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A prospective comparative randomized study comparing effect of induction chemotherapy (IC) followed by concurrent chemoradiation (CTRT) versus standard concurrent chemoradiation in locally advanced stage III & IV (M0) head and neck squamous cell cancer (LAHNSCC) patients

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Abstract

Introduction: Concurrent chemoradiation is currently the standard of care in LAHNSCC. Induction Chemotherapy (IC) causes tumor down staging, facilitating organ preservation, decreasing possibilities of residuals & recurrences and potential to prevent distant metastasis albeit at the cost of increased toxicities. Proposed study compared IC followed by CTRT versus CTRT alone in locally advanced, unresectable HNSCC to evaluate treatment response, toxicities and Progression Free Survival (PFS).

Materials and method: Patients with LAHNSCC of oral cavity, oropharynx, larynx & hypopharynx (AJCC Stage III-IVB) enrolled in study from April 2019 to August 2020 were randomized into two arms (84 in each). Study Arm A patients received three cycles of induction chemotherapy(IC) Paclitaxel 175mg/m^2 and Cisplatin 75mg/m^2 at three weekly interval followed by CTRT or CTRT alone in Control Arm B. EBRT dose was 66 Gy in 33# on Telecobalt along with weekly Inj. Cisplatin 30mg/m^2.

Results: After IC, Overall response was 76.2% (CR 21.43% & PR 54.76%). Response evaluation was done after 6 months of completion of CTRT in both arms showed complete response (CR) 67.86% & 52.40% in Study arm A & Control arm B respectively while partial response (PR) was 23.81% & 38.09%. Overall response rate (OR=CR+PR) was 91.67% in Study arm and 90.47% in Control arm.CR was better in study arm but not statistically significant. Grade ≥ 3 acute toxicities included nausea & vomiting (17.86%), myalgia (5.9%), neutropenia (5.9 %), and anemia (4.8%) during IC. During CTRT acute toxicities like

nausea/vomiting, mucositis, dermatitis were more in arm A but statistically not significant.

Conclusion: We conclude that Induction chemotherapy paclitaxel & cisplatin with sequential chemoradiation is more suitable in terms of complete response rate (CRR), compliance with manageable toxicity in LAHNSCC.

Keywords: Induction chemotherapy, Concurrent chemoradiation, complete response rate.

INTRODUCTION

Cancer is second leading cause of death globally (first cardiovascular diseases) and currently the cause of 12% of all deaths (estimated 9.6 million deaths in 2018) worldwide. Overall, 60% of global head and neck cancers (excluding esophageal cancers) occur in Asia especially in India. In India, cancer ranks third as a cause of death and accounts for 9.5% (3.8 million) of all mortality[1]. Head and Neck Carcinomas constitute the most common malignancy amongst men and 17.1% overall as compared to the developed countries (around 4.65%). More than 2 lakh new cases of head and neck cancer are diagnosed each year in India with 1.4 lakh deaths (almost 15%) in a year [3].The vast majority present in locally advanced stages i.e. stage III & IV with only 25-30% presenting in early stages (GLOBOCAN 2018)[2,3]. Due to advanced disease, these tumors can cause varying degree of functional and cosmetic deformity and can be permanent despite best treatment.

Oral cancer is the most common type of HNC, accounting for over 60% of all HNSCC in the country[4,5]. Almost 1.20,000 cases are diagnosed annually. Prognosis is poor for LAHNSCC. Among treated patients almost 8 to 10% have residual disease, 40% to 60% of patient with relapse/local disease recurrence within 2 years and 30 to 50% of patients live for less than 3 years despite surgery or radiation therapy or both in LAHNSCC.

Multiple trials established superior role of CTRT over RT alone for LAHNSCC in terms of improvement of progression free survival & overall survival. The MACH-NC meta-analysis updated in 2009[4] proved an improved absolute survival, 4% at 5 years in advanced HNSCC with higher benefit 8% using chemotherapy concomitantly to radiotherapy over radiotherapy alone. Induction chemotherapy followed by curative chemoradiotherapy has not demonstrated superior clinical results in comparison to concomitant chemo-radiation in most trials. However NACT can help to reduce the initial bulk of disease, thereby improvement in symptoms and quality of life and results in better organ preservation in extensive locoregional disease with overt symptoms. NACT is also beneficial in control of distant metastasis as well as in achievement of more chances of complete response (CR).

