ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 07 | July - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

"CLINICAL ASSESSMENT OF TREATMENT RELATED TOXICITY AND RESPONSE BY CONCOMITANT CHEMORADIATION THERAPY IN LOCALLY ADVANCED HEAD AND NECK CARCINOMA"

Oncology

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

Dr.Rinki Saha Associate Professor . Department of Ophthalmology, KPC Medical College , Kolkata.

ABSTRACT

Introduction: Head and neck cancer is the commonest malignancy in India. Most of the cases present are at a locally advanced stage. Concurrent chemo radiotherapy is one of the treatment options in locally advanced Head & Neck Cancer patients. **Materials & Methods:** Locally advanced head and neck cancer patients attending the Out Patient Department of Radiotherapy from May 2018 to February 2020. Patients were treated with concurrent chemoradiation and followed for a minimum period of 9 months. **Results:** On analysing the pattern of response, it was noted that, in the chemoradiation complete response was seen in 20 patients (66.66%), partial response in 6 patients (20%), stable disease in 2 patients (6.66%) and progressive disease in 1 patient (3.33%). In our study, complete Response in case of Stage III was seen in 18 patients and other form of response was seen in 3 patients . In case of Stage IV A and IV B , Complete Response in 2 patients and other form of response was in 6 patients respectively. Haematological toxicities like neutropenia (3.3%), thrombocytopenia (0%) and anaemia (3.3%) were seen. Acute toxicities like oral mucositis and skin reaction were observed 10% in both the cases. **Conclusions:** The present study, Concomitant chemoradiotherapy improved overall survival and locoregional control. Preservation of function is a major endpoint of interest.

KEYWORDS

Head and Neck cancers, Locally advanced Carcinoma, Concurrent Chemoradiation, Cisplatin

INTRODUCTION:

Head and Neck Cancer is one of the commonest cancers seen in developing countries, including India, constituting up to 25% of the overall cancer burden[1] . In India, out of over 200,000 cases of HNCs, only 60% patients presents with locally advanced but non metastatic disease [2]. Oral cancer is the common head and neck cancer for both sexes [3]. In India the incidence among males is 12.48 and females is 5.52 per 1,00,000 population [4]. Head and Neck cancers occurs due to high consumption of tobacco, alcohol, cigarettes smoking, cigars, pipes, and using snuff and Epstein-Barr virus (EBV). Poor care of the mouth and teeth has been suggested as a factor that may increase the risk of head and neck cancer [5]. Human papillomavirus infection (HPV;most commonly HPV-16) plays a role in the development of certain head and neck cancers, particularly in oropharynx[6].[7].

Concurrent chemoradiotherapy has a central role in the management of locoregionally advanced head and neck cancers and organ preservation and a survival benefit for this approach in comparison to radiation alone is now widely accepted.[8-10]

MATERIALS AND METHODS:

A total of 40 patients with Locally advanced Head and neck carcinoma were enrolled, ultimately 30 patients were included in the study. Patients with locally advanced head and neck cancer attending the Radiotherapy Out Patient Department (OPD), from May 2018 to February 2020 , meeting specified Inclusion and Exclusion Criteria, were willing to participate in the study.

INCLUSION CRITERIA :

- Adult patients (Age 50 to 70 years)
- Cytologically/Histologically confirmed patients of squamous cell carcinoma of head and neck; stage III, IVA & IVB
- ECOG Performance Status 0 – 2
- Normal baseline complete blood counts, liver function test, renal functions test.
- Signed informed consent to participate in the study.

EXCLUSION CRITERIA:

- Maligancies originating from oral cavity, nasopharynx, paranasal sinus, salivary gland, thyroid and External auditory canal.
- Malignant neck node enlargement with unknown primary.
- Prior radiation / surgery (excepting neck node biopsy) / chemotherapy.
- Preexisting co-morbid medical conditions.
- Pregnancy or lactation.
- Participation in any other study on head and neck cancer
- No other synchronous or metachronous primary malignancy.
- History of prior radiation therapy or cytotoxic chemotherapy.
- Patient's refusal

Patients were treated with. External Beam Radiation Therapy by Bhabatron 780 E CO 60 Telecobalt machine up to a total dose of 70Gy using standard fractionation along with concomitant chemoradiation 3 weekly Inj. Cisplatin 100mg/m^2 IV infusion ,with necessary premedications and adequate hydration.

Response was assessed using the Response assessment Criteria In Solid Tumors(RECIST) version 1.1. Acute and Late Toxicities were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. During treatment patients were reviewed weekly. After treatment completion, patients were reviewed monthly for eight months.

RESULTS:

This study was conducted in the Department of Radiotherapy in Goverment Medical College from May 2018 to February 2020. The study included a population predominantly male .1 patient expired during treatment due to chemotherapy related toxicity .

