Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Conventional Radiotherapy versus Accelerated Fractionation Radiotherapy in Squamous Cell Head and Neck Cancers – A Prospective Comparative Study

B Rajkumar

Senior Resident, Department of Radiotherapy, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India

Abstract

Introduction: Treatment of locally advanced lesions of head and neck cancers includes a combined modality approach such as surgery, radiotherapy (RT), and chemotherapy.

Aim: The aim of the study was to study the treatment response by locoregional control and radiation toxicity of conventional and accelerated fractionation RT in squamous cell head and neck cancers.

Materials and Methods: A total of 30 patients were included in each group, Group A received accelerated six fractions per week and Group B received conventionally fractionated radiation therapy. The patients were assessed for locoregional disease response and radiation toxicities weekly during RT and at the end of treatment.

Results: In this study, 4 patients were dropped out and 26 patients completed the treatment in each group. About 86% of the patients in the accelerated fractionation arm and 82% of the patients in conventional arm showed complete response. Radiation toxicities were slightly higher in accelerated fractionation compared to conventional fractionation RT.

Conclusion: Accelerated fractionation with concurrent chemotherapy can be considered as an alternative treatment strategy to conventional chemoradiation.

Key words: Accelerated fractionation, Conventional fractionation, Head and neck cancer, Radiation toxicity

INTRODUCTION

Radiotherapy (RT) is an extremely effective treatment for head and neck cancer, both as a primary modality and as an adjuvant treatment following surgery. RT causes significant acute (during and up to 3 months post-radiation) and late toxicities when used at doses required to sterilize the locoregional disease (radical doses). The acute toxicities of RT include mucositis, dysphagia, xerostomia, dermatitis, and pain. Radiation-induced mucositis of the upper aerodigestive tract results in significant morbidity and altered quality of life during RT.[1]

Access this article online

www.ijss-sn.com

Month of Submission : 09-2019
Month of Peer Review : 10-2019
Month of Acceptance : 11-2019
Month of Publishing : 11-2019

The conventional system of fractionation, i.e., 60–70 Gy in 2 Gy per fraction 5 times a week as the optimal way of delivering RT in all circumstances is highly debatable.[2] While treating head and neck cancers with radiation, a balance is to be maintained between four parameters, i.e. total radiation dose, dose per fraction, overall treatment time, and the irradiated volume.[3] One of the most important biological factors hindering the local control is accelerated repopulation of tumor cells after the initiation of treatment. Treatment with chemotherapy or radiation triggers the surviving cells in a tumor to divide faster than before and a larger proportion of tumor clonogenic comes to the replication pool.[4] This can make the tumor resistant to conventional fractionation of radiation as well as to chemotherapy. There are a number of clinical reports which prove that a decrease in treatment time has improved the clinical outcomes which is clinically and biologically documented.[5]

Shorter treatment time can be achieved by applying a higher dose per fraction which may increase the rate of

Corresponding Author: Dr. B Rajkumar, Department of Radiotherapy, Tirunelveli Medical College, Tirunelveli, Tamil Nadu, India.

complications disproportionately. Hence, the number of fractions delivered per week is increased without increasing the dose per fractions. This fractionation is called accelerated RT, i.e., 60–70 Gy in 2 Gy/fractions, 6 times a week, and Monday to Saturday. Accelerated fractionation shortens overall treatment time, minimizes tumor repopulation during treatment and therefore increases the probability of tumor control for a similar total dose.[6]

In conventional fractionation RT (CFRT), the patients were given a total dose of 60–70 Gy in 2 Gy/fractions, 5 times a week, and Monday to Friday. The main aim was to assess whether similar disease control could be achieved with accelerated fractionation RT (AFRT) as compared with CFRT in head and neck cancers in the Indian population.[7]

Aim

The aim of the study was to study the treatment response by locoregional control and radiation toxicity of conventional and AFRT in squamous cell head and neck cancers.

MATERIALS AND METHODS

This is a prospective comparative study conducted in the Department of RT at Tirunelveli Medical College in patients with squamous cell head and neck cancers.

Inclusion Criteria

Patients with squamous cell head and neck cancers confirmed with malignant histology, no prior treatment (surgery or neoadjuvant chemotherapy), and no evidence of distant metastases.

