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Original Research Article

Concurrent paclitaxel versus cisplatin with external beam radiotherapy in locally advanced head and neck cancer patients: a comparative study

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ABSTRACT

Background: The management of locally advanced head and neck cancer (HNC) requires a multidisciplinary approach. With a paradigm shift towards organ preservation, concurrent chemo radiation (CCRT) has taken a more centralized place in the management of HNC. This study aimed to compare the efficacy of CCRT with weekly paclitaxel versus weekly cisplatin in locally advanced squamous cell carcinoma of the head and neck (SCCHN).
Methods: This quasi-experimental study was conducted at the Department of Oncology, Khwaja Yunus Ali Medical College and Hospital (KYAMCH), Enayetpur, Sirajganj, from June 2019 to December 2020. A total of 64 patients were selected by purposive sampling technique. Study subjects were divided into 2 arms- arm A and arm B, each arm contained 32 patients.
Results: In Arm A, 53.12% showed complete response (CR) whereas in arm B, CR showed 62.5%. Partial response was 31.25% and 28.12% in Arm A & B, respectively. Stable disease was 9.37% & 6.25% in Arm A & B, respectively. Two patients in Arm A and one patient in Arm B showed progressive disease at the final follow-up. The difference was statistically not significant ($p>0.05$).
Conclusions: This study concludes that patients receiving paclitaxel showed comparatively more response to treatment than those receiving cisplatin. So, CCRT by low dose weekly Paclitaxel given in conventional fractionation can be substituted to concurrent Cisplatin in locally advanced SCCHN in terms of efficacy and some manageable local toxicities.

Keywords: External beam radiotherapy, Efficacy, Head and neck cancer, Histopathology

INTRODUCTION

Cancer is a heterogeneous group of diseases based on presentation and location but homogenous in cellular mechanisms. The core principle of cancer is abnormal and uncontrolled cell growth resulting in invading local sites or metastasizing to distant parts of the body.[1] According to the Cancer Registry Report 2015-2017 published by the National Institute of Cancer Research and Hospital (NICRH), a total of 14,044 newly diagnosed cancer patients attended at outpatient department in NICRH. Among them, total head and neck cancer (HNC) patients were 1,470 (10.5% of total patients) and male patients were 914 (62.17%) and female patients were 556 (37.82%). The most common site of the tumor was the lip and oral cavity 802 (54.56%), followed by the hypopharynx 202 (13.74%), oropharynx 188 (12.79%), nasopharynx 39 (2.65%) and larynx 17 (1.16%).[2] NCCN

guidelines recommended combined modality therapy for approximately 60% of patients with locally or regionally advanced disease at diagnosis.[3] Concurrent platinum-based chemoradiation regimens have demonstrated improved disease control rates compared to those obtained using radiotherapy alone and are the most commonly used chemotherapeutic agent in clinical use4 but with the cost of increased high-grade mucositis, weight loss, hematologic and renal toxicity. In efforts to enhance outcomes and pinpoint agents with reduced toxicity compared to platinum-based drugs, researchers have explored a range of newer and potent radio sensitizing chemotherapies administered concurrently with radiation therapy in patients with head and neck squamous cell carcinoma (HNSCC).The nitroimidazoles metronidazole, misonidazole, etanidazole, and nimorazole, which enhance the radiosensitivity of hypoxic cells, have also been extensively evaluated in phase I, phase II**,** and phase III trials. Newer agents undergoing evaluation include paclitaxel, docetaxel, ifosfamide, topotecan, vinorelbine, gemcitabine, and terapazamine.[5,6] The taxoids represent a new class of agents having both a specific chemical structure and mechanism of action.[7] Paclitaxel is one of the most active agents for SCCHN in metastatic and recurrent settings and is a radio sensitizer for the human SCCHN cell line. In a single small phase III trial, a weekly paclitaxel concurrent regimen appeared equivalent to a weekly cisplatin concurrent schedule. However, the data must be considered limited. In recent trials, paclitaxel has been studied concurrent with RT, as a prolonged infusion, weekly infusion, or in combination with different cytotoxic agents with long-term local control and survival in patients with SCCHN.[8] These have been studied and well-established in preclinical studies in several head and neck squamous cell lines.[9-11] This radio-sensitizing effect is seen even on exposure to a sub-cytotoxic dose as low as 10 nmol/l. Based on this background the present study may give us more information about another option of radiosensitizer in the management of advanced HNC. The aim of the study was to compare the efficacy of CCRT with weekly paclitaxel versus weekly cisplatin in locally advanced SCCHN.

