CCRT in LACC have shown superiority over CCRT alone, but most of these data are from western literature with some disparity.[18-20] OS rates >80% to 90% achieved with CCRT followed by the ACT were higher than the 60% to 65% rates obtained with CCRT alone.[21] As chemotherapy can cause toxicities, potential survival advantages should outweigh these disadvantages. Due to paucity of data on safety and tolerance of ACT in LACC in Indian scenario, a prospective study was conducted to study the toxicity profile of double-agent ACT after CCRT and intracavitary RT (ICRT) in LACC and to compare it with standard chemoradiation protocol.

Materials and Methods

Study design

This is an experimental prospective randomized study; comparative and interventional in nature; that was carried out at the Oncology Center of a tertiary care super-specialty hospital of government setup in a developing country over 2 years duration.

Sample size

The following formula was used to calculate the required number of patients in the study: $N = 4\ PQ/L^2$; Where P is the prevalence of cervical cancer, which is 10% approximately at this Hospital; Q is 100-P and L = Permissible Error = 10%. Hence, $n = 4 \times 10 \times 90/100 = 36$ (approximated to 40). Thus, at least 40 patients needed to be enrolled, 20 in each arm.

Inclusion criteria

The inclusion criteria were histologically confirmed squamous cell carcinoma/adenocarcinoma cervix, stage IIB to IVB (limited to paraaortic lymph node involvement without any distant metastasis), no previous malignancy/radiation to pelvis/chemotherapy, age group <70 years, Karnofsky performance status (KPS) ≥50%, nonpregnant, nonnursing females, without renal or liver abnormalities, and who consented for the study.

Treatment protocol

There were two arms of the study, Conventional Arm (Arm 1) and Interventional arm (Arm 2) having 23 and 24 patients, respectively. The patients were randomized by simple random sampling technique (Chit-Pull system). In Arm 1, patients were managed by the standard protocol of weekly injection cisplatin 40 mg/m^2 concurrently with pelvic RT, followed by ICRT. In Arm 2, after this standard CCRT and ICRT protocol, patients were further offered ACT with 3 cycles of ACT using injection paclitaxel (155 mg/m^2) and injection carboplatin (AUC 5.0) every 3 weekly. In both arms, patients received pelvic RT 5040cGy/28 fractions @180cGy per fraction over 5–6 weeks; and in patients with evidence of paraaortic lymph node involvement on imaging, a paraaortic field was added to a dose of 4500cGy/25 fractions. This external beam radiotherapy was followed by ICRT with high dose rate brachytherapy (BCT) in the form of 03 fractions of 7 Gy each. During treatment and up to 3 months posttreatment, the patients were monitored for therapy-induced acute toxicities and were reviewed thereafter every 12 weekly for delayed toxicities.

Results

Patient-related characteristics

The mean age of the patients was 56.4 years (range: 39–69 years) and 52.7 years (range: 33–70 years) in Arms 1 and 2, respectively. The age-wise distribution of the 2 arms is summarized in Table 1. Maximum incidence of the disease was seen in the age group of 61–70 years in the conventional arm while 41–50 years in the interventional arm. 6/23 patients in each Arm (26% and 25% in Arms 1 and 2, respectively) had comorbidities such as hypertension, diabetes mellitus, and hypothyroidism. The KPS of patients in both arms were 90% for all the patients at the time of pretreatment evaluation excluding three patients in Arm 1 and one patient in Arm 2 with KPS of 80%. The average pretreatment hemoglobin in Arm 1 was 11.04 g/dl and in Arm 2 was 11.13 g/dl.

Disease-related characteristics

All patients had squamous cell carcinoma histopathology, except for 1 patient in Arm 1 and 2 patients in Arm 2 who were having adenocarcinoma cervix. The distribution of patients as per FIGO staging 2009 is shown in Figure 1; the distribution in Arm 1 was 8/23 (35%) in stage IIB,

Table 1: Age distribution of patients

Age group (years)	Arm 1	Arm 2	Total	χ^2	*P*
<40	1	2	3	2.062	0.56
41-50	7	10	17		
51-60	6	7	13		
61-70	9	5	14		
Total	23	24	47		

Arm 1 – Conventional arm (n=23); Arm 2 – Interventional arm (n=24)