The tumor sites include the oral cavity, oropharynx, hypopharynx, and larynx. The tumor stages were confined to Stages I-III. All patients had regional nodal metastases. About 30 patients were enrolled in each arm. The patients were randomly assorted into two groups.

- Group A – Received accelerated six fractions per week, Monday to Saturday, 2 Gy/day up to 66 Gy in 5.3 weeks.
- Group B – Conventionally fractionated radiation therapy – Received conventional five fractions per week, Monday to Friday, 2 Gy/day up to 66 Gy in 6.3 weeks.

During radiation treatment, the field of radiation included the gross primary tumor with a generous margin (2–3 cm) with a bilateral neck. After 44 Gy, the posterior neck field was reduced to spare spinal cord. All the patients were treated in tele cobalt machine. Mostly opposing lateral fields were used. During treatment adequate nutritional support, aggressive hydration, antiemetic therapy, and psychological support were given. All patients were encouraged to complete the full treatment schedule in the allotted time period. Some patients had minor interruption due to toxicity. Common radiation-induced toxicities encountered were anemia, mucositis, skin reactions, and dysphagia, which were managed with intensive care.

The patients were assessed for locoregional disease response and radiation toxicities weekly during RT and at the end of treatment. The locoregional response was considered to be complete if there was complete regression of the disease with no visible or palpable disease, partial, if there was more than 50% regression in the lesion, stable, if lesion regressed <50% and progressive, and if lesion increased by 25% or appearance of new lesion. During the course of radiation execution, tolerance to treatment was assessed by noting the weight, performance status, and radiation reactions. The radiation toxicity was assessed according to radiation therapy oncology group toxicity criteria.

RESULTS

In this study, 30 patients were recruited in both groups and 4 patients were dropped out in the study for various reasons. All the patients are male with a mean age of 58.4 in Group A and 56.2 in Group B. Figure 1 shows the site of the tumour.

In the end, a total of 26 patients were available for analysis in both groups. At the end of treatment, a complete response (CR) was identified in 86% of patients in accelerated fractionation group (Group A) and in 82% of patients in conventional fractionation group (Group B) Figure 2. During treatment, patients in Group A found difficult to complete the treatment compared to Group B due to the higher incidence of radiation toxicity. Acute skin reactions were observed in both arms which were slightly more in Group A. Acute mucositis was the most important

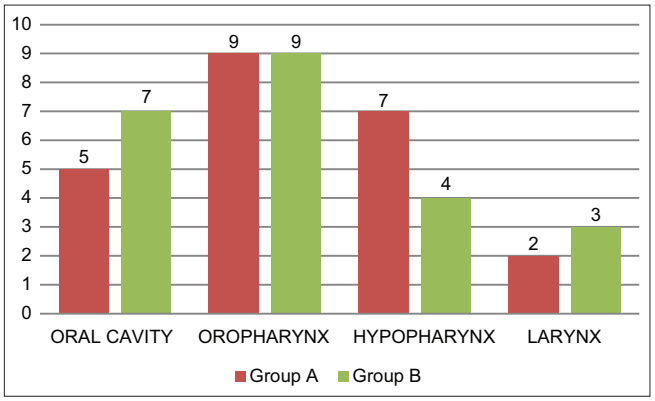

Figure 1: Tumor site

toxicity observed in both groups and appeared early in the accelerated fractionation group. Furthermore, the onset of dysphagia was earlier in Group A, although the severity of dysphagia was the same by the end of treatment. Anemia and neutropenia were encountered in both groups. The toxicities were treated intensively with intravenous fluids, blood transfusion, colony-stimulating factors, antibiotics, etc. All the patients were given psychological support and were encouraged to complete the treatment without increasing the treatment period Figure 3.

DISCUSSION

Head and neck squamous cell carcinomas are notorious for accelerated repopulation during the course of RT. This phenomenon usually sets in after 4 weeks of radiation therapy and to counteract this, 0.6 Gy of extra dose per day is needed.[8] To increase local control and survival, in the past decade, altered fractionation regimens have been assessed for the treatment of head and neck squamous cell carcinomas. The most commonly used altered fractionation schedules for the RT of advanced head and neck cancers are: Hyperfractionated RT to exploit the differences in radiosensitivity of cancer and normal cells to increase the therapeutic ratio; accelerated RT to overcome tumor repopulation; and accelerated-hyperfractionated RT to combine the effects of the two irradiation regimens.

