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NEOADJUVANT CHEMOTHERAPY FOLLOWED BY CONCURRENT CHEMORADIATION IN LOCALLY ADVANCED SQUAMOUS CELL CARCINOMA OF HEAD AND NECK REGION: A SINGLE INSTITUTIONAL STUDY

Dr. Swapan Kumar Mallick*[1], Dr. Ghafran Nahid[2] and Dr. Rajiv Lochan Jena[3]

[1]Associate Professor, Department of Radiotherapy, Malda Medical College, Malda.

[2]RMO Cum Clinical Tutor, Department of Radiotherapy, Malda Medical College, Malda.

[3]Medical Officer Radiotherapy, Department of Radiotherapy, Malda Medical College, Malda.

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***Corresponding Author**
Dr. Swapan Kumar Mallick
Associate Professor, Department of Radiotherapy, Malda Medical College, Malda.

ABSTRACT

Introduction: Head and neck cancer is amongst the commonest malignancy in India. Overall 57.5% of global head and neck cancer occur in Asia especially in India. Most of the cases present at a locally advanced stage. Concurrent chemoradiotherapy with or without neo-adjuvant chemotherapy are both viable treatment options in locally advanced cases. **Materials & Methods:** 30 biopsy proven cases of locally advanced head and neck cancer attending the Out Patient Department (OPD) of Radiotherapy from March 2016 to August 2017, meeting specified Inclusion and Exclusion Criteria, willing to participate in the study were included. Patients were treated with neo-adjuvant chemotherapy followed by concurrent chemoradiation and followed for a minimum of 8 months. The toxicity and loco-regional control data were assessed. **Results:** At last follow-up Complete Response, Partial Response, Stable Disease and Progressive Disease was observed in 76.66%, 3.33%, 10% and 3.33% of cases respectively. Haematological toxicities like neutropenia (13.3%), thrombocytopenia (10%) and anemia (20%) were seen. Acute toxicities like oral mucositis and skin reaction were observed in 33.3% and 30% cases respectively and late toxicity like xerostomia was observed in 40% of the cases. Hoarseness and dysphagia were observed in 30% and 56.66% respectively. **Conclusions:** Neo-adjuvant chemotherapy followed by concurrent chemoradiation gives good locoregional response, but is associated with substantial haematological, gastrointestinal and mucosal toxicity, which is manageable. Thus, neo-

adjuvant chemotherapy followed by concurrent chemoradiation is a good option in locally advanced head and neck cancer, which is to be administered weighing the pros and cons of the therapy.

KEYWORDS: Neoadjuvant chemotherapy; Concurrent chemoradiation; Locally advanced head and neck cancers.

INTRODUCTION

Head and neck cancer comprises a huge burden of disease worldwide. It is the fifth most common malignancy globally among adults.[1] It is amongst the commonest malignancy in India. Overall 57.5% of global head and neck cancer occur in Asia especially in India.[2]

Over 200,000 cases of head and neck cancers occur each year in India.[3] It accounted for 30% of all cancer in males and 11-16% of all cancer in female in India. Among them, Oral cancer is the most common head and neck cancer for both sexes.[4] In India the incidence among males is 12.48 and females is 5.52 per 1, 00,000 population.[5] The mortality rates due to this cancer among males and females are 3.48 and 1.34 per 1, 00,000 population respectively.[5]

Concurrent chemoradiation therapy (CRT) has become the standard of care in the nonsurgical management of most locally advanced head and neck cancer. Neo-adjuvant chemotherapy followed by concurrent chemoradiation is effective in locally advanced head and neck cancer. Neo-adjuvant chemotherapy for locally advanced HNSCC has also shown high overall responses rate (RR), including complete response (CR).[6] Many patients of locally advanced squamous cell cartcinoma of head and present with extensive locoregional disease with overt symptoms. In them, neo-adjuvant chemotherapy (NACT) can help reducing the initial bulk of disease, reducing the rate of distant metastasis, improving Overall survival, resulting in better organ preservation and thereby improving symptoms and quality of life.[7] [8] Thus we have designed a study to evaluate neoadjuvant chemotherapy using injection docetaxel and injection cisplatin and injection 5FU followed by 3 weekly cisplatin based concurrent chemoradition.