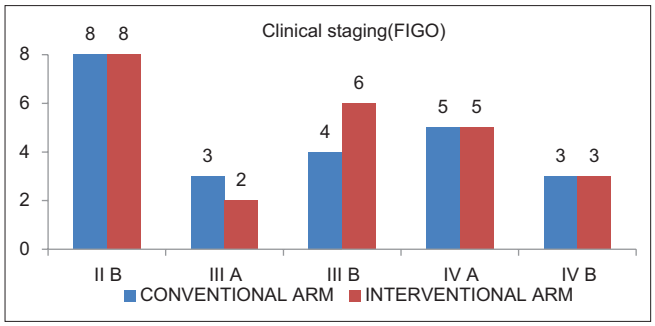

Figure 1: Clinical Stages in Arm 1 (Conventional Arm, *n* = 23); and Arm 2 (Interventional arm, *n* = 24)

3/23 (13%) in IIIA, 4/23 (17%) in IIIB, 5/23 (22%) in IVA, and 3/23 (13%) in IVB. In Arm 2, the stage distribution was 8/24 (33%) in stage IIB, 2/24 (8%) in IIIA, 6/24 (25%) in IIIB, 5/24 (21%) in IVA, 3/24 (13%) in IVB. Thus, the most common stage of presentation was FIGO stage IIB followed by stage IIIB and IVA in both the arms. The incidence of metastasis to pelvic, inguinal, and paraaortic lymphnodal groups based on imaging (CECT/PET CT) in both the arms is depicted in Table 2. In Arm 1, incidence of involvement of pelvic, inguinal and paraaortic group of lymph nodes is 20/23 (86%), 0/23 (0%), and 3/23 (13%), respectively, whereas in Arm 2, the corresponding figures were 19/24 (79%), 1/24 (5%), and 3/24 (12.5%), respectively.

Treatment-related characteristics

Majority of patients in both the treatment arms (16/23 and 19/24 in Arms 1 and 2, respectively) received 5 or more cycles of weekly concurrent injection cisplatin along with radiation. Four patients each in Arms 1 and 2 received 4 cycles of concurrent chemotherapy while remaining patients received <4 cycles. Thus, overall, 35 out of 47 patients (74%) in both arms could tolerate the desired 5 or more cycles of weekly concurrent chemotherapy. The mean treatment time of completing definitive CCRT followed by ICRT in Arm 1 was around 63.7 days (range: 56–78 days) and in Arm 2, it was 64.4 days (range: 57–71 days).

Toxicities-related characteristics

The site-specific acute and delayed toxicities are summarized in Tables 3 and 4, respectively.

Acute toxicities

Acute toxicities were observed in a small subset of patients of both the study arms up to first 3 months of follow-up. Acute toxicities were graded as per "Common Terminology Criteria for Adverse Events (CTCAE)," i.e., CTCAE version 4.03. Grades are divided from scale of 0–5 in which 0 stands for nil toxicity and 5 for death related to adverse events.

Anemia

In Arm 1, 14/23 (58%) of the patients had anemia of whom 50% (7 patients) had Grade 1, 22% had Grade 2 (3 patients) and 28% (4 patients) had Grade 3. In Arm 2, 12/24 (50%) of the patients had anemia, of whom 17% (2 patients) had Grade 1, 58% (7 patients) had Grade 2 and 25% (3 patients) had Grade 3. Thus, among

Table 2: Loco regional lymphnodal involvement based on imaging in both arms

	Arm 1	Arm 2	Total	Pearson χ^2	*P*
Pelvic LNs					
No	3	5	8	0.505	0.477
Yes	20	19	39		
Inguinal LNs					
No	23	23	46	0.979	0.322
Yes	0	1	1		
Para-aortic LNs					
No	20	21	41	0.003	0.955
Yes	3	3	6		

Arm 1 – Conventional arm (*n*=23); Arm 2 – Interventional arm (*n*=24); LNs – Lymph nodes

Table 3: Acute toxicities in both arms

Toxicity	Grade	Arm 1	Arm 2	Total	Pearson χ^2	*P*
Nausea/ vomiting	0	15	19	34	1.268	0.53
	1	1	1	2		
	2	7	4	11		
AKI	0	19	23	42	2.361	0.307
	1	3	1	4		
	3	1	0	1		
Anaemia	0	9	12	21	4.93	0.177
	1	7	2	9		
	2	3	7	10		
	3	4	3	7		
Neutropenia	0	19	16	35	1.57	0.21
	3	4	8	12		
Skin reaction	0	20	19	39	4.673	0.097
	1	2	0	2		
	2	1	5	6		
Neuropathy	0	23	15	38	10.668	0.005
	2	0	7	7		
	3	0	2	2		
Cystitis	0	19	18	37	2.007	0.367
	2	3	6	9		
	4	1	0	1		
Proctitis	0	21	17	38	5.902	0.052
	2	1	7	8		
	4	1	0	1		
Enteritis	0	21	16	37	1.139	0.286
	2	2	4	6		
Vaginal stricture	0	21	20	41	2.004	0.367
	1	2	2	4		
	2	0	2	2		
Alopecia	0	23	20	43	4.19	0.041
	1	0	4	4		
Total		23	24	47		