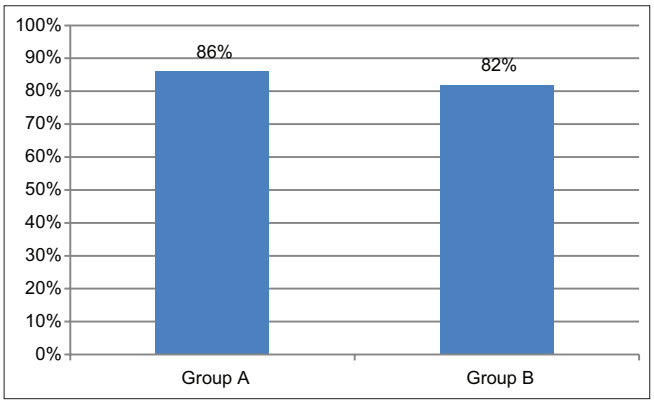

Figure 2: Complete response immediately after the end of the treatment

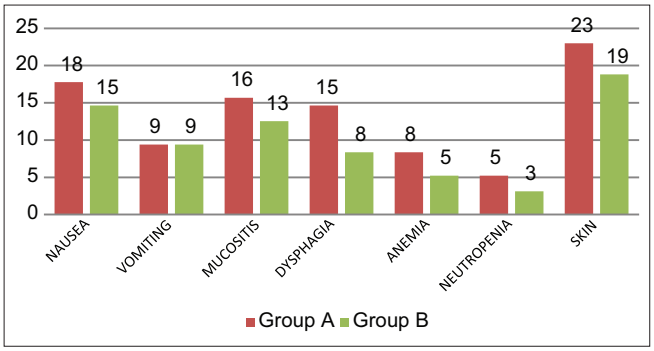

Figure 3: Distribution of toxicity

Several prospective randomized studies have shown that accelerated RT improves locoregional control in squamous cell carcinoma of head and neck. However, accelerated regimens have been shown to increase treatment-associated acute morbidity, which in severe cases might lead to an increase in late radiation effects. This study was conducted with the objective that pure accelerated RT with concomitant chemotherapy would result in better treatment outcomes compared to conventional chemoradiotherapy. Another objective was to find out whether patients can tolerate the new accelerated schedule.

In a prospective study by Gupta *et al.*,[9] at first follow-up, 90.9% had a CR at the primary site and 89.1% had a CR at the nodal site in the accelerated arm and in conventional RT arm corresponding figures were 81.5% and 75.9%, respectively. At a median follow-up of 43 months, CR was seen in 29 patients (52.7%) in the accelerated RT arm and 24 patients (44.4%) in the conventional RT arm. Although the difference in locoregional control was not statistically significant, this study clearly indicates a trend toward the improved outcome. In Danish head and neck cancer study group study,[10] locoregional tumor control improved significantly in the accelerated fractionation group compared with that in the conventional RT group (70% vs. 60% 5 years actuarial rate, $P = 0.0005$). There was 10% statistically significant improvement in locoregional disease control in the accelerated arm. In the International Atomic Energy Agency – ACC study by Overgaard *et al.*,[11] the 5-year actuarial locoregional control was 42% in the accelerated versus 30% in the conventional group ($P = 0.004$).

CONCLUSION

In this study, there was no statistically significant difference, in the efficacy was noted whereas in the centers with high patient load can consider accelerated fractionation an alternative treatment strategy to conventional fractionation which is radiobiologically superior and also beneficial in squamous cell head and neck cancers.

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How to cite this article: Rajkumar B. Conventional Radiotherapy versus Accelerated Fractionation Radiotherapy in Squamous Cell Head and Neck Cancers – A Prospective Comparative Study. Int J Sci Stud 2019;7(8):1-4.

Source of Support: Nil, **Conflicts of Interest:** None declared.