MATERIALS AND METHODS

Patients with locally advanced head and neck cancer attending the Radiotherapy Out Patient Department (OPD) from March 2016 to August 2017, meeting specified Inclusion and

Exclusion Criteria, willing to participate in the study were included. Patients were treated with neo-adjuvant chemotherapy followed by concurrent chemoradiation and followed for a minimum of 8 months.

Patients were treated with Neo-Adjuvant Chemotherapy with Inj. Docetaxel 75 mg/m^2 IV infusion over 60 minutes, Inj. Cisplatin 75mg/ m^2 IV infusion over 60 minutes on day 1 and Inj. 5 FU 750 mg/ m^2/day continuous IV infusion starting from day 1 to day 5, administered for three cycles every 21 days. This was followed by Concomitant chemoradiation with 3 weekly Inj. Cisplatin 100mg/m^2 IV infusion[9] with necessary premedications and adequate hydration alongwith External Beam Radiation Therapy by Bhabatron 780 E CO 60 Telecobalt machine upto a total dose of 70Gy using standard fractionation. Concomitant chemoradiation was started 3 weeks after last neoadjuvant chemotherapy cycle. Response was assessed using the Response assessment Criteria In Solid Tumors(RECIST) version 1.1.[10] Acute and Late Toxicities were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0.[10] During treatment patients were reviewed weekly. After treatment completion, patients were reviewed monthly for eight months.

RESULT

This single institution study was conducted from March 2016 to August 2017. Total 40 patients were assessed for eligibility. Ultimately, 30 patients were included in the study.

1 patient in the study expired during treatment and 1 patient stopped treatment due to toxicity and subsequently was lost to follow up.

Among the patients included In the study only 1 patient was female. The baseline characteristics, toxicities, namely, neutropenia, thrombocytopenia, anemia, mucositis, dermatitis, xerostomia, hoarseness, dysphagia, emesis and responses were reported. Further, we performed stage-wise outcome analysis.

Table-1:

1. DISTRIBUTION OF AGE OF PATIENTS	
AGE GROUP	**NO. OF PATIENTS (%)**
50-55 yrs	5 (16.7)
56- 60 yrs	13 (43.3)
61-65 yrs	9 (30)
66 – 70 yrs	3 (10)
2. DISTRIBUTION OF STAGE OF DISEASE	
STAGE OF DISEASE	**NO. OF PATIENTS (%)**
Stage III	16 (53.3)
Stage IV	14 (46.7)

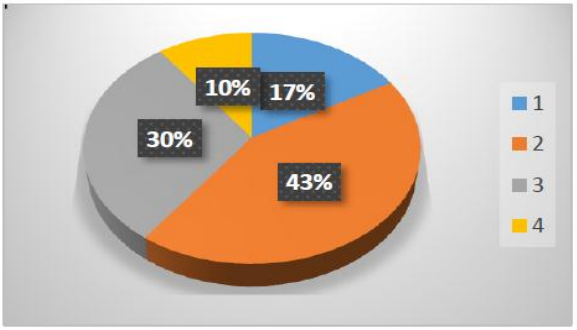


Figure 1: Distribution of age of patients.

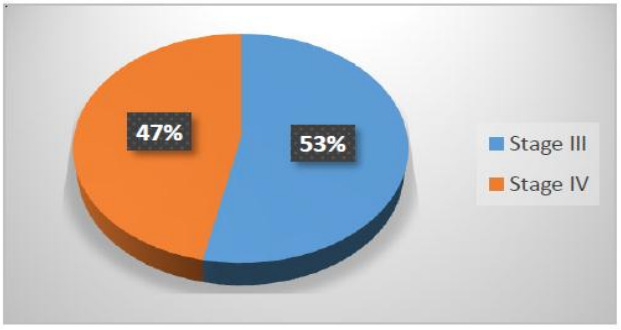


Figure 2: Distribution of stage of patients.

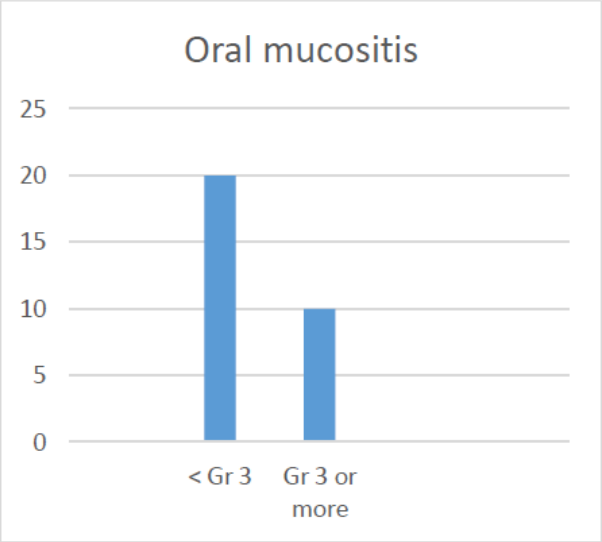
Table 2: Hematological toxicities.

