Original Article

Palliative Hypo-fractionated Radiotherapy in Locally Advanced Head and Neck Cancer with Fixed Neck Nodes

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Abstract

Background: The locally advanced head and neck cancer with fixed nodes are incurable and has a short survival. This study aims to evaluate the symptom relief, disease response and acute toxicity after palliative hypo-fractionated radiotherapy.

Methods: Between December 2010 to June 2011, previously untreated 50 patients who had histopathologically proved of head and neck squamous cell carcinoma with fixed node of stage IV, Eastern Cooperative Oncology Group (ECOG) performance status 2-3 were offered palliative radiotherapy (20 Gy/5Fr/5 Days). Patients were evaluated at 15th and 30th day after completion of treatment for disease response (WHO), palliation of symptoms using symptomatic response grading and acute toxicities (Radiation Therapy Oncology Group, RTOG).

Results: The most common presenting complaint was pain followed by dysphagia. Majority of patients (60-70%) had appreciable relief in their presenting symptom. In our study, we observed Partial Response (PR) in majority of patients (92 %); no patient had progressive or stable disease. None of the patients experienced radiation toxicities that required hospital admission. Almost all patients showed grade one and two acute skin and mucosal toxicities one month after completion of treatment.

Conclusion: Advanced head and neck cancer with fixed neck node should be identified for suitable palliative hypo-fractionated radiotherapy to achieve acceptable symptom relief in great proportion of patients.

Keywords: Cancer of head and neck; Lymph nodes; Palliative therapy

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Introduction

The most common head and neck cancer is oropharyngeal carcinoma (28.6%) followed by esophageal and oral cavity cancers (19.4%) and (16.3%), respectively. With respect to oral cavity and oropharynx, the most common site of involvement is the tongue (32.7%) [1].

Among Indian population, incidence of head and neck cancer had estimated 12.48 and 5.52 per 100,000 populations in male and female respectively. Estimated mortality is about 3.48 and 1.34 per 100,000 in male and female, respectively [2].

At our center, the registry of year 2010 recorded 1741 new cases of head and neck cancer which constitute about 28.3% of total registered patients. The common malignancies registered were carcinoma of tongue: 287 (16.48%), larynx: 214 (12.29%), tonsil: 160 (9.19%), laryngopharynx: 66 (3.7%), nasopharynx: 24 (1.38%) and post cricoid 71(4.08%). Metastatic squamous cell carcinoma of neck with unknown primary was about 10%. Majority of head and neck cancer patients present with advanced, incurable stage and around 50% dying from uncontrolled locoregional disease.

The word fixed node is interpreted in different ways by different authors. This difference in usage would explain the varying proportion of fixed nodes in different series from about 5% by Philip M Stell [3] (1984) to as many as 35% in G B Snow (1982) [4].The rate of treatment failure is high, particularly for large tumors or advanced disease, which lowers the overall cure rate and survival.

Strategies that modulate the biological response of tumors or normal tissues to radiation include

altered fractionation schedules, combined modality treatments using chemotherapeutic agents and more recently biological agents targeting molecular processes and signalling pathways. Altered fractionation schedules seek to improve the therapeutic ratio between tumor cell kill and normal tissue damage by exploiting the dissociation between acute and late radiation effects. There is no doubt that hypo-fractionation offer potential benefits to the patients and economy of health system, but their clinical implementation should not be at the expense of a lower likelihood of tumour control or a greater adverse effect on normal tissue.

In the developing world, approximately 75% of patients with head and neck malignancies present with locally advanced disease. These patients are often found unfit for radical surgical treatment or combined modality due to poor nutritional status. A short course of hypo-fractionated radiation is often effective for palliation to relieve the symptoms quickly with manageable side effects.

This prospective observational study is designed to quantify the response and radiation toxicity of short course hypo-fractionated radiation for locally advanced head and neck cancer with hard fixed cervical nodes and to assess the improvement of signs and symptoms on the basis of clinical observation and subjective feeling.

Materials and Methods

In our study, 50 previously untreated patients with histopathologically proved locally advanced head and neck squamous cell carcinoma with hard fixed cervical node(s) were included from December 2010 to June 2011.