Although TPF is widely used as combination of use for induction chemotherapy in head and neck cancers because of edge they have in terms of disease response and possible survival benefit over other combinations but incidence of toxicities remains considerable. Toxicity imposes a financial burden on patient's family and healthcare system in general.

This study was conducted to test effectiveness of paclitaxel and cisplatin based IC followed by conventional CTRT in comparison to conventional CTRT alone in LAHNSCC in terms of locoregional response and toxicities.

In our settings patients tolerated a combination of paclitaxel and cisplatin or carboplatin fairly well. Toxicities are manageable. The main side effect of paclitaxel-cisplatin combination was nausea/vomiting, peripheral neuropathy, myalgia.

Materials and Methods

Study Area: Department of Radiation-Oncology, S.M.S. Medical College and attached group of hospitals, Jaipur, Rajasthan

Study Period: The recruitment of patients was started after approval of research review board and institutional committee from May 2019 to August 2020 and thereafter 4 months period taken for analysis of collected data.

Study Type and Design: Hospital based prospective comparative interventional study

Study Universe

A total of 168 patients of biopsy proven (oral cavity, oropharynx, larynx, hypopharynx) previously untreated inoperable locally advanced head & neck cancers (AJCC TNM group stage III, IV A & B) who attended Out Patient Department of Radiation-Oncology, S.M.S. Hospital, Jaipur. Eligible patients were randomized by chit & box method with replacement into two treatment groups. Study group (Arm A) 84 patients treated with three cycles of NACT (Inj. Paclitaxel 175 mg/m2 IV infusion over 3hrs followed by Inj. Cisplatin 75 mg/m2 over 1 hour repeated at 21 days interval) followed by concurrent chemoradiotherapy with weekly cisplatin 30 mg/m2 while Control arm (Arm B) received only concurrent chemoradiotherapy with weekly cisplatin 30 mg/m2. Radiotherapy consisted total dose of 66Gy in 33 fractions (2Gy daily fraction and five fractions per week) in both groups by conventional Telecobalt machine Bhabhatron.

Sample Size

Sample size was calculated 84 subjects each of two groups at alpha error 0.05 and power 80% assuring complete response rate in study group (IC+CTRT) and control group (CTRT) respectively 60.42% & 38.88% as per seed article. So further study purpose, 84 patients in each group were taken.

Inclusion Criteria

- Stage III to IVB histopathologically proven inoperable locally advanced head and neck squamous cell carcinoma.
- Age 25-70 years.
- Either sex.
- ECOG (Eastern Cooperative Oncology Group) performance status 0 to 2.
- Patients willing to give written informed consent.
- Patients fit to receive concurrent chemoradiotherapy with following parameters :
  - Hemoglobin> 9 gm/dl.
  - Absolute neutrophil count >1500 cells/mm^3.
  - Platelet count > 1lac cells/mm^3.
  - Serum bilirubin < 1.5 times upper limit of normal.
  - Serum creatinine<1.4 mg/dl.

Exclusion Criteria

- Head and neck malignancy other than squamous cell carcinoma of oral cavity, oropharynx, larynx, hypopharynx.
- No previous history of treatment with any of following modalities-surgery, radiotherapy, chemotherapy for head and neck cancer. No any other concurrent malignancies.
- No cardiac abnormality or any uncontrolled intercurrent co-morbidity.
- Patients were excluded if they had already been treated or metastatic or recurrent disease.

Patient Evaluation

- History and physical examination
- Histopathological examination
- CBC, kidney and liver function tests.
- HIV/HBsAg/HCV

- Chest radiograph/CECT CHEST
- Complete ENT evaluation including FOL
- CECT/MRI of head and neck

Selection of Patients

- A total of 168 locally advanced stages III to IVB LASCCHN fulfilling the eligibility criteria were selected.
- Patients were randomly assigned by Chit & box method with replacement into two treatment groups:

➢ Group A- Study group -84 patients

➢ Group B- Control group -84 patients

Induction Chemotherapy and Chemoradiation Schedule

All patients were pre-medicated before stating of NACT with ondensatron, dexamethasone, ranitidine and pheniramine. Inj G-CSF administration after 24hours of each induction chemotherapy cycle was implemented in study.

