International Journal of Current Advanced Research
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 10; Issue 03 (A); March 2021; Page No.23982-23988
DOI: http://dx.doi.org/10.24327/ijcar.2021.23988.4753

Research Article

A PROSPECTIVE COMPARATIVE STUDY TO COMPARE RESPONSE AND TOXICITIES OF CONCURRENT CHEMORADIATION WITH AND WITHOUT INDUCTION CHEMOTHERAPY (IC) IN LOCALLY ADVANCED STAGE III & IV (M0) HEAD AND NECK SQUAMOUS CELL CANCER (LAHNSCC)

Narendra Kumar Gupta., Rameshwaram Sharma., Vipul Mehta and Ramraj Meena

Department of Radiation Oncology, SMS Medical College, Jaipur (Rajasthan)

A R T I C L E I N F O

Article History:
Received 6th December, 2020
Received in revised form 15th January, 2021
Accepted 12th February, 2021
Published online 28th March, 2021

Key words:

Induction chemotherapy, Concurrent chemoradiation, Overall response rate

A B S T R A C T

Introduction: Concurrent chemoradiation is currently the standard of care in LAHNSCC. Most of head and neck cancer patients present initially as locally advanced disease. Induction Chemotherapy (IC) causes tumor down staging, facilitating organ preservation, decreasing possibilities of recurrences and potential to prevent distant metastasis. The purpose of the study was to assess effectiveness in treatment response and various toxicity profile between IC followed by concurrent chemoradiation (CTRT) and only concurrent chemoradiation in patients of locally advanced unresectable head and neck squamous cell cancer.

Materials and method: Patients with LAHNSCC of oropharynx, larynx and hypopharynx (AJCC Stage III-IVB) enrolled in study from April 2019 to August 2020 were randomized into two groups -68 subjects in study group and 66 subjects in control group. Study Group 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 Group B. The total dose of radiation was given in both the groups 66 Gray in 33 fractions, five fractions per week for 6.3 weeks on Telecobalt machine Bhabhatron along with concurrent chemotherapy Injection Cisplatin 30mg/m^2 weekly.

Results: Overall response was 79.4% (54 patients) including CR 23.5% (16 patients) & PR 55.9% (38 patients) after IC. Grade 3 toxicities nausea & vomiting (7.35%), neutropenia (6%), anemia (4.4%) and diarrhoea (4.4%) occurred during IC. Response evaluation was done after 6 months of completion of treatment in both groups showed complete response (CR) 76.5% & 59% in Study group A & Control group B respectively. Overall response rate (OR=CR+PR) was 92.7% in Study group and 90.8% in Control group. CR was better in study arm but not statistically significant. Significant grade ≥ 3 acute toxicities were nausea & vomiting 10.3% patients (p-value 0.038), mucositis 44.1% patients (p-value 0.047) in study group after completion of chemoradiation. Rest acute toxicities like dysphagia, dermatitis, nephrotoxicity and xerostomia were more in study group A but statistically not significant.

Conclusion: Our study induction chemotherapy paclitaxel & cisplatin with sequential chemoradiation is more suitable in terms of complete response rate (CRR), compliance with manageable toxicity in LAHNSCC.

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. 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 cancer is sixth most common malignancy worldwide with annual incidence is more than 5.5 lac cases with around 3 lac deaths in each year.

Corresponding author:* **Narendra Kumar Gupta
Department of Radiation Oncology, SMS Medical College, Jaipur (Rajasthan)

Overall, 60% of global head and neck cancers (excluding esophageal cancers) occur in Asia especially in India.. 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].

Smoked tobacco and alcohol are major causative factors for head and neck cancer worldwide, smokeless tobacco, betal-nut

and alcohol are etiological agents responsible for it in Asian population. The treatment of head and neck cancers has multimodality and multidisciplinary approach include surgery, radiotherapy, concurrent chemoradiation (CTRT). Among treated advanced stage patients almost 8 to 10% have residual disease, 50% to 60% have local disease recurrence within 2 years despite surgery or radiation therapy or both in LAHNSCC. Due to advanced disease, these tumors can cause varying degree of functional and cosmetic deformity and can be permanent despite best treatment.

