Breast Cancer : Current Research

Research Article Open Access

Short Course Hypofractionation- Palliative Radiation Regimen in Squamous Cell Carcinoma of Head and Neck

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Received date: October 06, 2021; **Accepted date:** October 20, 2021; **Published date:** October 27, 2021

Citation: Kumari **P** (2021) Short Course Hypofractionation- Palliative Radiation Regimen in Squamous Cell Carcinoma of Head and Neck. Breast Cancer : Current Research, Vol.6 Iss.1 No: 1.

Abstract

Aim: To evaluate the role of short course hypo-fractionated radiotherapy regimen in patients of locally advanced head and neck cancer(LAHNC)of advanced stage for symptomatic relief.In Indian setting, more than 70% patients present in locally advanced stage and with poor general condition and are suitable candidates for palliative radiotherapy. This is a prospective pilot study of a Regional cancer institute of North west zone.

Materials and Methods:36 patients with stage 3 and stage 4, head and neck cancer were treated with a short course of palliative radiotherapy [30 Gray (Gy)] in 10 fractions over 2 weeks). Baseline symptoms were assessed before the start of study for pain, dysphagia, respiratory symptoms, anxiety/depression and dyspnoea. First assessment for symptom relief was done at the completion of radiotherapy and then between 3 to 4 weeks aftercompletion ofradiotherapy.

Results: In the present study, out of total 36 patients, 72.22% were males and 27.78% were females and Median Karnofsky score was 60. Most common site was oropharynx in 14 (40%) patients followed by larynx was involved in 9 (24%) patients, hypopharynx was involved in 7 (17%) patients. 11 (31%) patients were found to be in stage III and 25 (69%) patients were found to be in stage IV of carcinoma. After completion of radiotherapy course and 3-4 weeks follow up, 88% patients had pain relief, 83% shown improvement in dysphagia, 81% patients shown improved sleep patterns and 65% improvement in respiratory symptoms. 75% patients had betterment in dysphonia. In 23 (65%) patients, Grade-I Mucositis was seen, 13 (35%) patients shown Grade-II mucositis, 15 (44%) patients had Grade-I skin toxicity and Grade-II skin toxicity was seen in 21 (56%) patients.

Conclusion:A short course of radiation promises to effectively relieve symptoms in locally advanced head and neck cancers and reduce the need of ongoing analgesic therapy and hospital visits. It reduces the need of continued supportive care and overall improves quality of patients' life. Reduces patients' frequent visits to hospital.

Keywords: Hypo-fractionationRadiotherapy, palliation, head and neck carcinoma

Introduction

Head and neck cancer accounts for 4.8% of all cancers globally and 14.3% of all cancers in India.Most of the cancers are diagnosed in III and IV stages in the developing countries like India and are considered incurable. The goal of treatment is to palliate symptoms including pain, dysphagia, dyspnea, bleeding, and ulceration and improve quality of life. Radiotherapy and chemotherapy can be useful modalities for symptom management and should be judiciously used in palliative care. Curative-intent radiation therapy is delivered with doses from 6000 to 7000 cGy divided into 180 to 200 cGy fractions and is often delivered with concurrent chemotherapy. Such regimens, although curative, are often highly toxic It is widely recognized that PRT (Palliative radiotherapy) provides effective palliation and improved quality-of-life in advanced incurable andin metastaticmalignancies.A number of different hypo-fractionated regimens have been used across the globe for treatment of locally advanced head and neck cancers.The present study was undertaken to evaluate the role of palliative radiotherapy in such type of patients [1].

Materials and Methods

This prospective single arm study was conducted at the AcharyaTulsi Regional cancer treatment and Research instituteBikaner between January 2018 to December 2018. A total of 35 biopsy proven cases of squamous cell carcinoma of head and neck region were enrolled. All patients had locally advanced disease and their Karnofskyperformance status ranged from 50 to 70. The patients were staged according to AJCC 2010 TNM staging system. Most of the patients at this centre were of other states [2].

Eligibility Criteria:The eligibility criteria were biopsy proven - squamous cell carcinoma of head and neck stage IV, stage III with poor performance status, no previous history of surgery, radiotherapy or chemotherapy,no recurrent disease, sites of tumors were oropharynx,larynx,hypopharynx, oral tongue,alveolus and retromolar trigone [3].