- Group A (Study arm): Patients group A was treated with three courses of paclitaxel (175mg/m2) and cisplatin (75mg/m2) for 3 cycles at every 21 days interval followed by concurrent chemoradiation (cisplatin 30mg/m^2 IV infusion every week with conventional radiotherapy).
- Group B (Control arm): Patients group B was treated with concurrent chemoradiation (cisplatin 30mg/m^2 IV infusion every week with conventional radiotherapy).

Radiation Technique

Curative irradiation started 3-4 weeks after last cycle of Induction Chemotherapy. External beam radiotherapy were given in total dose of 66 Gy in 33# (200cGy/fraction 5days in a week for 6.5 weeks) with conventional Telecobalt-60 machine to Gross Tumor Volume. We used two lateral fields to treat Gross Tumor and neck. .

Assessment of Tumor Response

Clinical evaluations were done after each cycle of NACT while radiological evaluations were done after 3 weeks of last cycle of NACT by CECT/MRI. All patients underwent dental evaluations before irradiation. Response was evaluated at completion, 3rd and 6th months of completion of chemoradiotherapy in both arms based on clinical examination, ENT evaluation and contrast enhanced CT/MRI scan of head and neck of each patient. Biopsy or FNAC was taken from any suspicious clinical or radiological residual tumour at primary site or nodal area. Then patients were categorized as per RECIST Criteria (Response Evaluation Criteria in Solid Tumors).

Assessment of Toxicities

All patients were examined once in 3 week during induction chemotherapy in study group & weekly during chemoradiation treatment in both groups. Any delay causing treatment interruption was noted and necessary gap correction for radiotherapy done. Patients were monitored for signs and symptoms of toxicity by physical examination and laboratory blood cell counts. Toxicities were graded according to Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 in Arm A during NACT and both arms during CTRT and grade reported was worst observed grade of each toxicity that occurred to patient. Appropriate measures were taken for management of toxicities.

Supportive care was given to all patients in form of dietary measures, antibiotics, multivitamins, anti-inflammatory drugs , gargle bottles and IV fluids after hospitalization if need to during treatment.

Statistical Analysis

Quantitative data was expressed in means with standard deviation and qualitative data was expressed in percentage proportions. Significance of difference in means of two groups was inferred with unpaired T test. Signification of difference in means at various follow up period was inferred with repeated ANOVA test. Significance of difference in proportion in two groups was inferred with Chi-square test. For significance P value less than 0.05 will be considered as significance.

The results of study group was analyzed & compared with control group in terms of various aspects like compliance, side effects, tumor response, & local disease status. The data thus collected were analyzed by using Chi-square test for correlation.

Results

Patient characteristics: All baseline patients and tumors characteristics were comparable between two arms and listed in Table 1.

Table 1: Patients baseline characteristics between study and control arm

Patients characteristics	Study Arm A (n=84), n (%)	Control Arm B, n (%)	P-value
Age			
Mean age± SD	52.08± 10.85	53.32± 10.76	Chi-square=0.6445 p-value=0.958 (NS)
Range	27-30 years	26-70 years	
Gender			
Male	68 (80.9%)	70 (83.3%)	Chi-square=0.1623 p-value=0.687 (NS)
Female	16 (19.1%)	14 (16.7%)	
ECOG PS			
0	49 (58.3%)	45 (53.6%)	Chi-square=0.4198 p-value=0.811 (NS)
1	31 (36.9%)	34 (40.5%)	
2	4 (4.76%)	5 (5.9%)	
Primary site			
Oral cavity	16 (19%)	18 (21.4%)	Chi-square=0.4234 p-value=0.935 (NS)
Oropharynx	34 (40.5%)	31(36.9%)	
Hypopharynx	13 (15.5%)	15 (17.9%)	
Larynx	21 (25%)	20 (23.8%)	
T-stage			
T1	0	0	Chi-square=0.8289 p-value=0.661 (NS)
T2	6 (7.1%)	9 (10.7%)	
T3	39 (46.4%)	40 (47.6%)	

