

Comparison of Conventional RT and CHART in Locally advanced head and neck

cancer: an Institutional experience

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ABSTRACT: **Abstract:** **Introduction:** Carcinoma of head and neck region are one of the commonest malignancies in India and contribute significantly to the annual morbidity and mortality rates. The decision of choosing modality of management rests on factors such as the functional and cosmetic results, general status of the patient and the desire of the patients.

Material and Method: The aim of study is to access the feasibility of using CHART and tolerance of this protocol over the conventional Chemo-radiotherapy by comparing the effects in terms of tumor regression and reaction during and after radiotherapy.

Results: The median age, ratio of male: female of the Control and Study arm was 56 and 53 years, 3.5:1 and 2.5:1 respectively. The most of the patients were stage III (T3 and N2) in both arms. Most of the patients have 0-1 ECOG performance status. The grade III/IV Skin reactions in Conventional versus CHART arm were 26.42 versus 77.78. (p value=0.001) The grade III/IV Mucositis in Conventional versus CHART arm were 33.96 and 70.38. (p value=0.001).

Conclusion: Even the reduction in total dose from 66 Gy to 54 Gy in CHART arm, the control rate of loco-regional disease and survival was non inferior together with the low incidence of long-term severe adverse events to those with CRT.

Introduction:

Carcinoma of head and neck region are one of the commonest malignancies in India and contribute significantly to the annual morbidity and mortality rates. The carcinoma of various anatomic sites of head and neck region share among themselves many similarities and are therefore, commonly grouped together under one heading as “head and neck carcinoma”. The carcinoma of head and neck region are commonly the disease of middle and old age. This is commonly found in persons having long standing habits of smoking, alcoholism or taking tobacco in any form and poor oro-dental hygiene etc. They are more common in males. They originate in the mucous membrane of upper aero-di-

gestive tract and histo-pathologically most of them are squamous cell carcinomas of varying malignant potential.

The decision of choosing modality of management rests on factors such as the functional and cosmetic results, general status of the patient and the desire of the patients. In most cases of advanced head and neck carcinomas, surgery alone may not be used as a curative modality because complete surgical excision of the advanced tumor may not be practically possible. Radiation therapy therefore, remains the main stay for the management in majority of cases of advanced head and neck carcinomas.

Various fractionated schedule in addition to the conventional radiation therapy, have also been tried from time to time on the basis of

radiobiological knowledge in order to achieve better results. In view of these advantages of CHART in locally advanced head and neck cancers, we planned a prospective comparative study between CHART and conventional chemo-radiotherapy in terms of tumor control and treatment toxicities.

Material and Method:

The aim of study is to assess the feasibility of using CHART and tolerance of this protocol over the conventional Chemo-radiotherapy by comparing the effects in terms of tumor regression and reaction during and after radiotherapy. 107 patients with histopathologically proved locally advanced squamous cell carcinoma of head and neck (III and IVa) were randomized in study and control arm. The inclusion criteria were age 18-70 years, European Co-operative Oncology Group (ECOG) performance status (0-2) and no prior treatment of malignancy.

Conventional and CHART group consisted of randomly selected previously untreated 53 and 54 patients of squamous cell carcinoma of head and neck. Radiotherapy was given three times a day with a dose of 150 cGy/ Fraction minimum 6 hours' interval for continuously 12 days by Cobalt-60 Theratron-780E/780C & Bhabhatron-II teletherapy units. In phase I a total dose of 4500 cGy was delivered in 30 fractions to the tumor and draining lymph nodes. After this dose, off-record planning with field size reduction to the main tumor bulk was done and further 900 cGy was delivered in 6 fractions to reach 5400 cGy. Patients were hospitalized if required to manage the acute radiation reactions. All patients were counseled regarding the requirements of Ryle's tube feeding. The control group patients were received injection Cisplatin 40 mg/m² weekly for 4-6 doses. All patients were received 6600 cGy

chemo radiation at 2 Gy/fr, 1fr/day, 5fr/week, in 6-7 weeks by cobalt-60 Theratron-780E/780C and Bhabhatron-II teletherapy units. In both arm initial treatment fields included the primary tumor with adequate safe margins and primary nodal drainage region.

