

Comparative Evaluation of Palliative Radiotherapy with Chemotherapy vs. Palliative Radiotherapy Alone in Locally Advanced Head and Neck Cancer

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Abstract

Background: The aim of the study was to evaluate and compare the efficacy, tolerability and toxicity of two palliative radiotherapy (RT) schedules in locally advanced head and neck carcinoma (LAHNC), i.e., Quad Shot schedule with chemotherapy and Quad Shot schedule alone.

Methods: The patients were randomly divided into two groups of 30 each. Group I patients were planned for 14.8 Gy in 4 fractions over 2 days every 3 weeks for three cycles. All these patients also received paclitaxel 60 mg/m² intravenous. Group II patients received 14.8 Gy in 4 fractions over 2 days every 3 weeks for three cycles alone. All these patients in Group I and II received total radiation dose of 44.4 Gy.

Results: At the end of treatment, complete tumor response (CR) in Group I was better than Group II (40% vs. 36.7%). Disease status (tumor+node) at the end of treatment in terms of complete response was 36.7% vs. 0% (11/30 and 0/30) in Group I and II. Disease status at 6 months of follow up was noted as follows: complete tumor response in Group I and II was 23.3% (7/30) vs. 10% (3/30) (p=0.012). Complete nodal response was 35.7% (10/28) in Group I and 6.67% (02/30) in Group II (p= 0.538). Overall, no evidence of disease was observed in 16.7% (5/30) in Group I and 3.3% (1/30) in Group II respectively (p<0.001).

Conclusion: This palliative schedule has been shown to provide good tumor response and palliation of symptoms. The toxicity profile remains low with the addition of paclitaxel. Further investigation is warranted in a larger trial. Palliation of symptoms resulted in improved quality of life for these group of patients

Keywords: Head and neck carcinoma; Palliative radiotherapy; Chemotherapy

Introduction

Globally, a major challenge of the 21st century is non-communicable diseases (NCDs). Of all cancers, Head and neck cancer accounts for 4.8% worldwide and 14.3% in India [1]. In India at the time of presentation 60-70% of patients are in locally advanced stage with 60-70% local failure rates [2]. Treatment with Radiotherapy (RT) achieved local control rates of 50-70% and disease-free survival rate in the range of 30-40% [3]. Because of advanced stage and poor general condition, some of the patients are suitable only for palliative RT. 30 Gy/2 weeks/10 fractions dose of Radiotherapy are used for palliation of symptoms [1]. The goal of treatment in these patients is to achieve immediate relief in symptoms. Combination of chemotherapy with palliative radiotherapy has been shown to improve good tumor response and palliation of symptoms. The present prospective, randomized study was planned to comparatively evaluate the efficacy, tolerability and toxicity of two schedules of palliative RT in LAHNC.

Materials and Methods

The present randomized, open label, parallel study was conducted on 60 treatment-naive, histopathologically proven patients of LAHNC. Patients receiving palliative RT for LAHNC from April 2014 to June 2016 were randomly divided by simple random sampling in two groups of 30 patients each. The study was carried out after the approval of the protocol by the institution's review board. Informed consent was obtained from all the patients before initiation of the study. The inclusion criteria for the patients selected for the study were: Karnofsky performance status (KPS) \geq 70, complete hemogram with hemoglobin >8 g/dL, total leucocyte count (TLC) >4,000/mm³, platelet count >100,000/mm³, renal function tests with blood urea <40 mg/dL and serum creatinine <1.5 mg/dL, liver function tests with Aspartate

transaminase (AST) and alanine transaminase (ALT) <35 IU/L, American Joint Committee on Cancer (AJCC) stage IV and a positive biopsy for squamous cell carcinoma of head and neck. The patients having distant metastases, prior radiation, surgery or chemotherapy, KPS <70, pregnant or lactating patients, histopathology other than squamous cell carcinoma were excluded from the study.

- Group I comprised of 30 randomly selected patients, having histopathologically proven squamous cell carcinoma of head and neck, suitable for palliative radiotherapy. All these patients received total radiation dose of 44.4 Gy. Radiation therapy was delivered in a dose of 2 daily fractions of 3.7 Gy for 2 days every 3 weeks for three cycles. All these patients also received paclitaxel 60 mg/m² intravenous 1 hour prior to the first day of each radiation cycle. Spinal cord sparing was done for last two fractions.
- Group II comprised of 30 randomly selected patients, having histopathologically proven squamous cell carcinoma of head and neck (Table 1), suitable for palliative radiotherapy. All these

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patients received only radiotherapy with total radiation dose of 44.4 Gy. Radiation therapy was delivered in 2 daily fractions of 3.7 Gy for 2 days every 3 weeks for three cycles. Spinal cord sparing was done for last two fractions. All the patients were treated in a supine position. Two-dimensional planning was performed with a pre-treatment simulation to work out the field borders which covered the primary tumor, disease extension and neck nodes. The patients were treated by parallel opposing fields and the dose was prescribed to the mid plane at the central axis. RT was delivered by cobalt-60.