T4	39 (46.4%)	35 (41.7%)	
N-stage			
N0	2 (2.4%)	5 (5.9%)	Chi-square=1.3846 p-value=0.709 (NS)
N1	32 (38.1%)	32 (38.1%)	
N2	47 (55.9%)	44 (52.4%)	
N3	3 (3.6%)	3 (3.6%)	
Histopathological grade			
G1	19 (22.62%)	24 (28.57%)	Chi-square=1.0029 p-value=0.606 (NS)
G2	61 (72.62%)	55 (65.48%)	
G3	4 (4.76%	5 (5.95%)	
Clinical stage			
III	21 (25%)	26 (31%)	Chi-square=1.5676 p-value=0.457 (NS)
IV A	57 (67.86%)	55 (65.48%)	
IV B	6 (7.14%)	3 (3.57%)	

Induction chemotherapy

In Study Arm A, all 84 patients completed planned 3 cycles of induction chemotherapy of Paclitaxel 175mg/m2 and Cisplatin 75mg/m2 three weekly. The overall clinical response obtained after completion of three cycles of induction chemotherapy in study arm (n=84) was 76.2% (64 patients) including complete response and partial response 21.43% (18 patients) & 54.76% (46 patients) respectively. Patients having stable disease were 14 (16.67%) while 6 patients (7.14%) progressed onto induction chemotherapy.

Patients with laryngeal and hypopharyngeal tumors were noted to have highest clinical response rates at primary site followed by oropharyngeal tumors whereas oral cavity tumors had lowest response.

Table 2: Treatment response after NACT/IC in study arm A

Response after NACT n=84 (%)	CR	PR	SD	PD
	18 (21.4%)	46 (54.8%)	14 (16.7%)	6(7.1%)

During induction chemotherapy, incidences of chemotherapy related toxicities were acceptable. In study arm during NACT (n=84), nausea & vomiting (17.86%), neutropenia (5.95%), anaemia (4.8%) and diarrhea (3.57%) appeared as grade 3 acute toxicities while peripheral neuropathy grade 1 symptoms was complained in 5 patients. Incidence of toxicities was higher in 2nd& 3rd cycle of NACT except nausea & vomiting & diarrhea (almost 50% reduction all grades in 3rd cycle of NACT). Incidence of febrile neutropenia was zero. No patients died while receiving chemotherapy. Delays in administration of induction chemotherapy cycles were not noted beyond three days in any patient.

Sequential Chemoradiation

All patients (168) started chemoradiation within an average of 3.5 weeks (range 3 to 5) of last cycle of chemotherapy. No delays in initiation of chemoradiation because of chemotherapy induced toxicity were noted. All patients successfully completed chemoradiation.

During chemoradiation, total 11/168 (6.55%) patients needed hospitalization for toxicity related causes including 8 in study arm and 3 in control arm. Among them 3/84 (3.57%) patients developed febrile neutropenia along with grade 3 mucositis, severe dysphagia and aspiration in study arm. Two patients hospitalized for emergency tracheostomy one in each arm. Toxicity related breaks occurred in 13 & 8 patients in study and control arm respectively during chemoradiation. No treatment related deaths occurred. Patients received six cycles of weekly cisplatin were 84.52% & 92.86% in study and control arm respectively.

Table 3: Treatment response

Response		Study Arm A (IC+CTRT)		Control Arm B (CTRT)		P-value
		No.	%	No.	%	
Response at 4-6 week after Treatment	CR	54	64.29	41	48.81	0.226 (NS)
	PR	23	27.38	35	41.67	
	SD	5	5.95	6	7.14	
	PD	2	2.38	2	2.38	
Follow up at 4 months	CR	57	67.86	44	52.38	0.210 (NS)
	PR	20	23.81	32	38.09	
	SD	5	5.95	6	7.14	
	PD	2	2.38	2	2.38	
Follow up at 6 months	CR	57	67.86	44	52.38	0.166 (NS)
	PR	20	23.81	32	38.09	
	SD	4	4.76	3	3.57	
	PD	3	3.57	5	5.96	

The clinical response rates obtained one month after completion of chemoradiation revealed that complete response (CR) was achieved in 54 patients (64.3%) in the Study group and 41 patients (48.8%) in the Control group. The partial response (PR) rates were 23 patients (27.4%) in Study group and 35 patients (41.7%) in Control group. Both CR and OR rates were not found to be statistically significant (p = 0.226).

At 4 months follow up period, CR was achieved 57 patients (67.9%) in the Study group and 44 patients (52.4%) in the Control group. The partial response (PR) rates were 20 patients (23.8%) in Study group and 32 patients (38.1%) in Control group. At 6 months follow up, CR & PR were similar as 4 months but three out of six stable disease patients converted in progressive disease patients In control arm while in study arm one out of five stable disease patients converted to progressive disease. The six months PFS were 96.34% and 94.04% in study arm control arm respectively.

