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CONTINOUS HYPER-FRATIONATED ACCELERATED RADIOTHERAPY (CHART) IN HEAD AND NECK CANCERS

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Abstract:

Background – head and neck malignancies are moderately radiosensitive. With the aim to increase loco-regional control Continuous Hyper-fractionated Accelerated radiotherapy has been studied in 50 patients with head and neck malignancies.

Patient and methods – 50 patients diagnosed with head and neck malignancies participated in the study between July 1996 – March 1997. Average age was 50 (30 – 70 yrs). 82% male patients and 18% female patients. Cancer of cheek, alveolar margin, tongue and tonsillar fossa accounts for 96% of patients. Daily dose of 1.4 Gy thrice daily in 6 hours interval were given for 12 consecutive days.

Results - follow up period 5 months – 15 months, primary site -80% had shown complete response while 20% have shown partial response for primary site. Nodal disease – 70% had shown complete response and 30 % had shown partial response. None of the patient had shown disease progression. Acute radiation reaction - 14%, 68% and 18% had shown grade 0, I, II grade acute radiation reaction, no grade III reaction have been observed in study group. Reoccurrence – 8 % at primary site, 12% had shown nodal recurrence.

Conclusion – CHART has shown better loco-regional control. It could be more effective in early stage disease. Acute radiation reaction is significant but manageable. Treatment volume has to be kept minimal to reduce radiation reaction.

Key words – head and neck cancers, CHART, loco-regional control,

Introduction

Cancer of upper airodigestive tract is collectively known as head and neck cancer arising from various sites such as tongue, cheek, lip, alveolar margin, tonsillar fossa, pharynx, larynx and nasal sinuses. It accounts for 30 – 35% of all malignancies in India[1]. These cancers are moderately radiosensitive and radiotherapy has the primarily role in overall management of head and neck malignancy either given alone or in combination with surgery and chemotherapy. Anatomy of Head and neck is complex and delicately architect, therefore if any treatment modality which delivers the equivalent result and simultaneously maintaining the cosmetic aspect of delicate architect is always welcomed. In general, curative radiotherapy should be delivered in as short an overall time as possible, using small fraction dose per fraction. Although 2 Gy five times a week may be 'reasonable average' treatment, greater individualization may be a research goal[2]. While radiotherapy is proceeding, tumour cells may proliferate. The use of small individual doses reduces late morbidity. The aim of radiotherapy planning is to deliver an adequate dose to the tumour volume so as to kill all the

malignant cells as well as the tumour cells produced by cell division of these malignant cells during the course of treatment and simultaneously sparing the normal tissue or more correctly with the repairable injury to the normal adjoining tissue[3]. In an attempt to get increase therapeutic gain and better tumour control CHART (continuous hyper-fractionated accelerated radiotherapy is undertaken)[4] in Jadav Ba cancer hospital, at Netaji Subash Chandra Bose Medical College, Jabalpur, MP, India.

Aims & Objectives – are clearly delineated to

- To evaluate the response of primary as well as nodal disease to CHART,
- To assess the acute radiation toxicity in the form of skin and mucosal reaction to see the feasibility of CHART,
- To assess the overall improvement in tumour control.

Material And Methods –

A detail history regarding age, sex, occupation, nature and duration of addiction, presenting complaint with duration and past history is obtained from each patient and is followed by thorough clinical examination in which assessment of primary site disease and adjoining lymph nodes are assessed clinically. Routine haematological and biochemistry tests were performed to rule out other chronic illness. Patient was staged according to TNM classification.

AJCC Staging

	T 0	T 1	T 2	T 3	T 4	Total
N-0	-	-	-	1	-	1
N-1	-	-	5	10	2	17
N-2	-	-	11	15	4	30
N-3	1	-	-	-	1	2
Total	1	-	16	26	7	50

All patients were biopsy proved squamous cell carcinoma with different degree of differentiation. Of all 54% patient were having moderately differentiated squamous cell carcinoma histopathology. One patient was having N3 nodal disease with occult primary.

Inclusion Criteria –

- WHO performance status 0 – 1
- Should not have distant metastasis
- Histological confirmation of squamous cell carcinoma
- Prior written consent to be a participant of study, all patient were explained the nature of treatment, its duration, efficacy and the side effects they are likely to face

Treatment Protocol –

all patients were treated on cobalt 60 – teletherapy unit. A total dose of 50.40 Gy was delivered in 36 fractions. 1.4 Gy per fraction given three times daily, with an inter-fraction interval of 6 hours. Treatment was given consecutively for 12 days without gap. All patients in the study group completed the treatment protocol successfully.

Criteria For Evaluation Of Response –

- Complete response (CR) – complete disappearance of primary as well nodal disease for a period of 8 weeks
- Partial response (PR) – 50% or more disappearance of tumour for a period of 8 weeks
- No regression (NR)– less than 50% regression in the size of tumour
- Progressive disease – increase in size of tumour during first 8 week of treatment

Observation –

Acute mucosal reaction – observed within 90 days from the commencement of treatment

GRADES	CASE NO.	%
Grade I	13	26
Grade II	31	62
Grade III	6	12

Majority of patients 62% has shown grade II mucosal reaction.

Acute skin reaction – observed within 90 days from the commencement of treatment

GRADES	CASE NO.	%
Nil	15	30
Grade I	33	66
Grade II	2	4
Grade III	-	-

Late mucosal reaction –

GRADES	CASE NO.	%
Grade 0	1	2
Grade I	34	68
Grade II	15	30
Grade III	-	-

Grade I & II Late mucosal reaction were observed in 98% of cases. No Garde III late mucosal reaction is observed in the study group.