Incidence of highest grade of neutropenia at any point of time during treatment	
Grade	**No. of patients (%)**
Less than grade 3	26 (86.7)
Grade 3 or more	4 (13.3)
Incidence of highest grade of thrombocytopenia at any point of time during treatment	
Grade	**No. of patients (%)**
Less than grade 3	25 (83.3)
Grade 3 or more	3 (10)
Incidence of highest grade of anemia at any point of time during treatment	
Grade	**No. of patients (%)**
Less than Grade 3	24 (80)
Grade 3 or more	6 (20)

Table 3: Other Toxicities.

Incidence of highest grade of Oral Mucositis at any point of time during treatment	
Grade	**No. of patients (%)**
Less than grade 3	20 (66.7)
Grade 3 or more	10 (33.3)
Incidence of highest grade of Skin reaction at any point of time during treatment	
Grade	**No. of patients**
Less than grade 3	21 (70)
Grade 3 or more	9 (30)
Incidence of highest grade of Xerostomia at any point of time during treatment	
Grade	**No. of patients (%)**
Less than grade 3	18 (60)
Grade 3 or more	12 (40)
Incidence of highest grade of Hoarseness at any point of time during treatment	
Grade	**No. of patients (%)**
Less than grade 3	21 (70)
Grade 3 or more	9 (30)
Incidence of highest grade of Dysphagia at any point of time during treatment	
Grade	**No. of patients (%)**
Less than grade 3	13 (43.3)
Grade 3 or more	17 (56.7)
Incidence of highest grade of Nausea and vomiting at any point of time during treatment	

Grade	No. of patients (%)
Less than grade 3	21 (70)
Grade 3 or more	8 (26.7)
Incidence of highest grade of weight loss at any point of time during treatment	
Grade	**No. of patients (%)**
Less than grade 3	21 (70)
Grade 3 or more	9 (30)



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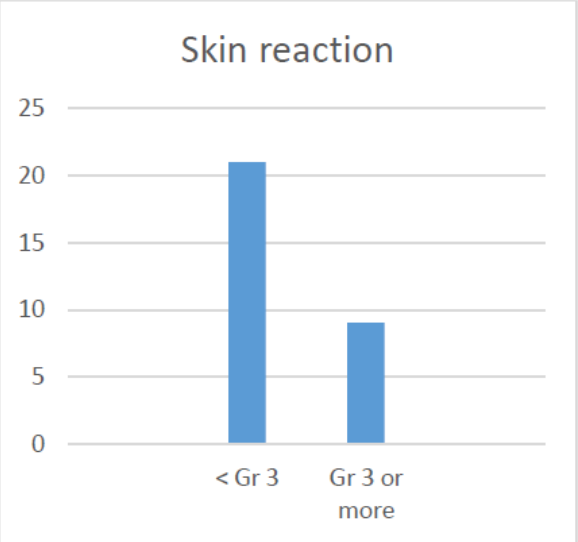

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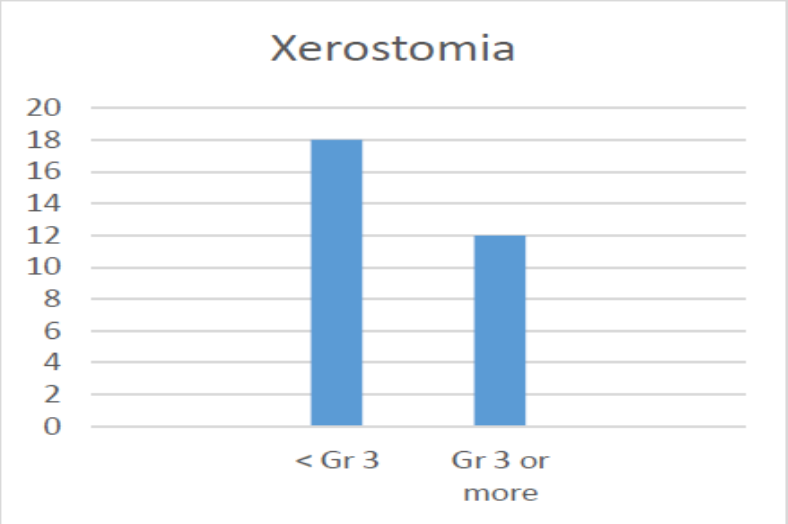