- **On each follow up patient were evaluated by:**

1 Clinical examination
2 Haematological investigation
3 Radiological investigations

Patients were assessed for toxicity profile every week. All patients after completion of treatment were assessed after 6 weeks, and three-monthly follow up thereafter. The prognostic outcome of each patient were assessed on the following parameters:

1. Acute and late Side effects (grading by RTOG criteria)
2. Disease free survival for minimum of 6 months
3. Loco-regional control for complete or partial response
4. Recurrence.

The baseline characteristic toxicities, namely, neutropenia, thrombocytopenia, anemia, mucositis, dermatitis, xerostomia,emesis were reported. Finally, we compared outcome in the form of Complete response , Partial response , Stable disease and Progressive disease.

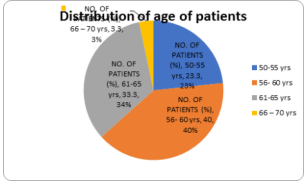

Fig 1:Distribution of age of patients

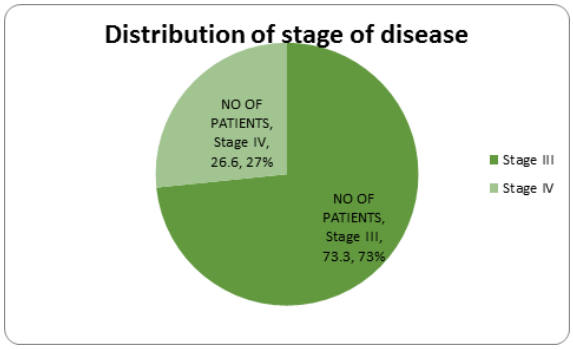

Fig 2:distribution Of Stage Of Disease

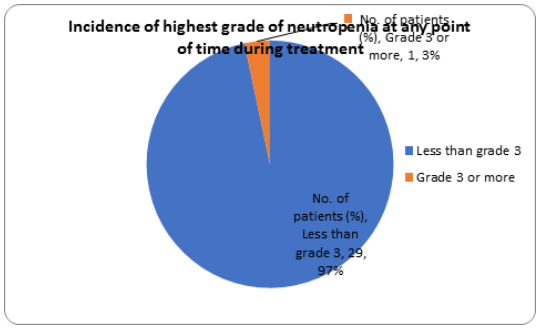

Fig-3:Incidence of highest grade of neutropenia at any point of time during treatment

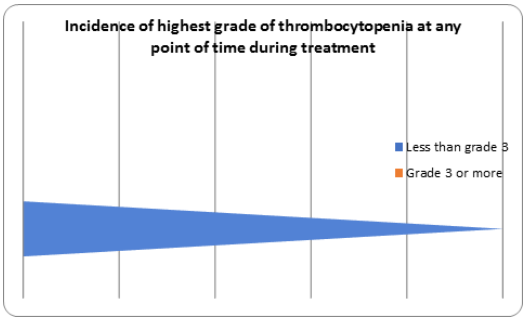

Fig 4: Incidence of highest grade of thrombocytopenia at any point of time during treatment

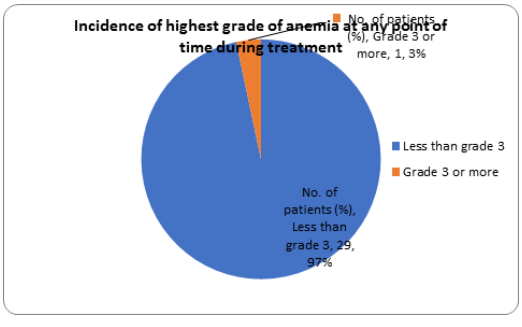

Fig 5 : Incidence of highest grade of anemia at any point of time during treatment

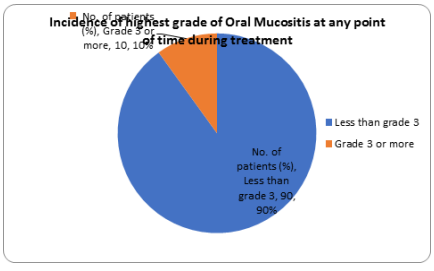

Fig-6: Incidence of highest grade of Oral Mucositis at any point of time during of treatment

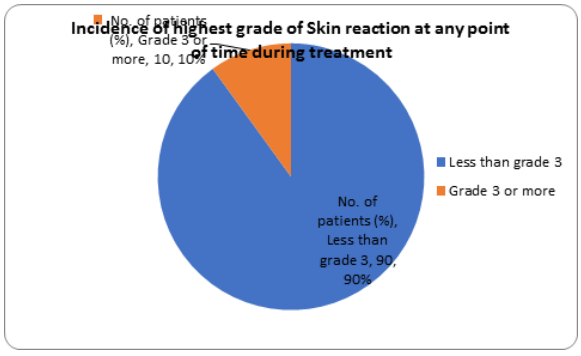

Fig 7: Incidence of highest grade of Skin reaction at any point of time during treatment