Patients with stage IV AJCC (American Joint Committee on Cancer) with hard fixed cervical nodes, European Cooperative Oncology Group (ECOG) performance status (2, 3) with life expectancy <1year were included. Patients were treated by external beam radiotherapy delivered by Cobalt-60 teletherapy machine (Theratron 780E/780C). A total dose of 20Gy was given in 5 fractions in 5 consecutive days with a dose of 4Gy per fraction. Treatment volume included primary tumor site plus neck region. Bilateral Parallel-opposed fields were planned where disease crossing the midline and had bilateral presentation and dose was being prescribed to midline. Surface bolus was used in fungating lymph nodes. These patients were evaluated on 15th and 30th day and assessed for treatment response in terms of disease control (tumor regression) using WHO criteria [5] and palliation of symptoms using symptomatic response grading. Acute skin and mucosal reactions grading was done as per RTOG (Radiation Therapy Oncology Group) toxicity criteria. Further treatment of patients was done according to tumor regression status.

Results

Characteristics of the patient, disease and treatment are shown in Table 1.Median age was 55 years and ranges from 40 to 65 years. Most of patients had ECOG performance status 2. Most common presenting complaint was pain followed by dysphagia. Tonsil and base of tongue were commonly involved primary sites. Commonly observed histology was moderately differentiated squamous cell carcinoma.

Treatment related toxicities are shown in Table 2. None of the patients experienced radiation toxicities that required hospitalisation. Almost all patients showed grade one and two acute skin and mucosal toxicities at one month after completion of treatment.

Symptom burden at presentation and symptomatic relief on follow-up visits are shown in table 3. Majority of patients (60-70%) had appreciable relief in their presenting symptoms.

Overall treatment response at one month follow-up is shown in Table 4. In our study, we observed Partial Response (PR) in majority of patients (92 %) and no patient had progressive or stable disease.

Discussion

Although it is appropriate to have a well-coordinated multimodal approach for advanced head and neck cancer, there are many grey areas in treatment since both III and IV stage and resectable/unresectable patients were combined in the reported studies. Recently Vikram et al. [6] has suggested that advanced head and neck cancers from developing countries do not show favourable outcomes and it would seem prudent for these patients to explore novel ways of providing relief. It is now realized that a proportion of advanced stage patients have life-limiting disease.

Eight hundred eight untreated head and neck cancer patients (91% stage IV) followed-up longitudinally; the median survival time was approximately100 days. It has further been studied that treated patients showed higher survival rates compared to best supportive group and type of treatment performed, even when aggressive, did not influence the survival. When the patient has more than 80% likelihood of death within 12 months, palliative treatment seems judicious and such practices have become standard therapeutic

decisions for many other advanced or metastatic solid tumors.

Weissberg et al. [7] evaluated conventionally fractionated versus hypofractionated palliative External Beam Radiation Therapy (EBRT) schedules for patients with locally recurrent or advanced head and neck cancers. That study compared 60 Gy to 70 Gy in 6 to 7 weeks versus 40 Gy to 48 Gy in 64 patients with stages III and IV surgically unresectable squamous cell carcinoma of the head and neck. No differences were noted in tumor control, acute side effects, or long term sequelae.

Sushmita Ghoshal et al. (2004) conducted another study to evaluate the role of palliative radiotherapy for symptom control in patients with locally advanced head and neck cancer. In this study, 25 patients with stage 3 and 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 using an 11 point numerical scale for pain, dysphagia, cough, insomnia and dyspnea. The primary end point was relief of symptoms in the fourth week after radiotherapy. All 22 patients with pain and 90% of patients with dysphagia, dyspnea and disturbed sleep had greater than 50% relief in symptoms after radiotherapy. Cough was relieved in 60% of cases [8]. In our study, 52% patients presented with main complaint of pain and 32% of patients with dysphagia, after radiotherapy more than 76% got relief from pain and more than 66% patients got relief from dysphagia.

In a large study, on 505 patients with stage IV head and neck squamous cell carcinoma, Mohanty et al gave a uniform regimen of 20 G_y/5 Fractions, once daily over 1 week. They reported good symptomatic relief (>50% for pain, 53% for dysphagia, 57% hoarseness, 47% otalgia, 76% for respiratory distress and 59% for cough). At one month assessment, 189 (37%) achieved a partial response and had ambulatory physical state suited for further curative-dose radiotherapy. The main acute toxicity of palliative radiotherapy was patchy oro-pharyngeal mucositis and dermatitis. Median overall survival was 200 days. One hundred fifty three patients who went on to receive further curative dose had significantly overall survival of 400 days [9].