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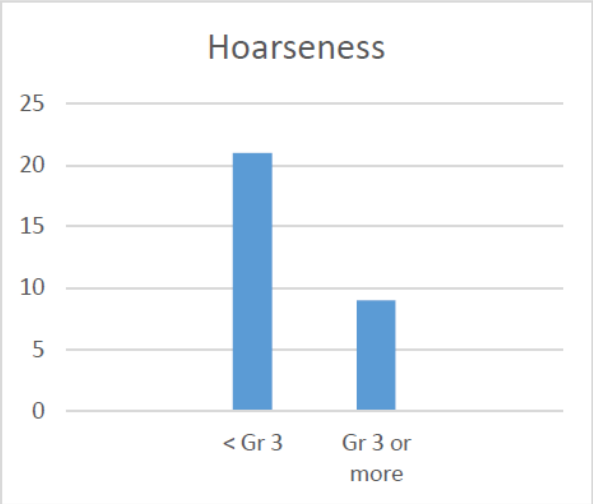

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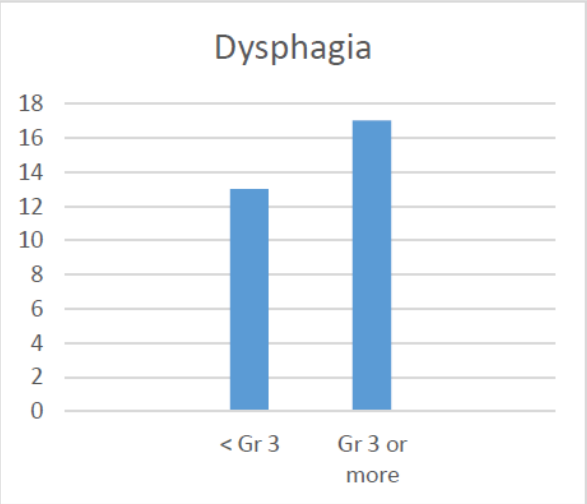

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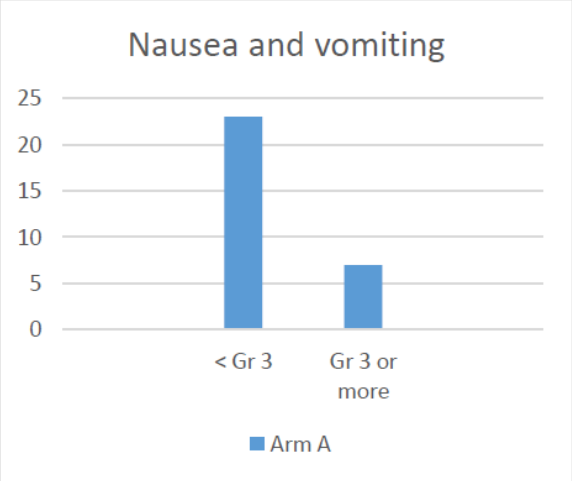

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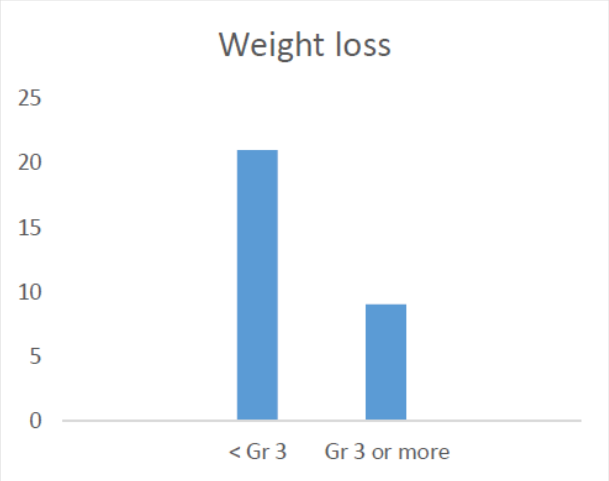

Figure-9:

Table-4:

Response to Treatment	
Type of response	**No. of patients**
Complete Response (CR)	23
Partial Response (PR)	1
Stable Disease (SD)	3
Progressive isease (PD)	1
Stage-Wise Response	
Response in cases of Stage III disease	
Response	**No. of patients (%)**
Complete Response	13 (81.2)
Other form of response	2 (12.5)
Response in cases of stage IVA and IVB disease	
Response	**No. of patients (%)**
Complete Response	9 (64.3)
Other form of response	3 (21.4)

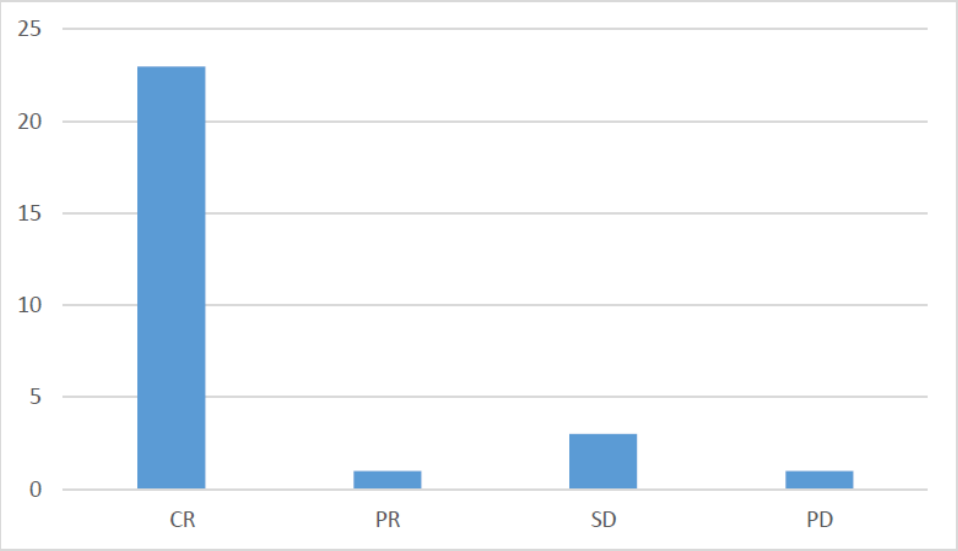

Figure-10: Response to Treatment.

DISCUSSION

Sqaumous cell carcinoma of head and neck is one of the commonest malignancy in India. In our present study we tried to assess the toxicity and locoregional control in case of induction chemotherapy followed by chemoradiation therapy in Stage III and IVA, IVB Sqaumous cell carcinoma of head and neck.

On assessing individual toxicity, it was seen that incidence of Grade 3 or more neutropenia was present in 13.3% of patients. In the study conducted by R. Hitt et al showed incidence of febrile neutropenia was more in TPF group.[11] Grade 3 or more thrombocytopenia and anemia was present in 10% and 20% of the patients respectively. Grade 3 or more oral mucositis, skin reaction and xerostomia was found in 33.3%, 30% and 40% of the patients.

Grade 3 or more nausea and vomiting was found in 26.7% of patients. A similar study conducted by Nikam B M et al on Indian patients showed similarly higher rate of oral mucositis, emesis and bone marrow toxicity in patients treated with neoadjuvant chemotherapy.[12]

At last follow-up Complete Response, Partial Response, Stable Disease and Progressive Disease was observed in 76.66%, 3.33%, 10% and 3.33% of cases respectively. This result closely resembles the result obtained in similar study on Indian population conducted by Jain P. et al. where taxane combined to cisplatin and 5 FU have been proved to be effective in locoregional control in locally very advanced head neck carcinoma.[13]

CONCLUSION

In the present study it was observed that in locally advanced squamous cell carcinoma of head and neck, neo-adjuvant chemotherapy with Docetaxel, Cisplatin and 5 Fluorauracil followed by conventional chemoradiotherapy showed good locoregional response. Use of neoadjuvant chemotherapy was associated with significantly increased haematological, gastrointestinal and mucosal toxicity, which was manageable. Neo-adjuvant chemotherapy (NACT) can help reducing the initial bulk of disease, reducing the rate of distant metastasis, improving Overall survival, resulting in better organ preservation and thereby improving symptoms and quality of life. Thus, neo-adjuvant chemotherapy followed by concurrent chemoradiation is a good option in locally advanced head and neck cancer, which is to be administered weighing the pros and cons of the therapy on a individualised basis.

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