Pre-treatment evaluation and symptoms:These patients were previously staged and decision for palliative radiotherapy as a single modality was made by multidisciplinary joint clinic at our centre. Family members of eachpatient was well explained about the incurability of the disease and benefit of short duration of therapy for quick symptom relief and written informed consent were taken. Baseline symptoms were assessed using a questionnaire incorporating a 11-point numerical scale. for scoring pain, dysphagia, cough, insomnia and dyspnoea. Symptoms were scored on a scale of 0-10 and graded as mild (score 1-3), moderate (4-6) and severe (>6). Analgesics were prescribed in accordance with the WHO pain ladder. Cough sedatives and anxiolytics were prescribed for relief of cough and insomnia [4].

Treatment plan: Most of the patients at this centre were of other states and were poor, so patient and family prefer continuous and short schedule.External beam radiotherapy was delivered in all these patients to a dose of 30 Gy in 10 fractions over 2 weeks. Radiotherapy was planned for Cobalt-60 teletherapy unit, and marking of patients was done around the gross tumor volume (primary tumor and involved nodes) with an additional margin of 1to 1.5 cm all around,bilateral oppose open wedged fields, once daily for five days a week.For this plan biologically equivalent dose (BED) for tumor and late reacting tissue is 39Gy10 and 32.5 Gy3, respectively. The equivalent dose to 2Gy /fraction schedule is 60 Gy10 for tumor and 36Gy3 for late reacting tissue [5].

Follow up and recordings:Primary end point of the study was prompt symptomatic relief 3– 4 weeks after the completion ofradiotherapy and secondary endpoints were objective response, toxicityand survival.All patients were reviewed at least once during radiotherapy for assessingtoxicity. The radiation therapy oncology group (RTOG) grading was used to document toxicity.

A provision was made in this study that patient achieving more than 50% symptomatic improvementand in a good general condition to perform their daily activities and may be in partial response or complete responseafter 3 or 4 weeks of radiotherapy, would be advised further radiotherapy for the curative intent.[8,9]To give curative dose to patient, further 2Gy/# was given to achieveradio-biologically equivalent dose of 66 Gy and spinal cord sparing was done at 44 Gy equivalents. This dose was calculated by the time- dose –fraction (TDF) method.Tumor response (both primary and nodal response) was assessed as partial response (PR), complete response (CR), stable disease,(SD), progressive disease (PD) or not evaluative (NE) by WHO response criteria either clinically or if needed, radiologically.Radiation reactions were assessed by Radiation Therapy Oncology Group (RTOG) criteria.

Results

Demographic Characteristics:

In the present study, out of total 36 patients, 26 (72.22%) were males and 10 (27.78%) were females. Median age was 59 years (range 31 to 86 years).

Karnofsky score:

Median Karnofsky score was found to be 60 (ranging from 50 to 70).

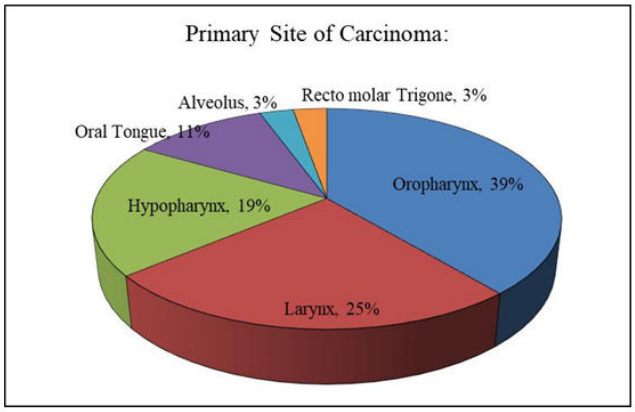

Figure1: Primary Site of Carcinoma.

Above figure shows that most common site was found to be oropharynx in 14 (40%) patients followed by larynx was involved in 9 (24%) patients, hypopharynx was involved in 7 (17%) patients. Lesser common sites affected were Oral Tongue, Alveolus and retromolar trigone involved in 4 (11%), 1 (3%) and 1 (3%) patients respectively. (Figure 1)

Stage of Carcinoma:

Out of 36 patients, 11 (31%) patients were found to be in stage III and 25 (69%) patients were found to be in stage IV of carcinoma.

