ORIGINAL ARTICLE

Life Saving New Modality in Advanced Cervical Carcinoma: Cisplatin Plus Radiation Therapy

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ABSTRACT

Background: Cervical carcinoma is linked with morbidity and high death rate among females globally. **Aim:** To determined the loco-regional control among advanced cervical carcinoma patients receiving concomitant chemo-radiation therapy.

Methodology: Following hospital's ethical committee approval, all patients (n=113) received cisplatin (40mg/m²) with radiation-therapyin two phases. All patients were evaluated for treatment response. Chi-square and Fisher's exact test was applied as p-value ≤ 0.05 was considered significant by using SPSS software, version 20.

Results: In present study, age (mean \pm SD) of the enrolled subjects (n=113) turned out to be 50.8 \pm 10.2 years with range 30 to 65 years. There was a good response shown to treatment given by the patients. In our study, 61 (54.0%) patients showed complete response, while in 32 (28.3%) patients partial response rate was observed. **Conclusion:** Treatment with concomitant chemo-radiation therapy showed good response (82.3%) in our enrolled patients. Hence, we concluded that CCRT treatment modality is more effective that radiation therapy alone in terms of response shown by the patients.

Keywords: Cervical carcinoma, Treatment Response and Concomitant Chemo-Radiation Therapy.

INTRODUCTION

Cervical malignancy is one of the most common malignancy in females globally. It is at second number after breast cancer occurring commonly cancer among women worldwide in low-and middle-income countries (LMICs) as well as worldwide. Globally, it caused approximately 234,000 deaths per year among Asian countries like Pakistan, India, Bangladesh etc. Though death rate is low in developed nations¹.

This inconsistency in death rate due to it among different countries is due to poor screening facilities. Results of Pap testing in low resource settings are neither reliable nor these screening test are done routinely. It is thought that use of vaccine against the human papilloma virus infection causing 99.7% cervical cancer cases, will decrease its incidence and death rate globally. It is thus a chief reason of morbidity and mortality from carcinoma. In 2018, new cases reported were 569847 and reported deaths were 311365/ year worldwide². In developing countries like Pakistan, India, Bangladesh and many others, it counts for more than 85% of these cases³.

Cervical carcinomas of various types are mainly due to many triggering factors like infections with viruses, family history, early sexual life, multiple partners, unprotected intercourses, and menstrual poor hygiene. They all spread human papilloma viruses⁴. Concurrent Chemo-radiation therapy (CCRT) has improved loco-regional control in even advanced carcinomas among developed countries.

Received on 15-02-2020 Accepted on 03-07-2020 In Pakistani population the evaluation of response treated with CCRT in locally advanced CA cervix has rarely been done. As we observe many CA cervix cases with short survival rate overall in our population. Thus we aimed to determine loco-regional control among advanced cervical carcinoma patients receiving concomitant chemoradiation therapy.

METHODOLOGY

This study with 113 enrolled female patients held at the department of radiation oncologyfollowing hospital's ethical committee approval. All patients received cisplatin (40mg/m²) with radiation-therapyin two phases. In phase I, all the patients were treated with a 2D simulation followed by external beam radiotherapy to the pelvis up to 45Gy in 25 fractions. Sample size of 113 was selected depending upon 327 hospital based cases of CA cervix, using a confidence level of 95% with a margin of error of 7.5% and an expected response rate of 50%⁵. Inclusion criteria included biopsy proven cases of Squamous cell or adenosquamous carcinoma of cervix with non-metastatic carcinoma cases. Those patients who failed to give informed consent, had any second malignancy and pregnancy were ruled out from the study.

Statistical analysis: The collected information was analyzed by SPSS version 23.0. Mean±SD was calculated for age. Frequency and percentages (%) were calculated for qualitative variables i.e. pre treatment loco regional disease FIGO stage on, histology, radiotherapy dose and response according to RECIST. Chi square test was used to determine the association of response rate with pretreatment loco-regional disease on histological basis. A p-value ≤0.05 was considered as significant.

RESULTS

Biopsy proven cases (113) of squamous cervix carcinoma were selected using non probability consecutive sampling. The mean age of the patients was 50.8 ± 10.2 years with range 30 to 65 years. The distribution of patients according to grades of cancer, TNM stage, risk group, concomitant ADT administration and radiation side effects according to CTCAE v.5 is given in table 1.