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. The first line treatment for Stages III & IV disease is concurrent chemoradiation which is standard of care. Induction chemotherapy followed by concurrent chemoradiation has not demonstrated superior clinical results in comparison to concurrent chemo-radiation in most trials. However IC can help to reduce the initial bulk of disease and distant metastases, thereby improvement in symptoms and quality of life and results in better organ preservation in extensive locoregional disease with overt symptoms. Induction chemotherapy is also beneficial in control of distant metastasis as well as in achievement of more chances of complete response (CR).

Most trials had used PF (Cisplatin and 5-FU) as induction chemotherapy before radiotherapy but two phase III trials revealed benefits of adding Docetaxel to PF as NACT before RT (TAX 323)[10] or before CTRT (TAX 324)[11,12] in terms of higher LRC, PFS and OS in TPF arm compared to PF arm in advanced unresectable HNSCC. The use of Docetaxel in these trials led to response rates of around 68% to 70% with significant toxicities. 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. IC with cisplatin showed response rate 80 to 90% with complete response rate was 20-40%.

In limited availability of supportive care resources ,in view of poor nutritional status along with considering patients 's financial difficulties, physicians often consider induction paclitaxel and cisplatin or carboplatin in locally advanced head and neck tumors. In our settings patients tolerated a combination of paclitaxel and cisplatin or carboplatin fairly well.

The purpose of the study was to assess effectiveness in treatment response and various toxicity profile between IC followed by concurrent chemoradiation (CTRT) versus only concurrent chemoradiation in patients of locally advanced unresectable head and neck squamous cell cancer.

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 134 patients of biopsy proven (oropharynx, larynx, and hypopharynx) previously untreated 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) 68 patients treated with three cycles of IC (Inj. Paclitaxel 175 mg/m2 IV infusion over 3hrs followed by Inj. Cisplatin 75 mg/m2 over 2 hour repeated at 21 days interval) followed by concurrent chemoradiotherapy with weekly cisplatin 30 mg/m2 while Control group (Arm B) 66 patients 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 taken 68 subjects in study group and 66 subjects in control group.

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 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 134 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. Two patients left treatment in control group at starting of chemoradiation.
- Group A- Study group -68 patients
- Group B- Control group -66 patients

Induction chemotherapy and chemoradiation schedule

All patients were pre-medicated before stating of IC and Inj G-CSF administration after 24 hours of each induction chemotherapy cycle was implemented in study.

- Group A (Study arm): 68 patients were treated with three courses of IC 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): 66 patients were 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 was given in total dose of 66 Gray 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 IC while radiological evaluations were done after 3 weeks of last cycle of IC by CECT/MRI. All patients underwent dental evaluations before irradiation. Response was evaluated at completion, 2^{nd} and 6^{th} months of follow-up in both arms based on clinical examination, ENT evaluation and contrast enhanced CT scan of head and neck of each patient was done . 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 Group A during IC and both groups 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 groups and listed in Table 1. No statistically significant difference was found in patients and tumor characteristics in both groups.

Table 1 Patients baseline characteristics between study and control group

Patients characteristics	Study Arm A, n=68(%)	Control Arm B, n=66(%)
Age		
Mean age± SD	53.15± 10.85	52.17± 10.76
Range	32-70 years	30-70 years
Gender		
Male	56 (82.4%)	55 (83.3%)
Female	12 (17.6%)	11 (16.7%)
ECOG PS		
0	40 (58.8%)	36 (54.5%)
1	25 (36.8%)	27 (40.9%)
2	3 (4.4%)	3 (4.6%)
Primary site		
Oropharynx	34 (50.0%)	31 (46.96%)
Hypopharynx	13 (19.1%)	15 (22.74%)
Larynx	21 (30.9%)	20 (30.30%)
T-stage		
T2	5 (7.4%)	7 (10.6%)
T3	32 (47.0%)	32 (48.5%)
T4	31 (45.6%)	27 (40.9%)
N-stage		
N0	2 (2.9%)	4 (6.1%)
N1	26 (38.23%)	25 (37.9%)
N2	38 (55.9%)	35 (53%)
N3	2 (2.9%)	2 (3%)
Histopathological grade		
G1	11 (16.2%)	10 (15%)
G2	53 (77.9%)	52 (78.9%)
G3	4 (5.9%	4 (6.1%)
Clinical stage		
III	18 (26.5%)	21 (31.8%)
IV A	47 (69.1%)	44 (66.7%)
IV B	3 (4.4%)	1 (1.5%)