METHODS

This quasi-experimental study was conducted at the Department of Oncology, Khwaja Yunus Ali Medical College and Hospital (KYAMCH), Enayetpur, Sirajganj, from June 2019 to December 2020. Patients who attended the KYAMCH oncology OPD were considered as the study population. A total of 64 patients were selected as study subjects as per inclusion and exclusion criteria. A purposive sampling technique was adopted in this study.

Inclusion criteria

Patients of age: 18 to 70 years and of both genders, linically diagnosed and histopathologically proved SCCHN, locally advanced (stage III or IV) disease, no previous history of treatment (surgery, chemotherapy or surgery), and patients having ECOG performance status up to 2 were included.

Minimum laboratory criteria were: hemoglobin more than 10 gm/dl or >60%, total WBC more than or equal to 4,000 cells/mm^3, platelet count more than or equal to 1, 50000/mm^3, serum bilirubin level less than 2 mg/dl, SGOT and ALP levels are not more than 2-3 times the upper limit, serum creatinine level equal to or less than 1.5 mg/dl, and creatinine clearance (CrCl) more than or equal to 60 ml/min.

Exclusion criteria

Patients with double primaries, pregnant or lactating woman, patient with serious concomitant medical illness including severe heart disease, uncontrolled diabetes mellitus, hypertension, or psychiatric illness, prisoner patients, and those who are not willing to be included in the study were excluded.

All data were collected using a pre-tested semi-structured questionnaire. Complete history & physical examination with special emphasis on the head and neck region. Histopathology or cytopathology reports (Biopsy/FNAC from tumor site). Necessary laboratory and radiological studies were done. Study subjects were divided into two arms- Arm A and Arm B. Each arm contained 32 patients. Arm A: CCRT has been given with weekly Cisplatin 40 mg/m2 in 500 ml normal saline over two hours about two hours before radiation treatment (RT). 500 ml normal saline along with steroid, anti-emetic, and H2 blocker was infused over one hour as prehydration. Post-hydration was given with one liter of normal saline along with a furosemide injection (20 mg) over 2 hours for each patient. Arm B: Concurrent chemotherapy with Paclitaxel 30 mg/m2 over one hour with normal saline in a glass bottle with codon set about four hours before RT. Patients were premedicated two days before chemotherapy with oral Dexamethasone and antihistamines. During the first 10 minutes of infusion pulse, blood pressure, and other vital signs were monitored carefully. All patients in both arms received EBRT 66 Gy 33 fractions two Gy per fraction five days per week in six and half weeks. After completion of treatment, patients were carefully followed up on the 6th, 12th, and 24th week respectively. Analysis of data was carried out by different statistical methods using a statistical package for social science (SPSS) 25.0 for Windows. After analysis, the data were presented in tables and charts. The p value of less than 0.05 was taken as significant. Ethical clearance was taken from the ethical committee of the Institutional Review Board of KYMCH. Informed written consent was taken from the participants.

RESULTS

Distribution of the patients according to age group 13 (40.63%) patients belonged to age 51-60 years in arm A and 12 (37.50%) in arm B. The mean age was found 53.4±8.2 years in arm A and 52.3±8.4 years in arm B. Only

6.25% and 9.8% of patients were below 40 years of age in both groups respectively. However, the difference was not statistically significant (p value >0.05) between the two groups (Figure 1). In this series, 52 (81.25%) patients were male and 12 (18.75%) were female. The male and female ratio was 4.3:1. Total of 25 (78.13%) patients were male in arm A and 27 (84.38%) in arm B. The difference was not statistically significant (p value >0.05) between the two groups (Figure 2).