Table-1: Distribution with	respect to FI	GO stage,	histology	and radiotherapy
among enrolled subjects				

Variable	Category	Frequency	%age
Pre-	1B1	10	8.8
treatment	IB2	11	9.7
Loco	IIA	18	15.9
Regional	IIA 1	11	9.7
Disease	IIA2	12	10.6
FIGO Stage	lIB	16	14.2
on	lliB	14	12.4
(PV/PS/MRI)	NA	21	18.6
	Squmaous	82	72.6
Histology	Adenocarcinoma	23	20.4
	Adenosquamous	8	7.1
Radiotherapy	EBRT + Brachy therapy	42	37.2
dose	Parametrial + EBRT + Brachy therapy	71	62.8

After a follow up period of 3 months, repeat MRI assessment of all the patients were done for the assessment of loco-regional disease control. Good response according to RECIST was regarded as loco-regional effectiveness and poor response was regarded as ineffective treatment. 61 (54.0%) patients showed complete response, while in 32 (28.3%) patients partial response rate was observed. Out of 113, disease was stable in 14 (12.4%) patients whereas disease progression was observed in 6 (5.3%) patients. In current project, overall good response rate (82.3%) and poor response rate (17.7%) was shown as summarized in table-3

The response rate after treatment among different histology results (i.e., squamous, adenocarcinoma, adenosquamous) were compared by Fisher's exact test. Results revealed that there was no significant difference in response rate among different histology groups (Table 4).

Table	2.	Response	rate	according	to	RECIST
Table	۷.	response	iale	according	ιU	ILCI01

Category	Frequency	%age
Complete Response	61	54.0
Partial Response	32	28.3
Stable Disease	14	12.4
Progressive Disease	6	5.3

Table-3: Distribution of response to treatment given among enrolled patients			
Category	Frequency	%age	
Good Response	93	82.3	
Poor Response	20	17.7	

Table-4: Treatment response on histological basis among enrolled subjects

Histology	Response		Total	
riistology	Good	Poor	Total	
Squmaous	71 (86.6%)	11 (13.4%)	82 (100%)	
Adenocarcinoma	16 (69.6%)	7 (30.4%)	23 (100%)	
Adenosquamous	6 (75.0%)	2 (25.0%)	8 (100%)	
ToP balu et al	93 (82.3%)	20 (17.7%)	113(100%)	
P value 0.143				

DISCUSSION

Radiation Therapy(RT) was planned for cervical carcinoma patients as it is the fourth most common malignancy in females globally. It was done to determine the loco-regional control after radical concomitant chemo-radiation in carcinoma of cervix stages IB-IVA after 3 months of treatment. Thus efficacy and safety of radical concomitant chemo-radiation was measured among our female patients⁶. There was significant clinical response to RT in our patients. To study treatment outcomes related to concomitant chemo-radiation after 3 months is not a routine. This disease has high burden among females in Pakistan due to limited resources and awareness.

Our number of patients (n=113) were in conformity with one Chinese study who enrolled 174 patients to determine clinical outcomes in advanced cervical cancer patients receiving concurrent chemoradiotherapy.⁷ Paradoxically, in one Indian study subjects enrolled were 87 cervical cancer patients.⁸

Age (mean \pm SD) of our enrolled subjects turned out to be 50.8 \pm 10.2 years in conformity with one previous study where age of their enrolled subjects (mean \pm SD) was 43.8 \pm 08 years.⁹ In many researches, the median of age (45 years) was used 45 with range (25–66 years).⁵

They were given total radiation dose 45-60 Gy given for 25 days (5weeks). Our work was in lines with many previous studies who prescribed 50Gys RT to whole pelvis of their patients in their studies.⁹

In our project, the complete response was observed in 61 (54.0%) patients while in 32 (28.3%) patients partial response rate was observed as shown in table-3. Paradoxically, in one study the complete response was observed in 95.5% patients while 4.5% patients showed partial response to treatment in their studies.¹⁰

In our study, response was categorized into good and poor response to treatment given. Results showed that good response (82.3%) whereas poor response (17.7%) was shown among our enrolled patients. Paradoxically, in one study good response shown by their patients was 33.1% whereas 66.9% showed poor response.¹¹

CONCLUSION

Treatment with concomitant chemo-radiation therapy showed good response (82.3%) in our enrolled patients. Hence, we concluded that CCRT treatment modality is more effective that radiation therapy alone in terms of response shown by the patients. **Limitations:** For logistical reasons, we limited sampling from one centre, INMOL, Lahore that limited the precision and accuracy of the results of current study. We did not perform PET scan and had limited financial resources. Conflict of interest: None

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