Arm 1 – Conventional arm (*n*=23); Arm 2 – Interventional arm (*n*=24); AKI – Acute kidney injury

Table 4: Late toxicities

Toxicity	Grade	Arm 1	Arm 2	Total	Pearson χ^2	*P*
Anaemia	0	10	14	24	14.106	0.003
	1	8	0	8		
	2	2	9	11		
	3	3	1	4		
Neutropenia	0	23	24	47		
Neuropathy	0	23	12	35	15.443	0.001
	1	0	1	1		
	2	0	10	10		
	3	0	1	1		
Cystitis	0	21	21	42	0.179	0.672
	2	2	3	5		
Proctitis	0	20	19	39	2.291	0.318
	2	2	5	7		
	3	1	0	1		
Vaginal stricture	0	13	19	32	4.217	0.239
	1	2	0	2		
	2	5	4	9		
	3	3	1	4		
Alopecia	0	23	20	43	4.19	0.123
	1	0	3	3		
	2	0	1	1		
Total	-	23	24	47	-	-

Arm 1 – Conventional arm (*n*=23); Arm 2 – Interventional arm (*n*=24)

patients developing anemia, higher proportion of patients in Arm 2 developed Grade 2 and Grade 3 anemia.

Nausea and vomiting

Nausea and vomiting (N/V) were observed in 8/23 (35%) patients of Arm 1 and 5/23 (22%) of Arm 2. Of these, 1 patient each in both arms had Grade 1 N/V while rest patients were of Grade 2. All were manageable on outpatient based symptomatic and supportive care.

Neutropenia

Neutropenia was observed in 4/23 patients (17%) of Arm 1 and 8/24 (33%) patients of Arm 2. All were Grade 3.

Neuropathy

In Arm 1, not even a single patient exhibited features of neuropathy, whereas in Arm 2, 9/24 (37%) of the patients had neuropathy, with 7/24 (29%) and 2/24 (8%) patients having Grade 2 and Grade 3 neuropathy, respectively.

Alopecia

In Arm 1, the incidence of alopecia as an acute toxicity was nil whereas in Arm 2, 4/24 (17%) of the patients had alopecia and all were Grade 1.

Miscellaneous

Apart from above mentioned toxicities, various other adverse events such as acute kidney injury, cystitis, enteritis, proctitis, skin reactions, and vaginal stricture were also noticed in small proportion of patients of both the arms within 3 months of their follow-up. They had no any significant correlation statistically and were comparable in both the arms.

Late toxicities

Late toxicities were charted in both the study groups starting after 3 months of completion of treatment protocol until the past follow-up of the patients. Late toxicities have been graded as per "Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer" criteria 2015 for radiation-related adverse events and CTCAE version 4.03 for chemotherapy-related side effects.

Anemia: In Arm 1, 13/23 (56.5%) patients had anemia, of whom 8, 2, and 3 patients (61.5%, 15% and 23%) had Grade 1, Grade 2, and Grade 3 anemia, respectively. In Arm 2, 10/24 (41.5%) of the patients had anemia, of whom 9 and 1 patients (90% and 10%) had Grade 2 and Grade 3, respectively. Thus, relative incidence of Grade 2 and 3 anemia is more in Arm 2.

Neuropathy: In Arm 1, not even a single patient exhibited features of neuropathy, whereas, in Arm 2, 12/24 (50%) of the patients had neuropathy, with 8.5% each (1/24) were having Grade 1 and Grade 3, while remaining 83% (10/24) were having Grade 2 neuropathy. Thus, considerably more number of patients in arm 2 developed neuropathy as compared to patients in Arm 1 (50% versus nil, respectively; $P = 0.001$).

Alopecia: In Arm 1, the incidence of alopecia as a late toxicity was nil, whereas in Arm 2, 4/24 (17%) of the patients had alopecia and they were Grade 1 (3/4, 75%) or Grade 2 (1/4, 25%).

Miscellaneous: Apart from above-mentioned toxicities, various other adverse events such as cystitis, enteritis, and proctitis were also noticed in patients of both the arms from 3 months to 6 months of their follow-up. All of them were observed almost equally in both the arms without any statistically significant correlation. No patient from any of the two arms developed neutropenia as a late toxicity.