Treatment response after IC in study group A

The overall clinical response obtained after completion of three cycles of induction chemotherapy in study group (n=68) was 79.4% (54 patients) including complete response and partial response 23.53% (16 patients) & 55.88% (38 patients) respectively. Patients with laryngeal and hypopharyngeal tumors were noted to have highest clinical response rates at primary site followed by oropharyngeal tumors. Grade 3 toxicities nausea & vomiting (7.35%), neutropenia (6%), anemia (4.4%) and diarrhoea (4.4%) occurred during IC while peripheral neuropathy grade 1 symptoms were complained in 3 patients.

Table 2 Locoregional Response after IC in study group A

Response after IC	N=68 (%)
CR	16 (23.5%)
PR	38 (55.9%)
SD	11 (16.2%)
PD	3 (4.4%)

Treatment response after Concurrent Chemoradiation

All patients (168) started chemoradiation within an average of 3.4 weeks (range 3 to 5) of last cycle of chemotherapy. All patients successfully completed chemoradiation. Patients received six cycles of weekly cisplatin were 73.5% & 90.9% in study and control group respectively.

Table 3 Disease response at 2 months of completion of treatment

Disease Response	**Study Group A IC+CTRT (n=68)**	**Control Group B CTRT (n=66)**
Complete response	49 (72%)	36 (54.5%)
Partial response	14 (20.6%)	24 (36.4%)
Stable disease	4 (5.9%)	5 (7.6%)
Progressive disease	1 (1.5%)	1 (1.5%)

P-value 0.195 (NS)

The clinical response rates obtained two month after completion of chemoradiation revealed that complete response (CR) was achieved in 49 patients (72%) in the Study group and 36 patients (54.5%) in the Control group. The partial response (PR) rates were 14 patients (20.6%) in Study group and 24 patients (36.4%) in Control group. Both CR and OR rates were not found to be statistically significant (p = 0.195).

Table 4 Disease response at 6 months of completion of treatment

Disease Response	**Study Group A IC+CTRT (n=68)**	**Control Group B CTRT (n=66)**
Complete response	52 (76.5%)	39 (59%)
Partial response	11 (16.2%)	21 (31.8%)
Stable disease	3 (4.4%)	3 (4.6%)
Progressive disease	2 (2.9%)	3 (4.6%)

P-value 0.161 (NS)

At 6 months follow up period, CR was achieved 52 patients (76.5%) in the Study group and 39 patients (59%) in the Control group. The partial response (PR) rates were 11 patients (16.2%) in Study group and 21 patients (31.8%) in Control group. In study arm one out of four stable disease patients converted to progressive disease while two out of five stable disease patients converted in progressive disease patients in control group. The six months PFS were 97% and 95.5% in study group & control group respectively. Loco-regional control was better in study group as compare to control group at 6 months.

Toxicities after Concurrent Chemoradiation

Table 4 comparison of toxicities between two groups during chemoradiation

Adverse events	**Study Group A IC+CTRT (n=68) , n (%)**			**Control Group B CTRT (n=66) , n (%)**			**P value**
	Grade 1	Grade 2	Grade≥3	Grade 1	Grade 2	Grade≥ 3	(only G≥3)
Anemia	37	19	2	27	18	1	0.761 (NS)
Neutropenia	21	7	2	12	1	0	-
Thrombocytopenia	6	2	0	3	2	0	0.669 (NS)
Nephrotoxicity	13	4	0	6	0	0	-
Nausea/Vomiting	29	23	7	25	7	1	0.038 (S)
Mucositis	4	34	30	7	43	16	0.047 (S)
Dermatitis	35	24	9	39	21	6	0.611 (NS)
Dysphagia	12	35	21	16	32	18	0.635 (NS)
Xerostomia	46	22	-	52	14	-	0.145 (NS)

In cumulative hematological toxicities anaemia was most common toxicity. Anaemia grade≤2 was present in 82.3% & 68.1% patients in study and control group respectively. Neutropenia grade≤2 was present in 41.2% & 19.7% patients in study and control group respectively. Two patients were of grade 3 neutropenia in study group A. Thrombocytopenia was least common hematological toxicity in both groups. In study group nephrotoxicity grade ≤2 was present in 25% patients while in control group shown only grade 1 nephrotoxicity (9%).