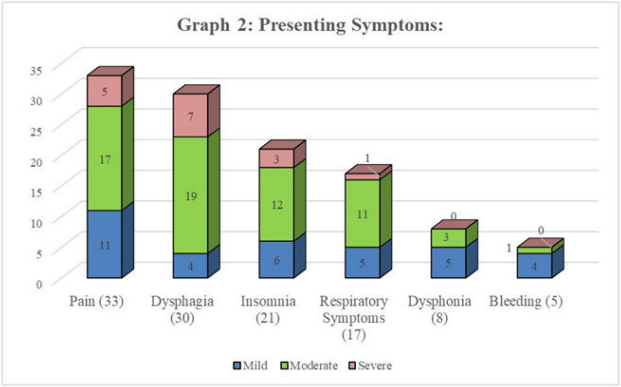

Figure2: Presenting Symptoms.

Histo-pathologically all cases were squamous cell carcinoma and most commonly presenting symptoms was pain seen in 33 (92%) patients followed by dysphagia in 30 (83%) patients, 21 (58%) patients had insomnia and respiratory symptoms were seen in 17 (47%) patients. Lesser common encountered were dysphonia and bleeding seen in 8 (22%) and 5 (1%) patients respectively. Seven patients required nasogastric intubation for absolute dysphagia. All of the symptoms were graded as mild, moderate and severe shown in table. (Graph 2)

Symptoms	Category	At RT Completion	%	At 3-4 weeks Follow Up	%	Pts with Better Symptoms

Pain (n=33)	Better	20	60.61%	9	27.27%	29 (88%)
	No Change	8	24.24%	2	6.06%	
	Worse	5	15.15%	2	6.06%	
Dysphagia (n=30)	Better	18	60%	7	23.33%	25 (83%)
	No Change	5	16.67%	2	6.67%	
	Worse	7	23.33%	3	10%	
Insomnia (n=21)	Better	11	52.38%	6	28.57%	17 (81%)
	No Change	10	47.62%	3	14.29%	
	Worse	0	0.0%	1	4.76%	
Respiratory Symptoms (n=17)	Better	7	41.18%	4	23.53%	11 (65%)
	No Change	8	47.06%	4	23.53%	
	Worse	2	11.76%	2	11.76%	
Dysphonia (n=8)	Better	4	50%	2	25%	6 (75%)
	No Change	3	37.50%	1	12.50%	
	Worse	1	12.50%	1	12.50%	
Bleeding (n=5)	Better	3	60%	2	40%	5 (100%)
	No Change	2	40%	0	0.0%	
	Worse	0	0.0%	0	0.0%	

Table 1: Impact of Radiotherapy on Symptoms.

Above table shows that, out of 33 patients who presented with pain, 20 (61%) shown improvement at completion of radiotherapy and out of remaining 13 patients, 9 (27%) patients improved after 3-4 weeks of follow up so total 29 (88%) patients had pain relief. Similarly for other complaints, after completion of radiotherapy course and 3-4 weeks follow up, 25 (83%) shown improvement in dysphagia, 17 (81%) patients shown improved sleep patterns, 11(65%) improvement in respiratory symptoms, 6 (75%) patients had betterment in dysphonia and all patients, 5(100%) noted improvement in bleeding tendency.

Response	Primary Site (%)	Nodal Site (%)
Complete Response	8 (22.22%)	8 (22.22%)
Partial Response	15 (41.67%)	13 (36.11%)
Stable Disease	7 (19.44%)	10 (27.78%)
Progressive Disease	6 (16.67%)	5 (13.89%)
Total	36 (100%)	36 (100%)

Table2: Response Rate (between 3-4 weeks).

In Primary disease over all response rate was 23 (64%) and in Nodal disease it was 21 (58%). (Table 2)

Radiation Reaction	Number	Percentage
Mucositis Grade-I	23	65%
Mucositis Grade-II	13	35%
Skin Toxicity Grade-I	15	44%
Skin Toxicity Grade-II	21	56%

Table 3: Radiation Reaction.

In 23 (65%) patients, Grade-I Mucositis was seen, 13 (35%) patients shown Grade-II mucositis, 15 (44%) patients experienced Grade-I skin toxicity and Grade-II skin toxicity was seen in 21 (56%) patients as radiation reaction. (Table 3)

Extent of Radiotherapy:

Out of total 36 patients who received radiotherapy, in 28 (78%) patients, only palliate radiotherapy was given, palliate radiotherapy followed by dose escalation was done in 8 (22%) patients.