Late skin reaction –

GRADES	CASE NO.	%
Nil	7	14
Grade I	34	68
Grade II	9	18
Grade III	-	-

In the present study undertaken, the relationship between the volume of tissue irradiated and the severity of skin and mucosal reaction was also observed. It has been observed that treatment volume exceeds 1400 cucm all patient had shown grade III mucosal reactions in the form of erythema, decreased salivation and ulceration of oral mucosa.

Immediate response of primary and nodal disease to CHART –

Site	Complete Resp. (Cr)	Partial Resp. (Pr)	Total
Primary	40 (80 %)	10 (20%)	50
Nodal	35 (70 %)	15 (30 %)	50

After 8 weeks of completion of CHART, immediate response was noted in present study. Out of complete responders 8% of patient had recurrence at primary site further reducing the complete responder to 72% for primary site. While 7 (14%) patients had nodal recurrence further reducing the complete responder to 56% for nodal site.

Discussion –

In the study undertaken 78 % patients were in the age group of 30 – 60 years. Higher incidence of head and neck cancer that too in advanced stage and radiotherapy being primary mode of treatment as a single modality or in combination with surgery or chemotherapy necessitates the radiation oncologist to understand the radiobiology of tissue reaction in the form of tissue reaction, altered dose fractionation, dose rate, volume effect, repopulation of tumour cells while on radiotherapy.[5] Multiple dose fractionation spares the normal tissue because of repair of sublethal damage between dose fractionation at the same time dividing the dose into number of fractions increases damage to the tumour because of reoxygenation and reassortment of cells into radiosensitive phase of cell cycle[6].

CHART combines the potential benefits of hyperfractionation and accelerated treatment. It would have less late effects as multiple small dose spares the late effect tissues more than that of acute effect tissue and tumour cells. Decreased repopulation of tumour cells because of shorter overall time[7].

According to AJCC pre-treatment clinical staging majority of patients were having locally advanced disease, with size of primary tumour were having T3 or T4 lesion (64%) and N 2 or N 3 nodal involvement in 64 % of cases.

Acute radiation reaction as was expected was higher with CHART[8 – 9]. Majority of patient has shown considerable mucosal reaction in the form of mild to moderate mucositis having complaint of pain, dysphagia, mucosal ulceration, and oral candidiasis. All patients were managed successfully with symptomatic treatment. In the latter half of study, patients were given weekly oral fluconazole prophylactically to prevent oral candidiasis which was seen frequently because of transient immune-suppressive state[10].

Late radiation reaction – includes both skin and mucosal, were those which were observed 90 days after the completion of CHART. 98 % of patients have shown either grade I (68%) or grade II (30%) skin and mucosal radiation reaction in the form of mucosal oedema, loss of

taste sensation, thick and viscid saliva, skin pigmentation, thickening, and telengiactasis. Resumption of taste sensation was usually seen after 5 – 7 months of completion of CHART, a delay which was observed while comparing with conventional radiotherapy.

Clinical response – out of 50 patients in the study group, 40 (80%) patients have shown complete regression of primary disease, while 10 (20) patients have shown partial regression. None of the patient have shown no regression or disease progression.

Reoccurrence – In the present study, patient were followed for a period of 5 months to maximum of 15 months. Majority of disease reoccurrence was seen in first 6 months of follow – up. Out of complete responders, 4 (8%) of them had disease reoccurrence at primary site, reducing the number for disease free survival to 72% for primary site. As far as nodal disease status is concerned 35 (70%), 7 patients had nodal reoccurrence further reducing the number to 28 (56%) who were found disease free on follow – up.

Results Of Other Studies At A Glance

Study name	patients no.	pri. site resp.	nodal resp.
Saunders & Dische et al[11] 54Gy/36F/3D/ 12CD/1.5Gy/F	67	87%	84%
Kumar HS et al 50.4 Gy/ 36F/ 3D/ 12CD/ 1.4Gy/F	28	86%	80%
Our Study 50.4Gy/ 36F/ 3D/ 12CD/ 1.4Gy/ F	50	80%	70%

Discussing the above observation, it is quite obvious CHART shows better results when we wish to treat locally advance head and neck cancers with curative intent on short term follow – up.

Altered fractionated radiotherapy improves survival in patients with head and neck malignancies[12].

Firm and final comment on CHART needs further clinical trial on large scale with prolong period of follow – up.

Acute radiation reaction are higher in CHART[8], but are managed successfully.

Conclusion –

From the above study we conclude clearly that CHART has shown encouraging initial result with acceptable acute radiation reaction and radiobiology of normal and malignant tissue can be explored with small doses per fraction and more doses per day and avoiding weekend off for radiotherapy.

Finally to summarize –

1. When it is clearly known that effect of radiotherapy delay in conventional format decreases overall local control and finally affects survival[13] CHART or other altered fractionation schedule can be explored keeping radiobiology of tissue in concern[14].

2. Anatomy of head and neck is complex with vital organs and is delicately architect. These malignancies are moderately radiosensitive and radiotherapy being a primary modality of treatment in all variety of settings, be it single or combined modality of treatment. Every possible efforts can be made to minimize cosmetic and other post surgical co-morbidities viz dysphagia, deglutition, voice, chewing etc.

3. If we could prevent late radiation damage, altered fractionation has to be explored extensively.

4. Treatment volume has to keep to minimum to avoid grade III acute skin and mucosal radiation reaction.

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