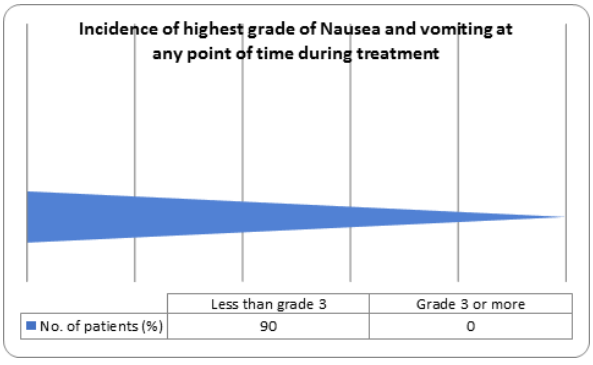

Fig 8: Incidence of highest grade of Nausea and vomiting at any point of time during treatment

Table 1:Subsite wise response

Subsite Wise Response	No. of patient	Response
Glottis	6	CR
	1	Other form of response
Sub glottis	3	CR
	1	Other form of response
Supraglottis	4	CR
	4	Other form of response
Oropharynx	7	CR
	3	Other form of response

DISCUSSION

The advent of concurrent chemoradiation has significantly contributed to the curability and an attractive organ sparing approach because it achieves locoregional control without surgical resection of important anatomical structures. The results of chemotherapy and radiation therapy in the treatment of patients with advanced Head and Neck cancers is preserving the larynx. Although local control and overall survival is significantly compromised among these patients [11]. Interestingly, the concurrent chemoradiation patients had the best results with an 8% overall survival benefit.[12]. However, treatment with RT alone or only therapeutic measures are poor with this treatment modality. RT alongwith chemotherapy has been used , in an effort to improve the therapeutic results. Concurrent administration of chemotherapy and radiotherapy is a promising approach for treating patients with locally advanced head and neck cancer. Moreover chemotherapy given as part of concurrent chemoradiation may act systemically and potentially eradicate distant micrometastases.[13,14] Concomitant chemoradiation treatment with platinum containing regimens particularly at the treatment of unresectable head and neck cancers has been used as an effective treatment as combined therapy has proven to be superior to radiotherapy alone in terms of overall survival, disease free survival and local control.[8-10,15]

In our study all patients were treated with Concurrent chemoradiation and 3 weekly cisplatin, provided good locoregional control for locally advanced head and neck cancers. This regimen, although toxic, is tolerable with appropriate supportive intervention. More than 50% of the patients who die from head and neck cancer have locoregional disease as the only site of failure [16]. Especially those with stage IV disease or unresectable cancers, Systemic chemotherapy was

introduced in the mid 1970s as part of the combined modality treatment[17].

In locally advanced head and neck cancers, 3weekly doses of cisplatin at 100 mg/m ^{2} concurrent with radiotherapy is routinely used in the western world [9],[17-19] and weekly cisplatin at 30–40 mg/m ^{2} in Asia.[20-24]

Acute reactions are markedly increased with chemo-radiation and patients need intensive supportive care for management of nutrition and pain. At our Institute, we have involved a team of pain and palliative care doctors along with radiation oncologists for the management of toxicity and pain. Dietary counseling is done periodically.

Maximum number of patients in our study group is 56-60 years (Fig.1) and number of patient in stage III is 73.3%(Fig. 2). In the study, incidence of grade 3 febrile neutropenia occurred in 97% patient (Fig.3) and less than grade 3 anaemia occured in 29 patients(Fig.5). Incidence of highest grade of nausea and vomiting occur at any point of time during treatment (Fig. 8) .Weight loss gradually increases with time (Fig.9).

Incidence of less than grade 3 oral mucositis occur in 90% patients (Fig.6) . Some sort of skin reaction occurred in all patients (Fig. 7). On analysing the pattern of response, it was noted that, in the chemoradiation , complete response was seen in 20 patients (66.66%), partial response in 6 patients (20%), stable disease in 2 patients (6.66%) and progressive disease in 1 patient (3.33%). One patient died during the course of treatment

As stage wise response assessment was carried out it was seen that 18 patients of stage III (81.8%) had complete response and 3 patients (13.6%) had poorer response. But in the case of stage IV disease, that is the group with locally very advanced disease the result is something different. Whereas, in the chemoradiotherapy , 2 patients (25%) had complete response and all other 6 patients (75%) had partial response, stable disease or progressive disease.

CONCLUSION

In our study, Concurrent chemoradiotherapy has a central role in the management of loco-regionally advanced head and neck cancers and a survival benefit for this approach in comparison to radiation alone is now widely accepted. Preservation of function is a major end point of interest, and concomitant chemoradiotherapy therapy are now considered as standards of care. Hence, the present study is intended to find the efficacy of concomitant chemoradiation with a single agent cisplatin in locally advanced Head and Neck cancer**.** It was observed that in locally advance squamous cell carcinoma of head and neck , concomitant chemoradiotherapy significantly improved locoregional response, improved overall survival and does not statistically increase severe late morbidity. Concomitant chemoradiotherapy was associated with significantly increased toxicity which being manageable, were not associated with increased mortality.

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