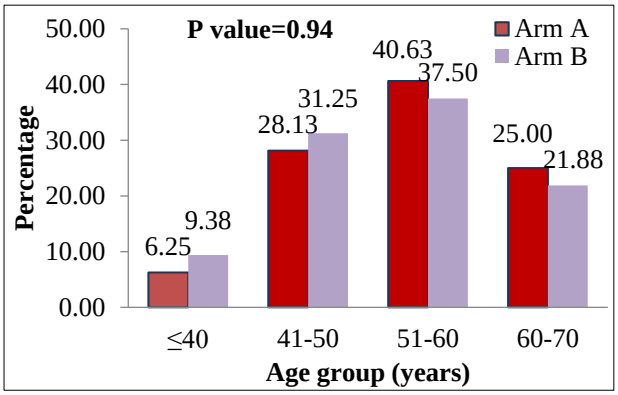

Figure 1: Distribution of the patients according to age group (n=64).

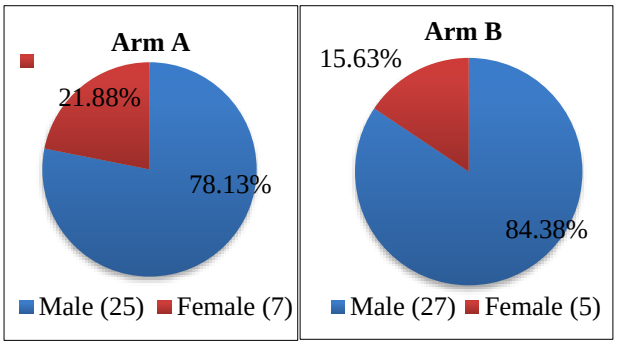

Figure 2: Distribution of the patients according to gender (n=64).

17 (53.13%) patients were found moderately differentiated in arm A and 13 (40.63%) in arm B. The difference was not statistically significant (p value >0.05) between the two groups. Poorly differentiated patients were less in both arms but the difference was not significant (Figure 3). Most of the patients were in stage III (59.38% and 56.25% in arm A and arm B respectively) and IVA (31.25% in arm A and 37.5% in arm B). However, the difference was not statistically significant (p value >0.05) between the two groups (Figure 4). The most common presenting complaints were voice change, sore throat, and neck swelling. Dyspnea, dysphagia, weight loss, and oral ulcer were also present but were not statistically significant (p>0.05) between the two groups (Table 1). In 1st follow-up, 13 (40.63%) patients were found to complete responses in arm A, and 17 (53.13%) in arm B. Radiological response was assessed in 2nd follow-up. 15 (46.88%) patients were found to complete response in arm A and 17 (53.13%) in arm B. In the final follow-up in the 24th week, the majority of patients showed complete response (53.13% in arm A and 62.50% in arm B). Only two (6.25%) patients in arm A and one (3.13) in arm B showed progression of disease. However, the difference between the two arms was not statistically significant (p>0.05). In the last follow up only three (9.38%) patients in arm A and two (6.25%) in arm B showed stable response. However, the difference was statistically insignificant (p>0.5) (Table 2).

Table 1: Distribution of the patients according to presenting complaints (n=64).

Presenting complaints	Arm A (n=32)		Arm B (n=32)		P value
	N	%	N	%	
Voice change	21	65.63	22	68.75	1.00
Pain oral cavity	10	31.25	13	40.63	0.43
Sore throat	21	65.63	19	59.38	0.61
Neck swelling	22	68.75	19	59.38	0.61
Dyspnea	1	3.13	2	6.25	0.50
Dysphagia	14	43.75	13	40.63	0.80
Weight loss	7	21.88	3	9.38	0.15
Oral ulcer	7	21.88	6	18.75	0.76