Discussion

Since carcinoma cervix is the most common gynecological cancer in developing countries including India, studies incorporating the use of ACT in LACC after CCRT in an attempt to improve survival merit consideration. In one such Asian study based on the use of ACT after CCRT in LACC, Ali *et al*.[22] reported the long-term outcome in lymph nodal–metastatic cervical squamous cell cancer after chemoradiation followed by ACT. CCRT consisted of cisplatin given once per week concomitantly with extended-field radiation therapy followed by high-dose rate BCT; while ACT comprised four courses of carboplatin and paclitaxel given every 3 weeks. The primary outcomes were local and distant failures. None of the patients had

local recurrence or distal failure after a minimum follow-up period of 3 years. The authors concluded that ACT after chemoradiation has a probable role in the management of lymph nodal–metastatic cervical cancer.

In our study, the use of injection paclitaxel and carboplatin (PC regimen) in postCCRT setting was well tolerated with manageable toxicities though some studies have found unfavorable toxicity profile of this regimen. Abe *et al*.[23] evaluated the efficacy and toxicities of the ACT with PC following cisplatin-based CCRT in patients with cervical cancer with lymphadenopathy (N1). Over a median 21.5months followup, no significant differences were found in the recurrence rate, PFS, OS, or median interval to recurrence with N1 cervical cancer patients between the two groups. Patients with paraaortic lymphadenopathy who received CCRT and ACT had a more favorable overall and diseasefree survival than those treated with CCRT alone. However, 16/17 patients developed Grade 3–4 leukopenia and 14/17 patients developed severe hematologic toxicity during ACT. The authors concluded that ACT consisting of full dose PC therapy after CCRT was not well tolerated in general and exhibited no benefit to N1 cervical cancer patients, but may be of therapeutic advantage over CCRT alone in cervical cancer patients with paraaortic lymphadenopathy.

In our study, only 3 patients had adenocarcinoma histopathology and most of the published data is based on results in squamous cell carcinoma of the cervix. Tang *et al*.[24] compared CCRT and adjuvant cisplatin-based chemotherapy with CCRT alone in 880 patients with clinical FIGO stages IIB-IVA cervical adenocarcinoma. The patients were randomized to receive either CCRT or chemoradiation with one cycle of neo-ACT with paclitaxel and cisplatin before receiving radiation and two cycles of consolidation chemotherapy with the same drugs after RT in 3-week intervals. 340 patients relapsed, with a median follow-up duration of 60 months. Patients who received chemoradiation with ACT showed a significantly longer disease-free ($P < 0.05$), cumulative survival ($P < 0.05$) and long-term local tumor control ($P < 0.05$). Patients who received CCRT alone had significantly more distant metastasis and pelvic failure than those who received chemoradiation with ACT ($P < 0.05$). The authors concluded that incorporating neoadjuvant and consolidation chemotherapy with paclitaxel and cisplatin into concomitant chemoradiation is highly effective and safe and treatment protocol for advanced cervical adenocarcinoma.

Apart from taxanes and platinum compounds which we used in our study, some other drugs have been studied in concurrent and adjuvant treatment in LACC, such as Gemcitabine, mitomycin C (MMC) and oral 5-fluorouracil (5FU). Alfonso Dueñas-González *et al*.[25] evaluated the role of the addition of gemcitabine to concurrent cisplatin chemoradiotherapy and as ACT with cisplatin in improving PFS at 3 years compared with current standard of care in LACC. The patients were randomly assigned to Arm A (cisplatin and gemcitabine weekly for 6 weeks with concurrent external beam RT followed by BCT, and then, two adjuvant 21-day cycles of cisplatin plus gemcitabine) or to Arm B of CCRT followed by BCT. 515 patients were enrolled (Arm A, $n = 259$; Arm B, $n = 256$). PFS at 3 years was significantly improved in arm A versus arm B. Grade 3 and 4 toxicities were more frequent in Arm A than in arm B (86.5% vs. 46.3%, respectively; $P < 0.001$), including two deaths possibly related to treatment toxicity in Arm A. The authors concluded that Gemcitabine plus cisplatin chemoradiotherapy followed by BCT and adjuvant gemcitabine/cisplatin chemotherapy improved survival outcomes with increased but clinically manageable toxicity when compared with standard treatment. In a similar Phase III study in 926 patients, Lorvidhaya *et al*.[26] found that MMC, and 5-FU together with conventional RT showed an improved survival rate when compared with conventional RT alone in patients with LACC.