Survival:

Follow up period ranged from 1 to 15 months. Median overall survival was 5.9 months (3 months to 12.5 months). Mainly survival was recorded telephonically, since patients were from distant sites.

Discussion

Management of locally advanced squamous cell carcinoma of head and neck has progressed over a period of time due to available research and literature and trials. Palliative treatment in patients with incurable disease, intensive radio therapy has not succeeded. [13] There are few studies available on palliative treatment for symptoms control in such type of cancers. [5] The present study tried to quantify the benefits of short course radiotherapy for locally advanced squamous cell carcinoma of head and neck with biological dose for sustained local control and symptoms relief.

In the present study, more males were seen (72% were males and 28% females). Median age was 59 years (range 31 to 86 years). Findings are comparable with study found that 73% were male and 27% patients were females showing male preponderance with mean age 55 years showing similar Karnofsky score. Common sites were oropharynx, larynx was and hypopharynx as found in study by. As in the present study, stage IV patients were more (69%), similar pattern was also seen in study found that 30% cancers were in stage III and 70% were found to be in stage IV. found 28% patients had Stage III disease and 72% had Stage IV.

In the present study, after completion of radiotherapy course and 3-4 weeks follow up, total 88% patients had pain relief, 83% shown improvement in dysphagia, 81% patients shown improved sleep patterns and 65% improvement in respiratory symptoms. carried out a study on 505 patients with stage IV HNSCC, gave a uniform regimen of 20 Gy in 5 fractions, once daily over 1 week. They reported good symptom relief in 57% for pain; 53% for dysphagia; 57% for hoarseness; 47% for otalgia and 76% for respiratory distress. The overall objective response and symptom control in the present study are comparable with this study. The two-week schedule used in a study by

[16] provided greater than 50% symptom relief in 90% of patients who had pain, dysphagia, dyspnoea and disturbed sleep.

Present study found that in Primary disease over all response rate was 23 (64%) and in Nodal disease it was 21 (58%). found that over all response rate was 73% but mentioned that 37% shown partial response. Performed studies describing short course of palliative radiation 3.5 Gy/fraction is given in 4 fractions in 2 days. Such two days regime has shown objective response, i.e., complete and partial response in 53% patients at the end of 6 weeks. Many Indian patients have advanced disease, poor nutritional and performance status and are found unfit for radical therapy. A short course of radiation is often effective in palliating symptoms in such patients.

In the present study, the radiation toxicities were mild (Grade-I Mucositis, 65%, Grade-II mucositis, 35%, Grade-I skin toxicity 44% and Grade-II skin toxicity 56%) as radiation reactions patients were treated with a short course of palliative radiotherapy [30 Gray (Gy)] in 10 fractions over 2 weeks.Found that the main acute toxicity of palliative radiotherapy was patchy oro-pharyngeal mucositis and dermatitis only. They gave a uniform regimen of 20 Gy in 5 fractions once daily over one week. Effective symptom relief was observed in half of all patients. Radiation toxicity was mild (grade 1- 2). an Australian Multicentric study , Grade 3 mucositis was seen in 26% patients. Radiation toxicities in the present study are less, which may be due to avoiding additional boost of radiation. Due to the palliative nature of treatment, late tissue morbidity is not significant issue in such patients treated with short course radiotherapy regimens. The incidence of grade 3 or worse toxicity is increased when concurrent chemotherapy is combined with conventional radical radiation. Such toxic treatment compromises the quality of life in these patients. The possible explanation for lower acute toxicity lies in the lower weekly accumulated dose of 8 Gy and time gap between two fractions resulting in a reduction in acute normal tissue reactions.

In present study, in 78% patients, only palliative radiotherapy was given, palliative radiotherapy followed by dose escalation was done in 22% patients. These findings are in accordance with a study done by this study, 74% of the patients completed the planned treatment.

Conclusion

The results from our study demonstratesthat a short course of radiation promises to effectively relieve symptoms in locally advanced head and neck cancers and reduce the need of ongoing analgesic therapy and hospital visits. It reduces the need of continued supportive care and overall improves quality of patients' life. It also helps in selecting patients for dose escalation. It is unsuitable for multi modality regimen measures as well as long duration conventional palliative radiotherapy. Dose escalate with smaller fraction sizes are advantageous for patients with a better performance status.

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