Radiation reactions were assessed by Radiation Therapy Oncology Group (RTOG) criteria [4]. Tumor response (both primary and nodal response) was assessed by World Health Organization (WHO) response criteria either clinically or if needed, radiologically [5]. From the commencement of treatment, all the patients were regularly assessed daily during treatment and weekly during planned gaps in treatment. Detailed clinical evaluations were done by thorough local examination of the patients and all the patients were followed up regularly on outpatient basis for a period of at least 6 months at 1month interval. The results of the study regarding completion of intended treatment, any interruptions in treatment, toxicity, local control rates and disease status at last follow-up in all the groups were documented.

Statistical analysis

The data, thus obtained, was assessed, analysed and compared to find out the difference in the two groups in terms of tumor response, side effects and toxicity. Quantitative data is presented as mean and standard deviation whereas qualitative data is presented as simple proportions and percentages. Qualitative variables were analysed using Chi-square test, Chi-square goodness of fit and Z test for proportions. For data analysis, SPSS version 20.0 was used. Statistical significance was considered when p value was less than 0.05.

Results

The patient's histopathological characteristics are shown in Table 1. The patient parameters were comparable in the two groups. The youngest patient was 40 years old in group I and 37 years in group II. Age of oldest patient in corresponding groups was 85 years and 80 years. The mean age at presentation in group I and group II was 58.70 years and 54.56 years respectively. The mean dose received by the patients was 43.41 Gy in both the groups. All patients in both the groups completed intended treatment. At the end of treatment, complete tumor response (CR) in group I was better than group II (40% vs. 36.7%). In T2 subgroup, complete tumor response was 100% vs. 50% (3/3 and 4/8), and in T3 and T4 subgroups CR was 33.3% vs. 33.3% (06/18 and 7/21

and 33.3% vs. 0% (3/9 and 0/1) in group I and II respectively. Overall, results were found to be in favour of group I, the difference being statistically significant (p=0.012). At the end of treatment, complete nodal response (CR) in N1 subgroup was 66.7% vs. 0% (2/3 and 0/1) and in N2 subgroup was 41.6% vs. 0% (10/24 and 0/28) for Groups I and II respectively. N3 subgroup in both the groups showed partial response. Overall results are in favour of Group I, but this difference was statistically insignificant (p=0.538). Disease status (tumor + node) at the end of treatment in terms of complete response was 36.7% vs. 0% (11/30 and 0/30) in group I and II respectively which is clearly in favour of group I and the difference was statistically significant (p<0.001) (Table 2 and Figure 1).

Grade II skin reaction at the 3rd, 4th, 5th, 6th week and at the end of treatment was seen in 3 (10%), 3 (10%), 18 (60%), 16 (53%) and 17 (56.7%) patients in group I and 3 (10%), 4 (13%), 17 (56.7%), 17 (56.7%) and 18 (60%) patients in group II respectively. No Grade III skin reactions were observed. Toxicities were comparable in both the groups and the difference was statistically insignificant (p>0.05). At the end of treatment, acute mucosal reactions were 40% vs. 47% in group I and II respectively and the difference was statistically significant (p<0.001). No Grade III mucosal reactions were observed in both the groups.

Disease status at 6 months of follow up was noted as follows: complete tumor response in group I and II was 23.3% (7/30) vs. 10% (3/30), better in group I (p=0.012). Complete nodal response was 35.7% (10/28) in group I and 6.67% (02/30) in group II, better in group I (p=0.538). Overall no evidence of disease was seen in 16.7% (5/30) patients in group I and 3.3% (1/30) in group II respectively (p=0.188).

Discussion

This study was carried out on sixty patients of locally advanced stage IV (A/B), histopathologically proven cases of squamous cell carcinoma of head and neck region. In LAHNC, surgery without postoperative RT is related with poor cure rates. Comparison of Surgery plus adjuvant RT with surgery alone, adjuvant RT gives benefit of 10% absolute increase in 5-year cancer-specific survival and overall survival. Immediate relief in symptoms is the main aim of palliative radiotherapy with minimum side-effects. This twice a day split course treatment format in patients with advanced cancer has been shown in the past to provide good palliation of symptoms with minimal acute and late toxicity. Historical response rates of 45–70% were acceptable but improvement without increasing the toxicity was desirable [6-8]. Because of the advanced stage at the time of presentation, the local failure rates are as high as 50-70%, despite improvement in treatment strategies for the management

Type	Group I (n=30) No. of Patients (%)	Group II (n=30) No. of Patients (%)	Overall (n=60) No. of Patients (%)
WDSCC	01 (03.33%)	00 (00.00%)	01 (01.00%)
MDSCC	27 (90.00%)	30 (100.0%)	57 (95.00%)
PDSCC	02 (06.67%)	0 (00.00%)	02 (3.33%)

WDSCC: Well Differentiated Squamous Cell Carcinoma; MDSCC: Moderately Differentiated Squamous Cell Carcinoma; PDSCC: Poorly Differentiated Squamous Cell Carcinoma

Table 1: Histopathological distribution of patients with locally advanced head and neck carcinoma.