P value reached from the Chi-square test and Fisher's exact test

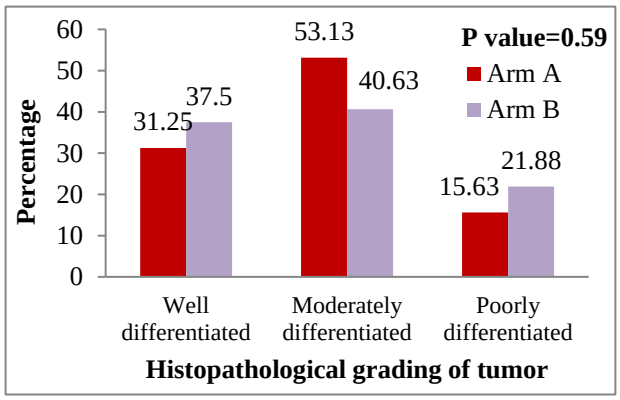

Figure 3: Distribution of the patients according to histopathological differentiation (n=64).

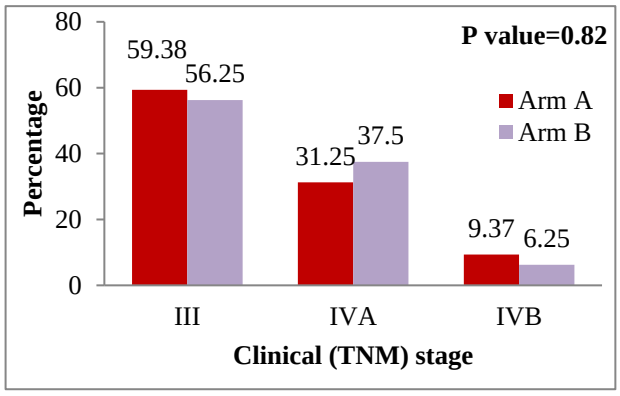

Figure 4: Distribution of the patients according to stage (n=64).

P value reached from the Chi-square test

Table 2: Distribution of the patients according to response in different follow up (n=64).

Clinical response	Arm A (n=32)		Arm B (n=32)		P value
	N	%	N	%	
1st follow-up (at 6th weeks)					
Complete response	13	40.63	17	53.13	0.60
Partial response	14	43.75	11	34.38	
Stable diseases	5	15.63	4	12.50	
Progressive disease	0	0.00	0	0.00	
2nd follow-up (at 12th weeks)					
Complete response	15	46.88	17	53.13	0.85
Partial response	11	34.38	9	28.13	
Stable diseases	4	12.50	5	15.63	
Progressive disease	2	6.25	1	3.13	
3rd follow-up (at 24th weeks)					
Complete response	17	53.13	20	62.50	0.84
Partial response	10	31.25	9	28.13	
Stable diseases	3	9.38	2	6.25	
Progressive disease	2	6.25	1	3.13	

P value reached from the Chi-square test

Table 3: Treatment response according to histopathological differentiation (n=64).

Histopathological differentiation and clinical response	Arm A (n=32)		Arm B (n=32)		P value
	N	%	N	%	
Well					
CR	7	70.0	7	58.33	0.87
PR	2	20.0	4	33.33	
SD	1	10.0	1	8.33	
Moderate					
CR	6	35.29	9	69.23	0.25
PR	7	41.18	3	23.08	
SD	2	11.76	0	0.00	
PD	2	11.76	1	7.69	
Poor					
CR	4	80.0	4	57.14	0.59
PR	1	20.0	2	28.57	
SD	0	0.0	1	14.29	

P value reached from the Chi-square test

Table 3 showed in the well-differentiated group seven (70.0%) patients were found to complete response in arm A and seven (58.33%) in arm B. In moderately differentiated tumors, six (35.29%) patients were found to complete response in arm A and 9 (69.23%) in arm B. Only four (80.0%) patients were found to complete response in arm A and four (57.14%) in arm B in the poorly differentiated group. The differences were not statistically significant (p value >0.05) between the two groups (Table 3). The above table showed complete response in both stage III (57.89% in arm A and 66.67% in arm B) and stage IV (46.15% and 57.14% in arm A and arm B respectively) was numerically more in paclitaxel arm than cisplatin arm. However, the difference is statistically insignificant. Only two (6.25%) patients in arm A and one (3.13%) patient in B showed progressive disease (Table 4).

Table 4: Treatment response according to stage of tumor (n=64).

