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A PROSPECTIVE OBSERVATIONAL STUDY TO DETERMINE RESPONSE AND QUALITY OF LIFE IN ADVANCED HEAD&NECK CANCERS FOLLOWING HYPOFRACTIONATED PALLIATIVE EXTERNAL BEAM RADIOTHERAPY.

Oncology

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ABSTRACT

Introduction: Squamous cell cancer of the head and neck (HNSCC) represents the sixth most common malignancy, with 6,50,000 new cases and 3,00,000 HNSCC related deaths reported annually worldwide. HNSCC constitutes approximately 90 percent of all head and neck cancers, and accounted for approximately 3 percent (about 50,000) of all new cancer cases and 2 percent (approximately 12,000) of all cancer deaths in 2010 in the United States. Overall, 57.5% of global head and neck cancers occur in Asia.

Aims And Objectives: To Determine Local Control And Quality Of Life in stage III & IV Advanced HNSCC Following Hypo Fractionated Palliative Radiotherapy. To study the response with hypo fractionated external beam radio therapy treatment using RECIST criteria (version 1.1).

Materials And Methods: At the completion of treatment both the primary and the node Response was assessed as per the RECIST 1.1 Response Criteria and Quality of life with QLQ H&N 35 module.

Results And Conclusion: At the completion of RT, 32.1% had CR, 50% had PR,14.3% had SD and 3.6% had PD. At 4 weeks of follow-up, 28.6% had CR, 53.6% had PR,14.3% had SD and 3.6% had PD. At 3 months of follow up 17.9% had CR, 60.7% had PR,10.7% had SD and 10.7% had PD. There is a statistically significant improvement in distressing symptoms like pain, swallowing difficulty, opening mouth difficulty. This fractionation schedule allowed treatment to be completed in a short overall period with good tolerance and clinically acceptable toxicities.

KEYWORDS

Head and neck (HNSCC), oropharyngeal squamous cell cancer(OPSCC) and Oral squamous cell carcinoma (OSCC).

INTRODUCTION

Squamous cell cancer of the head and neck (HNSCC) represents the sixth most common malignancy, with 6,50,000 new cases and 3,00,000 HNSCC related deaths reported annually worldwide. HNSCC constitutes approximately 90 percent of all head and neck cancers, and accounted for approximately 3 percent (about 50,000) of all new cancer cases and 2 percent (approximately 12,000) of all cancer deaths in 2010 in the United States. Overall, 57.5% of global head and neck cancers occur in Asia [1].

Head and neck cancer is one of the highly prevalent cancers in developing countries like India.[2], Population-based cancer registry in India projects that the number of tobacco- related cancer and head and neck cancer would be 3,16,734 and 2,18,421, respectively, by 2020. The epidemiology and biology of head and neck cancer in developing countries are different from that of developed countries. Therefore, the treatment data from Western literature should be extrapolated with caution in developing countries like India.

In India, HNSCC constitutes upto 25% of the overall cancer burden.[3] Over 200,000 cases of head and neck cancer occur each year in India. Oral squamous cell carcinoma (OSCC) and Oro pharyngeal Squamous cell carcinoma(OPSCC)are among the most common cancers worldwide, with an estimated 400,000 incident cases and 223,000 deaths during 2008. The annual estimated incidence is around 275,000 for Oral squamous cell cancer(OSCC) and 130,000 for oropharyngeal squamous cell cancer(OPSCC) with two-third of these cases occurring in developing countries.

Nearly 80,000 OSCC are diagnosed every year in India. Tobacco and alcohol are the strongest risk factors for both OSCC and OPSCC [4]. In India, 60 % to 80 % of patients present with advanced disease as compared to 40% in developed countries. Large majority of them present in advanced incurable stage which carries a poor prognosis with patients dying of uncontrolled Loco-regional disease.

Locally advanced head and neck cancer is generally incurable and has a short survival rate.In most cases, due to extensive locoregional involvement, poor general condition of the patient, or comorbid conditions curative treatment is not possible. Therefore, the relevance of aggressive treatment in unresectable locally advanced head and neck cancer has been questioned.The intent of treatment in such cases is to improve the quality of life of the patients keeping their socioeconomic condition in mind and judiciously utilizing the precious resources for curable conditions.