Groups	Stage	Total no. of patients	Disease status		p-value
			CR	PR	
I	IV	30	11 (36.6%)	19(63.3%)	0.038
II	IV	30	00 (00.0%)	30 (100.0%)	<0.001

Abbreviations used: CR, complete response; PR, partial response

Table 2: Comparison of disease status at the end of treatment in both the groups.

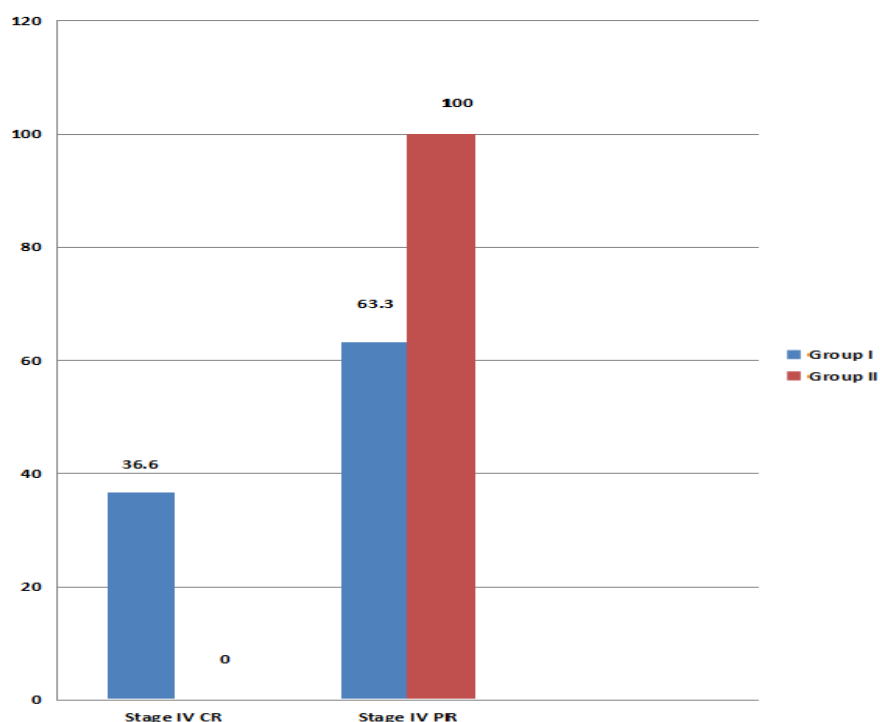


Figure 1: Bar diagram representing disease status at the end of treatment in both the groups.

of LAHNC [9]. For this group of patients with a limited life span and who are ineligible for curative therapy, the addition of paclitaxel may serve as a small step toward the goals of optimal palliation—excellent tumor response, low treatment-related toxicity and limited time in the hospital or treatment centre.

The cutaneous radiation reactions follow a definite pattern following conventional RT. In the present study, the skin changes were consistent with those described in literature [4]. Hypo fractionation has been known to produce greater overall toxicity in head and neck cancer patients. In this study, disease status (tumor+node) at the end of treatment in terms of complete response was 36.7% vs. 0% (11/30 and 0/30) in group I and II respectively which is clearly in favour of group I and the difference was statistically significant ($p < 0.001$). No Grade III skin reactions were observed in the patients. Toxicities were comparable in both the groups. The differences in two groups for grade II reactions were statistically insignificant at 5th and 6th week and at the end of treatment ($p < 0.05$). Hypo fractionated twice daily split course treatment is known to produce similar reactions in head and neck cancer patients [10-17].

Mucosal reactions were comparable in both the groups. No grade III mucosal reactions were observed in both the groups. The difference in observations was statistically significant ($p < 0.05$). In group I, our results are comparable to Carrascosa et al. [15] and Paris et al. [18] in providing good tumor response and palliation of symptoms [15-19]. Late radiation toxicity was observed in accordance with that reported by Ghoshal et al. [19], Corry et al. [20] and Soni et al. [21].

The patients were followed for a period of 6 months. Disease status at 6 months of follow up was noted as follows: Complete tumor response in group I and II was 23.3% (7/30) vs. 10% (3/30) respectively ($p = 0.012$) while complete nodal response was 35.7% (10/28) in group I and 6.67% (02/30) in group II ($p = 0.538$). Overall no evidence of disease

was observed in 16.7% (5/30) in group I and 3.3% (1/30) in group II respectively ($p = 0.188$).

Conclusion

Based on the comparison of treatment response in both the groups, it may be concluded that paclitaxel based chemotherapy plus palliative radiotherapy is better as compared to palliative radiotherapy alone in terms of better tumor control, better tolerability and low toxicity profile. Addition of paclitaxel to palliative RT may serve as a small step towards the goal of improving the quality of life by achieving optimal palliation; good tumor response, low toxicity and shorter hospital stay though the claim needs to be reinforced by similar supporting studies in larger sample size.

Conflicts of Interest

The authors declare no conflicts of interest.

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