Stage and clinical response	Arm A (n=32)		Arm B (n=32)		P value
	N	%	N	%	
III					
CR	11	57.89	12	66.67	0.72
PR	5	26.32	5	27.78	
SD	2	10.53	1	5.56	
PD	1	5.26	0	0.00	
IV					
CR	6	46.15	8	57.14	0.95
PR	5	38.46	4	28.57	
SD	1	7.69	1	7.14	
PD	1	7.69	1	7.14	

P value reached from the Chi-square test

DISCUSSION

In this series, the majority 13 (40.63%) patients belonged to the age 51-60 years in arm A (cisplatin group) and 12 (37.50%) belonged to the age group 51-60 years in arm B (paclitaxel group) respectively. The mean age was found 53.4±8.2 years in arm A and 52.3±8.4 years in arm B. Bari et al found mean ages were 54.7±7.91 and 56.6±7.9 in arm A and arm B respectively.[12] In this series, 52 (81.25%) patients were male and 12 (18.75%) were female. Maring et al described males as 81 (78.0%) and females as 23(22.0%).[13] In this study, in 1st follow-up, 13 (40.63%) patients were found to complete response in arm A and 17 (53.13%) in arm B. In 2nd follow-up, 15 (46.88%) patients were found to complete response in arm A and 17 (53.13%) in arm B. In 3rd follow-up at 24 weeks, 17 (53.13%) patients were found complete response in arm A and 20 (62.50%) in arm B. Only 9.38% in arm A and 6.25% of patients in arm B were stable disease. A total of 3 patients showed progressive disease in both arms. The differences were not statistically significant (p>0.05) between the two groups. A study by Das et al observed that on follow-up, up to 6 months, 51.85% of cases are disease-free in the control arm (cisplatin) and 50.66% of cases in the study arm (paclitaxel arm).[14] Persistent disease at the treatment end is 27.16% in the control arm and 25.33% in the study arm. Recurrence in primary only is 9.87% in the control arm and 8% in the study arm. Only nodal recurrence is 6.17% in the control arm and 12% in the study arm. Locoregional recurrence is 3.70% in the control arm and no locoregional recurrence in the study arm.

Kanotra et al reported that in group A CR was seen in 72.7% and PR in 27.3%.[15] In group B, CR was seen in 52% and PR in 48%. At the primary site, CR was seen in 34 out of 44 patients in group A (77.2%). This was significantly higher (p value <0.05) than that seen in group B (52%). Overall, the CR with paclitaxel was significantly higher (p<0.05) as compared to cisplatin. Drau et al stated that response assessment was done 6 weeks after the completion of treatment.[16] CR was achieved in 69.2% of patients in arm 1 versus 57.7% for arm II. PR was achieved in 11.5% versus 15.4% in arms I, and II respectively but the difference was statistically insignificant (p value=0.859). A 69.2% CR was achieved with paclitaxel versus 57.7% with cisplatin in patients with advanced HNSCC. In a study of Jain et al observed that response assessment was done after 1 month of completion of treatment.[17] CR rates were 73 and 64% respectively for arm A and arm B. There was no statistically significant difference observed in the groups (level of significance p<0.05). On follow-up of 3-10 months 59 and 42% of cases are alive and disease-free in arms A and B respectively. A 73% CR was achieved with paclitaxel versus 64% with cisplatin in patients with highly advanced HNSCC.

Limitations

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community. Moreover, the study was a non-randomized quasi-experimental study, it failed to prevent selection bias.

CONCLUSION

This study concludes that patients receiving paclitaxel showed comparatively more response to treatment than those receiving cisplatin. So, CCRT by low dose weekly Paclitaxel given in conventional fractionation can be substituted to concurrent Cisplatin in locally advanced SCCHN in terms of efficacy and some manageable local toxicities.