Hypofractionated treatment delivers palliation that is time efficient, cost effective. These regimes should theoretically produce worse late effects than conventional fractionation. But patients who are treated for symptom palliation are unlikely to survive to face the increased risk of long-term side effects. Hence, shorter courses like hypofractionation are ideal in advanced stage setting with the sense that a modest potential for increased late toxicity was not a major concern in patients with limited life expectancy.

To Determine Local Control And Quality Of Life In stage III & IV Advanced HNSCC Following Hypo Fractionated Palliative Radiotherapy.

1. To study the response with hypo fractionated external beam radio therapy treatment using RECIST criteria (version 1.1).
2. To assess the quality of life using Questionnaire QLQ-C30 (Head & Neck cancer module: QLQ-H&N35).

MATERIALS AND METHODS

Source of data:-

This prospective observational study was conducted at Saroj Gupta Cancer Centre and Research Institute, Kolkata, between October 2015 till November 2016 Data were collected from all patients who had been cytological/ histopathologically and radiologically proven locally advanced stage III & IV HNSCC; fulfilling eligibility criteria were recruited after obtaining informed consent.

Inclusion Criteria

1. Histological/Cytological proven Primary HNSCC Stage III, IVA and IVB.
2. ECOG score ≤ 2.
3. Age group 30-60 yrs.
4. Hb> 10 g/dl
5. Absolute Neutrophil Count > 1500/ mm3
6. Platelet count > 100,000/mm3
7. BUN < 25 mg/dl
8. Serum Creatinine < 1.5 mg/dl
9. Serum Bilirubin < 1.5 mg/dl
10. ALT& AST within normal limits.

Exclusion Criteria

1. Patient with distant metastasis.
2. Patient unsuitable for radiation therapy due to Medical Co morbidities like Autoimmune diseases, Immunodeficiency .
3. Restless Patient.
4. Pregnant or breast feeding woman.
5. History of allergic reaction to iodinated contrast media.
6. Previous history of radiotherapy/chemotherapy.

RESULT AND DISCUSSION

The present study was undertaken in Department of Radiotherapy, SGCCRI Kolkata. The patients with newly diagnosed, histological proven stage III and IV, Advanced HNSCC were presented in hospital tumour board and after board decision, treatment was decided as Palliative Hypofractionated RT.

Out of 28 cases analysed, 78.57% patients were males and 21.42% patients were females with a male to female ratio of 4:1. Study by Okamiet al [5] also demonstrated male to female ratio of 4:1. It has been widely approved that the cancer of head and neck regions appear more frequently in the sixth and seventh decades of life compared to younger age groups as reported by Robert et al [6] In our study, the highest incidence of cancer was seen in the fifth to seventh decades of life. The median age of presentation was 55 years. As a universally accepted fact, this study also emphasized the overwhelming predominance of males over females to develop malignancy of head and neck region. The male predominance in head and neck cancer can be attributed to the fact that habits like tobacco smoking, alcohol and pan chewing are more prevelant among males

RESPONSE EVALUATION

Hypofractionated RT is good treatment option for patients who are unsuitable for chemoradiaion due to medical co-morbidities, distant metastatic disease, very advanced loco-regional disease or a combination of these factors who require some form of treatment for their loco-regional disease. Various trials that have evaluated the role of hypo fractionated palliative radiotherapy have found good response rate and good relief of symptoms with this approach. This approach is also suited in areas where there is a high burden of patients on machines especially in developing countries. The long term toxicity may not be a major concern for these patients as they may not survive that long for late toxicity to appear.

In our study, we reported the Response rates at completion of treatment, at 4 weeks and 3 months after treatment completion. At completion of treatment, 32.14% had CR, 50% had PR, 14.28% had SD and 3.57% had PD. Our results are in conjunction with the results of Nguyen et al study [7].