Use of Cisplatin has been compared with Cisplatin-Paclitaxel (C + P regimen) in postRT cervical cancer in anecdotal studies. Moore *et al*.[9] studied whether C + P improved response rate, PFS, or survival compared with cisplatin alone in patients with stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix in postradiation therapy scenario. Among 264 eligible patients, 134 received cisplatin and 130 received C + P. The majority of all patients had prior radiation therapy. Objective responses occurred in 19% (6% complete plus 13% partial) of patients receiving cisplatin versus 36% (15% complete plus 21% partial) receiving C + P ($P = 0.002$). The median PFS was 2.8 and 4.8 months, respectively, for cisplatin versus C + P ($P < 0.001$). Grade 3–4 anemia and neutropenia were more common in the combination arm. The authors concluded that C + P is superior to cisplatin alone with respect to response rate and PFS with sustained QOL.

In our study, we used single agent injection cisplatin in concurrent setting which is considered as the standard of care. Doublet chemotherapy as part of CCRT in LACC has been tried anecdotally in the Indian scenario. Varghese *et al*.[2] assessed whether the combination of paclitaxel and cisplatin with radiation was feasible in Indian women with cervical cancer FIGO stages IB2 to IIIB; treated with weekly injections of cisplatin 30 mg/m^2 and paclitaxel 40 mg/m^2 for 4 weeks along with RT. A total of 25 patients were enrolled in this study. A total of 23 patients completed the intended treatment. There was a complete response rate of 88%, 12% were not available for response assessment. The major toxicity was Grade 3 diarrhea (48%). The mean duration of treatment was 58 days. The authors concluded that combination chemotherapy with cisplatin and paclitaxel along with RT in patients with LACC had

a high incidence of acute toxicity. There was no increase in immediate tumor response and PFS with this treatment regimen. Hence, this regimen offers no added benefit when compared to the chemoradiation with cisplatin alone.

Some researchers are concerned about toxicities of use of Inj Cisplatin in CCRT and have replaced it with injection carboplatin. Sangkittipaiboon[27] studied the treatment outcomes of CCRT with weekly carboplatin in 105 patients with LACC. The most acute toxicities were in Grade 1–2 (Grade 3 hematological toxicities were 3.80%). Complete response was achieved in 95 patients (90.5%). Among the 95 responders, 27 experienced recurrences: local recurrences in eight (8.4%), distant failure in 17 (17.9%), and both local and distant failure in two (2.1%). Five-year disease-free survival rate was 52.38% while 5-year OS rate was 56.19% (61.45%, 42.11%, and 0% in stage IIB, III, and IVA, respectively). The authors concluded that concurrent weekly carboplatin and radiation therapy yields high response rate with modest disease-free and OSs in LACC. The regimen is feasible with minimal toxicities but is not considered as the standard of care.

The PC regimen which we used here in the ACT has also been tried for NACT in LACC. McCormack *et al.*[28] investigated the feasibility of dose-dense NACT with PC regimen before CCRT and assessed the response rate to such a regimen. Patients received dose-dense carboplatin (AUC2) and paclitaxel (80 mg m^{-2}) weekly for six cycles followed by CCRT (40 mg m^{-2} of weekly cisplatin, 50.4 Gy, 28 fractions plus BCT). The primary end-point was response rate 12 weeks postCRT. Complete or partial response rate was 70% (95% confidence interval [CI]: 54–82) postNACT and 85% (95% CI: 71–94) postCRT. Overall and PFSs at 3 years were 67% (95% CI: 51–79) and 68% (95% CI: 51–79), respectively. Grade 3/4 toxicities were 20% during NACT (11% hematological, 9% nonhematological) and 52% during CRT (hematological: 41%, nonhematological: 22%). The authors opined that a good response rate is achieved by dose-dense weekly NACT with carboplatin and paclitaxel followed by radical CCRT; and is a feasible regimen as evidenced by the acceptable toxicity of NACT and by the high compliance to RT (98%).

Conclusion

Exhibition of ACT with injection paclitaxel and injectioncarboplatin-based protocol in locally advanced carcinoma cervix after the conclusion of CCRT followed by ICRT is a technically viable option with manageable toxicity and does not add on to any significant morbidity/mortality. Judicious follow-up and supervision is required for the patients who receive ACT so that the toxicity, if any, can be managed early in an outpatient or inpatient setting as clinically indicated. More multicentric studies should be envisaged in urban and rural settings, and data should be analyzed to evaluate further any benefit in OS and locoregional control by addition of ACT in locally advanced cervical carcinoma.

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Conflicts of interest

There are no conflicts of interest.

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