Loco-regional control was better in study arm as compare to control arm at 6 months.

Table 4: comparison of toxicities between two arms during chemoradiation

Adverse events	Study Arm A (n=84) , n (%)			Control Arm B (n=84) , n (%)			P value
	Grade 1	Grade 2	Grade≥3	Grade 1	Grade 2	Grade≥ 3	(only G≥3)
Anemia	42	23	2	45	19	2	1 (NS)
Neutropenia	18	5	0	15	1	0	-
Thrombocytopenia	4	5	0	6	3	0	-
Nephrotoxicity	17	5	0	8	0	0	-
Nausea/Vomiting	35	31	8	26	13	3	.119 (NS)
Mucositis	6	44	34	12	48	24	.105 (NS)
Dermatitis	42	30	12	48	28	8	.341 (NS)
Dysphagia	19	42	28	23	40	21	.234 (NS)
Xerostomia	65	19	-	66	18	-	-

In cumulative hematological toxicities anaemia was most common toxicity. In both arm 50% patients developed grade 1 anaemia while grade 2 anaemia was present in almost one quarter patients. Thrombocytopenia was least common hematological toxicity which was present in 10.7% patients in both arms. Neutropenia grade≤2 was present in 27.4% & 19% patients in respective arm. In study arm nephrotoxicity grade ≤2 was present in 26.2% patients while in control arm shown only grade 1 nephrotoxicity (9.5%).

In cumulative non hematological toxicities, nausea vomiting grade≥2 was present in 46.4% & 19.1% patients in study and control arm respectively which was statistically significant in 6th & 7th week of chemoradiation. Most of patients developed grade 1 mucositis, dysphagia, xerostomia and skin reaction 3rd week onward which converted to grade 2 or 3 toxicity later during chemoradiotherapy course. An average 30% patients developed grade 3 mucositis & dysphagia in both arms, more in study arm but statistically not significant. All grade 3 toxicities were managed conservatively which required hospitalization.

None of cumulative hematological and non-hematological toxicities were statically significant.

Discussion

Induction chemotherapy to curative chemoradiation in treating HNSCC had been studied in several trials. At present, no schedule can be considered standard of care in this setting. The indications for NACT are not well defined in clinical practice while role of CTRT as an effective treatment option in inoperable LAHNSCC has been proved long back with few drawbacks such as chances of residual/recurrence of tumors and distant metastasis[6,7]. Most patients with HNC present at locally advanced stages. Induction chemotherapy is used keeping in mind that it could help in control of micrometastasis and might downstage the tumor and hence helping in improvement of normal tissue sparing during radiotherapy planning as well as making tumors operable[8,9]. Conformal radiotherapy and IMRT facilities are not widely available and having high cost if available so here induction chemotherapy make

normal tissue sparing possible during treatment on conventional Telecobalt.

Most of trials (TAX 323[10], TAX 324[11], Hitt R et al[13]) and meta-analysis (Qin et al[14], Blanchard et al[15]) compared three drug regimen (TPF) versus two drug regimen (PF) as induction chemotherapy and found better results with three drug regimens.

The TAX 323 trial[10] revealed benefits of adding Docetaxel to PF as NACT before radiotherapy in terms of significantly higher ORR, PFS and OS with TPF versus PF arm in unresectable LAHNSCC. However there were higher neutropenia in TPF arm and thrombocytopenia and stomatitis in PF arm. The TAX 324 trial[11] also showed significantly higher median OS, PFS and LRC along with grade 3 or higher neutropenia and thrombocytopenia in TPF arm compared to PF arm. The long term results of TAX 324[12] came out with median follow-up period of 72 months which also showed significantly better OS and PFS with TPF.

A phase III trial[13] by R. Hitt demonstrated that NACT followed by CTRT significantly increases TTF (Time to Treatment Failure) and loco-regional control compared with CTRT alone in LAHNSCC patients. Another study by Paccangnella et al[16] over 101 patients of LAHNSCC, CR rates were significantly better with TPF followed by CTRT compared to CTRT alone with no negative impact on CTRT feasibility in NACT arm. Toxicities were similar in both arms.