Ling SM et al. [10] assessed the effect of Electron Beam Intraoperative Radiotherapy (EB-IORT) on local-regional control and any associated complications in patients with locally advanced or

Table 1. Patient characteristics

Variable		Number of patients
Sex	Male	40 (80%)
	Female	10 (20%)
ECOG	2	32 (64%)
	3	18 (36%)
Main complaint	Pain	48 (96%)
	Dysphagia	16 (32%)
	Hoarseness	11 (22%)
	Respiratory distress	10 (20%)
	Other	3 (6%)
Primary site of disease	Tonsil	12 (24%)
	Base of tongue	11 (22%)
	Hypo-pharynx	14 (28%)
	Larynx	6 (12%)
	Other	7 (14%)
Primary tumor stage	T3	27 (54%)
	T4	23 (46%)
Nodal stage	N2	20 (40%)
	N3	30 (60%)

Table 2. Acute reactions

Time of follow-up	Acute skin reaction				Acute mucosal reaction			
	Grade I	Grade II	Grade III	Grade IV	Grade I	Grade II	Grade III	Grade IV
15th day	10 (20%)	0	0	0	7 (14%)	0	0	0
30th day	31 (62%)	19 (38%)	0	0	27 (54%)	21 (42%)	2 (4%)	0

recurrent head and neck cancer. In this study, 25 patients were included with recurrent or persistent disease despite previous treatment with full-course external-beam radiotherapy and/or one or more resections. EB-IORT was given as a single fraction of 1500 cGy to the 90% isodose with 6 or 9 Mev electrons. With a median follow-up time of 30 months, nine patients (27%) had only local recurrence. Of these, only one recurrence was inside the EB-IORT field and eight were outside the EB-IORT field. Two patients (7%) developed distant metastases only and one patient (3%) had both local recurrence and distant metastasis. Seven patients died, five with disease. Twenty-two patients are known to be alive, 15 (68%) of whom have no evidence of disease. One patient was lost to follow-up after 12 months; when last examined he was free of disease. Five patients (16%) have had mild-to-moderate transient complications probably related to EB-IORT. The 3-year actuarial local-regional control rate was 60%.Due to unavailability of IORT in developing countries this modality remains underused.

Our study which was also conducted in similar way, reported good symptomatic relief (more than 76% for pain, 66% for dysphagia, 50% hoarseness, 35% otalgia and 70% for respiratory distress). The main acute toxicity of palliative radiotherapy was similar to above study. At one month assessment 92% patients achieved partial response.

In our study, we observed that two-third of the patients experienced multiple symptoms and the short course of palliative radiotherapy provided durable symptom relief to more than 50% of the patients.

Fraction size is the dominant factor in determining late effects but overall treatment time has little influence on these effects. In patients having poor survival, late effects are meaningless; it is a determining factor in providing good quality of life.

Thus, patients in whom disease progressed in spite of hypo-fractionated radiotherapy were offered palliative symptomatic treatment.

It is concluded that unfavourable advanced stage head and neck cancer can be identified for a suitable short course palliative radiotherapy which will achieve growth restraint and symptom relief in sizeable proportions of patients. This study tries to strike a balance between economic burden, treatment time and hospital stay and machine load.

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Conflict of Interest

The authors have no conflict of interest.

Table 3. Symptomatic relief in main complaints

Main symptom on presentation (No. of Patients)	Symptom Relief		
	No Relief (%)	Partial Relief (%)	Appreciable Relief (%)
Pain (48)	0 (0.0)	18 (37.5)	30 (62.5)
Dysphagia (16)	0 (0.0)	4 (25.0)	12 (75.0)
Hoarseness of voice (11)	1 (9.1)	2 (18.20)	8 (72.7)
Respiratory distress (10)	1 (10.0)	2 (20.0)	7 (70.0)

Appreciable relief means ≥ 50% symptomatic relief
Partial relief means < 50% symptomatic relief

Table 4. Overall treatment response during follow up

Response	Number of patients	
	15th day	30th day
CR	2 (4%)	4 (8%)
PR	26 (52%)	46(92%)
SD	22 (44%)	0

Authors' Contribution

Rajan Paliwal and Arvind Patidar designed the study and analysed the data. Rahul Walke and Pushpendra Hirapara contributed to the data entry and literature review. Sandeep Jain and Megh Raj Bardia contributed to the study design and writing-up process.

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