In cumulative non hematological toxicities, nausea vomiting grade≥2 was present in 44.1% & 11.8% patients in study and control group respectively which was statistically significant (p-value 0.038). 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. Grade 3 mucositis developed in 44.1% patients in study group while 24.2% patients in control group which was statistically significant (p-value 0.047). Dysphagia, dermatitis and xerostomia were more in study group in comparison to control group but statistically not significant. All grade 3 toxicities were managed conservatively which required hospitalization. During chemoradiation, total 8/134 (6%) patients needed hospitalization for toxicity related causes including 5 in study arm and 3 in control arm. Among them 3/68 (4.41%) 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 12 & 8 patients in study and control arm respectively during chemoradiation. No treatment related deaths occurred.

DISCUSSION

Treatment of head and neck cancer is a multimodality approach, requiring surgery, chemotherapy and radiotherapy based on site and stage of tumor. Induction chemotherapy followed by concurrent 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 IC 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].

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 IC 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 s. 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 IC 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 IC arm similar toxicities 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 IC 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. Subset analysis of the DeCIDE trial showed lower number of distant metastatic events with IC, proving it ability to eradicate micro metastatic disease. Meta-analysis by Zhang *et al*[21] of 5 RCT with 922 patients compared IC followed by CTRT versus CTRT alone and found significantly decreased distant metastasis rate and improved CR in IC f/b CTRT arm. Our study grade 3 toxicities neutropenia, mucositis and nausea/vomiting were more in study arm. Rest toxicities like dysphagia, dermatitis and anemia were similar in both groups.

Most of these trials showed grade 3-4 neutropenia with decreased distant metastasis and improved CR in IC arm compare to CTRT alone.

IC has encouraged its use by virtue of functional organ preservation despite risk of increased toxicity[20]. More studies is going on chemo selection which can increase survival, disease control and functional preservation of larynx and pharynx with reducing unwanted toxicity[28].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 79.4% (54 patients) with complete and partial response rates of 23.5% and 55.9% respectively. These results overlap with high response rates observed in other studies in which paclitaxel is used as induction combinations[5,24]. High CR 76.5% has been observed at completion of chemoradiation in sequential chemoradiation arm. Responses were radiologically evaluated two month and sixth month after completion of chemoradiation. The primary endpoint was complete radiographic response. The study showed sequential chemoradiotherapy group (IC followed by CTRT) to be better than concurrent chemoradiation group (CTRT alone) with higher complete response rates 76.5% (52 patients) for sequential CTRT versus 59% (39 patients) for concurrent CTRT arm at 6 months. Three patients (4.41%) developed febrile neutropenia in sequential chemoradiation group 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 after IC. At completion of CTRT overall responses were 97.7% (42 patients) including CR 46.5% & PR 51.2%. Another study by Fornari *et al*[29] (Paclitaxel and Carboplatin based NACT before definitive CTRT in LAHNSCC) demonstrated CR+PR: 77% for T stage and 60% for N stage. Along with most prevalent toxicity G3-4 neutropenia 81.8% showing similar overall response as our study 76% with no G3-4 neutropenia. After induction followed by CTRT demonstrated CR+PR: 90.8% for T stage and 75% for N stage similar to our study but very high mucositis 77.3% G3-4 and neutropenia 59% G3-4 in comparison to our study(G3 mucositis 44% and neutropenia 2.9%). In an analysis by M. Nikam[26] ORR after IC and after chemoradiation was 89.1% & 83.34% respectively but higher grade 3 mucositis and skin reaction compare to our study. Aparna G *et al*[27] 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.

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[28,29]. 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. Longer duration follow-up is necessary to comment on overall survival and progression free survival. 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 large volume LAHNSCC to downstage tumor thereby decreasing symptoms with improved treatment response.

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How to cite this article:

Narendra Kumar Gupta *et al* (2021) 'A Prospective Comparative Study To Compare Response And Toxicities of Concurrent Chemoradiation With And Without Induction Chemotherapy (IC) In Locally Advanced Stage III & Iv (M0) Head And Neck Squamous Cell Cancer (LAHNSCC)', *International Journal of Current Advanced Research,* 10(03), pp. 23982-23988. DOI: http://dx.doi.org/10.24327/ijcar.2021.23988.4753

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