Recommendations

CCRT with weekly paclitaxel may be considered in the treatment of locally advanced SCCHN by considering clinical and radiological outcome profiles. Further studies in multiple centers of Bangladesh with larger sample sizes and ample time should be carried out to get robust data.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Weinberg RA. The Biology of Cancer. 2nd Edition. W. W. Norton & Company. 2013.
2. National Institute of Cancer Research & Hospital, Hospital Cancer Registry Report 2015-2017. Mohakhali, Dhaka. Available at: https://nicrh.gov.bd/images/reports/5bd09-hbcr-2015-2017. Accessed on 12 September 2024.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines Oncology. 2020. Available at: www.nccn.org/professionals/physician_gls/default.aspx. Accessed on 12 September 2024.
4. Pignon JP, Le Maitre A, Maillard E, Bourhis J; MACH-NC Collaborative Group. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): an update on 93 randomized trials and 17,346 patients. Radiother Oncol. 2009;92(1):4-14.
5. Overgaard J, Hansen HS, Overgaard M, Bastholt L, Berthelsen A, Specht L, et al. A randomized double-blind phase III study of nimorazole as a hypoxic radiosensitizer of primary radiotherapy in supraglottic larynx and pharynx carcinoma. Results of the Danish Head and Neck Cancer Study (DAHANCA) Protocol 5-85. Radiother Oncol. 1998;46(2):135-46.
6. Forastiere AA, Shank D, Neuberg D, Taylor SG 4th, DeConti RC, Adams G. Final report of a phase II evaluation of paclitaxel in patients with advanced squamous cell carcinoma of the head and neck: an Eastern Cooperative Oncology Group trial (PA390). Cancer. 1998;82(11):2270-4.
7. Schrijvers D, Vermorken JB. Role of taxoids in head and neck cancer. Oncologist. 2000;5(3):199-208.
8. Citrin D, Mansueti J, Likhacheva A, Sciuto L, Albert PS, Rudy SF, et al. Long-term outcomes and toxicity of concurrent paclitaxel and radiotherapy for locally advanced head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2009;74(4):1040-6.
9. Pradier O, Laurent D, Schmidberger H, Rave-Fränk M, Rubisch K, Krebeck M, et al. In vitro study of a paclitaxel-radiotherapy combination on a human epidermoid tumor cell line. Cancer Radiother. 1999;3(1):51-6.
10. Smith RE, Thornton DE, Allen J. A phase II trial of Paclitaxel in squamous cell carcinoma of the head and neck with correlative laboratory studies. Semin Oncol. 1995;22(3):41-46.
11. Posner MR, Haddad RI, Wirth L, Norris CM, Goguen LA, Mahadevan A, et al. Induction chemotherapy in locally advanced squamous cell cancer of the head and neck: evolution of the sequential treatment approach. Semin Oncol. 2004;31(6):778-85.
12. Bari MA, Alam S, Sharmin S, Nahar S, Uddin J, Aslam N. Outcome of Concurrent Chemoradiotherapy and Radiotherapy Alone Following Induction Chemotherapy in Locally Advanced Squamous Cell Carcinoma of Head and Neck. Bangl Med Res Council Bull. 2018;44(2):93-7.
13. Posner MR, Haddad RI, Wirth L, Norris CM, Goguen LA, Mahadevan A, et al. Induction chemotherapy in locally advanced squamous cell cancer of the head and neck: evolution of the sequential treatment approach. Semin Oncol. 2004;31(6):778-85.

14. Das TK, Chatterjee K, Das S. A prospective comparative study. International Journal of Medical Science Public Health. 2020;9(1):97-100.
15. Kanotra SP, Kanotra S, Gupta A. Chemoradiation in advanced head and neck cancers: a comparison of two radiosensitizers, Paclitaxel and Cisplatin. Indian J Otolaryngol Head Neck Surg. 2011;63(3):229-36.
16. Drau HK, Devi YS, Singh LJ. A study of weekly paclitaxel vs weekly cisplatin with concomitant chemoradiation in locally advanced head and neck cancer. Int J Res Med Sci. 2017;5(11):4895-902.
17. Jain RK, Kirar P, Gupta G, Dubey S, Gupta SK, Goyal J. A comparative study of low dose weekly paclitaxel versus cisplatin with concurrent radiation in the treatment of locally advanced head and neck cancers. Indian J Cancer. 2009;46(1):50-3.

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