Mohantiet al. [8] evaluated 20 Gy in 5 fractions palliative radiotherapy in advanced HNC patients. Symptom relief ranged from 47% to 76% for pain, dysphagia and respiratory distress. June Corry et al [9] in the QUAD shot study evaluated 14 Gy in 4 fractions over 2 days and repeated every 4 weeks for 3 sessions in palliative cases of head and neck. The study found median overall survival of 5.7 months, median progression free survival 3.1 months. Agarwal JP et al [10] reported in a single institution experience that hypofractionated radiotherapy regimen evaluated is an effective treatment modality for sustained symptoms relief with good response rates and acceptable toxicity. GhoshalS et al [11] studied the role of palliative radiotherapy with a dose of 30 Gy in 10 fractions over 2 weeks. All patients with pain and 90% of patients with dysphagia, dyspnoea and disturbed sleep had greater than 50% relief in symptoms after radiotherapy. Porceddu SV et al89 in hypo trial treated advanced HNSCC with 30 Gy in 5 fractions and assessed rate of tumor response which showed 56% CR, 19% had PR, 15% had SD, at primary site and 44% CR,19% PR, 15% SD, 11% PD in nodal region response. The median time to progression and death was 3.9 and 6.1 months, respectively.

Quality of life Assessment

Although, the information about the optimal palliative regimen for incurable HNSCC in the current literature is scanty, an optimal palliative RT schedule is one that would provide worthwhile regression of the tumor and local symptoms within a short OTT with minimal toxicity. From radiobiological, economic and logistical points of view, a hypofractionated schedule would be the most suitable option. In Quality of life assessment majority of scales demonstrated a worsening of QOL during treatment as evident by increased mean scores observed Immediately after RT inparameters of pain(HNPA), swallowing (HNSW), Sensory problems (HNSE),Trouble with Social eating (HNSO),opening mouth (HNOM), Dry mouth (HNDR), Sticky saliva(HNSS) Coughing (HNCO), Feltill (HNFI), Nutritional Supplements (HNNU) Feeding tube(HNFE) attributed to RT related toxicity with a corresponding improvement in QOL 4 weeks post-treatment and 3 months after treatment. The subsequent relatively good scores at 4 weeks and 3 months of follow up indicate that most symptoms are transient and resolve after treatment cessation. Speech(HNSP),Problems with Teeth (HNTE), Pain killers usage(HNPK) had no change in Score immediately following RT and Trouble with Social contact(HNSC) had decreased score following RT. The above observations is in conjunction with Desmond Curranet al98study which proposed that majority of scales demonstrated a worsening of QoL during treatment, with a corresponding increase in QoL post-treatment.

When baseline Scores are Compared with Scores 3 months after RT pain(HNPA) (P=<0.0001), Speech(HNSP) (P=0.0002), Trouble with Social eating(HNSO) (P= <0.0001), Trouble with Social contact (HNSC) (P= <0.0001), Pain killers (HNPK) (p<0.0001), Nutritional Supplements (HNNU) (P=0.0002), had significant decrease in score which implies significant improvement in Quality of life. When baseline Scores are Compared with Scores 3 months after RT Problems with Teeth (HNTE) (P=0.9031), Dry mouth (HNDR)(P=<0.0001), Sticky saliva (HNSS) (p=0.0001), coughing (HNCO) (P=<0.0001), Felt ill (HNFI) (P=0.0014), had only slight decrease in score which implies only slight improvement in Quality of life. When baseline Scores are Compared with Scores 3 months after RT swallowing(HNSW)(P=.00234), Sensory problems(HNSE) (P=0.0093), opening mouth(HNOM) (P=0.9704),Feeding tube(HNFE) (P= <0.0001), weight Loss (HNWL) (P=<0.0001), weight Loss(HNWG)(P=0.5458) had only increase in score which implies decrease in Quality of life. Our Results are in conjunction with S das et al [12] study who showed that there was improvement in all the aspects of the quality of life (physical, social, emotional, and functional well-being) at the end of radiotherapy. A statistically significant improvement in social well -being was noted after treatment (17.4 vs. 20.01, P = 0.03).

S das et al [12] in an observational study which included 36 patients with inoperable head and neck cancer who received 40 Gy in 10 fractions with 2 fractions per week. Treatment-related toxicity was assessed using RTOG criteria. Functional Assessment of Cancer Therapy (Head and Neck, FACT H and N) quality of life (QOL) tool was administered before starting and at the completion of radiotherapy.