On the contrary, studies including Haddad et al[17] phase III trial (PARADIGM study), Balerampas et al[18] retrospective analysis, Cohen W et al[19] (DeCIDE trial), Hitt et al[20] phase III trial, meta-analysis by Zhang et al[21] & Budach et al[22], study by Takacsi-Nagy et al[23] compared CTRT alone versus NACT followed by CTRT which did not show statistically significant differences in OS, PFS, ORR or LRC between IC followed by CTRT versus CTRT alone in LAHNSCC. Most of these trials showed grade 3-4 neutropenia with decreased distant metastasis and improved CR in NACT arm compare to CTRT alone.

Hitt et al[20] (2004) replaced Docetaxel with Paclitaxel and significantly better CRR and median TTF in Paclitaxel arm (PCF) versus CF.

Most of regimen consisting 5-FU which is commonly causing mucositis and diarrhea so that alternative treatment regimen platinum with taxanes (paclitaxel-carboplatin, paclitaxel-cisplatin) were used omitting 5-FU.

In our study, we used paclitaxel and cisplatin as induction chemotherapy regimen. After induction therapy overall response rate was 76.2% (64 patients) with complete and partial response rates of 21.43% and 54.76% respectively. These results overlap with high response rates observed in other studies in which paclitaxel is used as induction combinations[5,24]. High CR 64.3% has been observed at completion of chemoradiation in study sequential chemoradiation arm. Responses were radiologically evaluated two month and four month after completion of chemoradiation. The primary endpoint was complete radiographic response The study showed sequential chemoradiotherapy arm (NACT followed by CTRT) to be better than concurrent chemoradiation arm (CTRT alone) with higher complete response rates 64.3% (54 patients) for sequential CTRT versus 48.8% (41 patients) for concurrent CTRT arm. At 4months, CR increased 67.9% & 52.4% in sequential & concurrent chemoradiotherapy arm respectively. Locoregional control was better in NACT arm as compare to CTRT alone but was not statistically significant. Three out of six stable disease patients converted in progressive disease in concurrent chemoradiotherapy group while

one out of five stable disease patients converted to progressive disease in sequential chemoradiotherapy group. Loco-regional control was better in study arm as compare to control arm at 4 months. Three patients (3.57%) developed febrile neutropenia in sequential chemoradiation arm and all survived with meticulous care in ICU with support of broad spectrum antibiotics and G-CSF support. Stefano Pergolizzi et al[25] conducted study with IC paclitaxel along with cisplatin 3 courses at 21 days interval in advanced HNSCC and noted ORR 74.4% (32 patients) including CR 20.93% & PR 53.48% almost comparable to our study. At completion of CTRT overall responses were 97.7% (42 patients) including CR 46.5% & PR 51.2%. Aparna G et al[26] conducted a study with paclitaxel-cisplatin 3 courses three weekly interval and found overall response rate after IC was 89.2% and at chemoradiation completion was 89.7% (CR 85.8%) with febrile neutropenia 3.4%(7/207). Both ORR and incidence of febrile neutropenia was similar to our study. In an analysis by M. Nikam ORR after IC and after chemoradiation was 89.1% & 83.34% respectively but higher grade 3 mucositis and skin reaction compare to our study.

No significant differences in response rate (ORR & CR) were observed among patients who received paclitaxel-cisplatin or TPF. The results indicate paclitaxel-cisplatin is more tolerable. The strategy of chemo selection helps to reduce unwanted toxicity in patients by identifying only those who derive benefit in terms of disease control and functional outcomes[27,28]. A regimen like paclitaxel-cisplatin combination which is more compliant, cost effective and less toxicity is of utmost importance in our scenario, and carries significance in treatment of locally advanced head and neck cancer.

However results require further evaluation owing to limited number of patients being studied and shorter duration of follow-up. Our patients received conventional radiotherapy. Exploration should be done on conformal techniques and IMRT. Perhaps result might differ with advanced radiotherapy techniques.

Conclusion

In conclusion results of our study indicate induction chemotherapy with paclitaxel and cisplatin followed by concurrent chemoradiation is superior to chemoradiation alone in terms of complete radiological response and locoregional control with acceptable toxicity profile. It can be of some potential benefit in patients of LAHNSCC to downstage tumor thereby decreasing symptoms with improved treatment response.

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