Parallel opposed bilateral fields were planned. The doses were prescribed at midline. Treatment interruptions were strongly discouraged. Treatment breaks were clearly indicated in the treatment record when they occur and time corrections were made.

Results:

The median age, ratio of male: female of the Control and Study arm was 56 and 53 years, 3.5:1 and 2.5:1 respectively. The Base of tongue was the most common malignancy site in both arm followed by tonsil, soft palate and vallecula. The most of the patients were stage III (T3 and N2) in both arms. Most of the patients have 0-1 ECOG performance status. The grade III/IV Skin reactions in Conventional versus CHART arm were 26.42 versus 77.78. (p value=0.001) The grade III/IV Mucositis in Conventional versus CHART arm were 33.96 and 70.38. (p value=0.001). After 6 months of treatment completion, the primary site response rate was superior in CHART patients. The patients were follow-up for a period of 24 months since treatment. Loco-regional control at 2 years is 51% versus 46% for CHART and CRT arm respectively. (p value=0.611)

Discussion:

The fractionated schedules are in the form of hyper-fractionation, hypo-fractionation and accelerated fractionation besides conventional radiotherapy. Each of these had their own advantages and disadvantages. Studies on cellular kinetics using bromo-deoxyuridine (Wilson et al 1988)^{1,2} have shown a high rate of cell division

in tumors during the treatment i.e. in between the two fractions and this could be a major factor leading to treatment failure. Some studies have suggested that certain tumor cells have a short doubling time and squamous cell carcinoma of head and neck is one of them. The potential doubling time of tumors of head and neck region is five days or less.³

During a conventional course of radiotherapy given over 6-7 weeks, accelerated repopulation of tumor cells might be an important cause for treatment failure. It has been established that giving ionizing radiation in multiple small fractions may lead to a reduced incidence of late radiation change. The above observation suggests using a fractionated regime, in which the treatment can be completed at the earliest possible time with minimal complication rate and good patient tolerance. This prompted the radiation oncologists to combine the accelerated and hyper-fractionated regimes which will satisfy both condition i.e. early completion of treatment (accelerated) and lesser complication by use of hyper-fractionation.

More than half of the patients attending the department of Radiation oncology at Regional cancer center which is situated in the middle of desert. They generally belong to remotely placed villages and mostly belong to low socio economic group. They find it very difficult to complete the long radiotherapy course (a minimum period of 6 weeks) delivered by conventional radiotherapy technique. If a proper dose per fraction (optimum dose) could be evaluated and established by combining accelerated and hyper-fractionation techniques (CHART), then it can be of great help to these poor patients, in terms of time and money and comfort.

Accelerated fractionation is shortening the overall treatment duration of a regimen using conventional dose fractionation. The aim is to

reduce the tumor growth rate during the treatment period by irradiating the tumor at an accelerated rate. This is achieved by giving 2 or 3 fractions daily. Total dose is similar to conventional radiotherapy given in multiple fractions.^{4,5,6} Acute mucosal toxicity occurs at an increased rate in patients receiving CHART.⁷ During the past 20 years, several experiments and clinical studies were carried out on these radiobiological factors to find out an optimum time dose fractionation strategy, which would help in improving the clinical results of radiotherapy. Various experimental studies prove that active regeneration in skin starts by the third week and regeneration in oropharyngeal mucosa begins 10-14 days after the start of a conventional radiotherapy regimen.^{8,9} Experimental and clinical studies reported by Horiot et al have shown that regeneration begins earlier if the initial treatment is accelerated and proceeds more rapidly during prolonged gap in radiotherapy.¹⁰ Thames et al have published various radiobiological experimental data and radiobiological reviews.¹¹

Conclusion:

Even the reduction in total dose from 66 Gy to 54 Gy in CHART arm, the control rate of loco-regional disease and survival was non inferior together with the low incidence of long-term severe adverse events to those with CRT. These outcomes suggest that CHART is a treatment option for patients with especially for early locally advanced oro-pharynx.

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