QOL assessment showed improvement in social well -being (17.4 vs. 20.01, P = 0.03) after treatment. Reduction of pain was observed in 88% patient s and 60% patients had improvement of performance status. AbrahimAl-mamgani A et al [13] studied 16 fractions of 3.125 Gy per fraction and QoL of patients was assessed using the QLQ H&N-35 module, dry mouth and sticky saliva were ranked amongst the highest scores, followed by swallowing problems.

Corry et al [9] inthe QUAD shot study evaluated 14 Gy in 4 fractions over 2 days and repeated every 4 weeks for 3 sessions in palliative cases of head and neck reported improvement in QoL in 44% of patients after RT for incurable HNSCC.Sandro V. Porceddu et al. [14] in hypo trial treated advanced HNSCC with 30 Gy in 5 fractions and assessed rate of tumor response and QOL using FACT-HN in which 62% patients showed over all improvement in quality of life(QoL), 14% no change in QOL and 24% showed deterioration of QoL.

Desmond Curran et al [15] in a randomized, phase III study, quality of life(QoL) was assessed in 424 patients with locoregionally advanced squamous cell carcinoma of the head and neck (HNSCC)after high-dose radiotherapy alone or in combination with cetuximab.They have concluded that the addition of cetuximab to radiotherapy significantly improved locoregional control and increased overall survival without adversely affecting QoL.

Over all Survival (OS) and Progression Free Survival(PFS)

During our study period Patients treated with hypo fractionated radiotherapy were followed up for 1 year and 1 year Overall survival was seen in 28.57% patients and Median OS was 5.5 months and Median PFS was 3.5 months.

Results of our study are in conjunction with study of S.Das et al [12] with a 1 year overall survival of 30% and **Agarwal et al** [10] study with a Median overall survival of 5.7 months, with a median progression-free survival of 3.1 months.

Table: Distribution Of Response at Various Follow Up

		Frequency	Percentage
At completion of RT	**CR**	9	32.1%
	PR	14	50.0%
	SD	4	14.3%
	PD	1	3.6%
4 weeks after RT	**CR**	8	28.6%
	PR	15	53.6%
	SD	4	14.3%
	PD	1	3.6%
3 Months after RT	**CR**	5	17.9%
	PR	17	60.7%
	SD	3	10.7%
	PD	3	10.7%

SUMMARY AND CONCLUSION

- The study titled “A Prospective Observational Study To Determine Response And Quality Of Life In Advanced Head&Neck Cancers Following Hypo Fractionated Palliative External Beam Radiotherapy”, was performed in the department of Radiotherapy, Saroj Gupta Cancer Centre & Research Institute, Kolkata from October 2015 to November 2016.
- 30 patients of Head and Neck cancers of stage III, IVA & IVB satisfying the eligibility criteria were enrolled for the study. In this study we have given Palliative Hypo fractionated RT for 3 ½ weeks. The radiation dose delivered was 40Gy in 16 fractions (2.5 Gy/fraction/5 days/week). Out of 30 patients, 2 patients defaulted the treatment protocol. Total 28 patients were taken for final analysis. The age range of patient population was 33-68 years with median age of 55 years.22 patients were male and 6 Patients were female. All the patients had ECOG performance status ranging from 1-2.
- It is recommended to consider a proper efficacy judgement criteria for palliative head and neck radiotherapy where the primary endpoints are symptom relief and not survival.
- There is a statistically significant improvement in distressing symptoms like pain, Swallowing difficulty, opening mouth difficulty. Thus, hypofractionated radiotherapy regimen evaluated in the present study is an effective treatment modality for sustained symptomatic relief producing good Quality of life with good response rates.
- This fractionation schedule allowed treatment to be completed in a short overall period with good tolerance and clinically acceptable toxicities.
- Good patient compliance, high response rates and improvement in QoL has been observed in the present study indicating the usefulness of palliative hypofractionated radiotherapy in routine clinical practice. However a prospective Randomized control trial with a large number of patients and longer followup is required to establish this treatment regimen in day to day radiotherapy practise

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