



Mucosal And Skin Reactions In Altered Fractionation Radiotherapy In Locally Advanced Oropharyngeal Carcinoma

Authors

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ABSTRACT

INTRODUCTION: *Mucositis and skin reactions are the most commonly encountered acute toxicities in head and neck irradiation. This is significantly higher in altered fractionation regimens. This study highlights the reactions in two different altered fractionation schedules of radiotherapy.*

AIM: *to study the acute mucosal and skin reactions in altered fractionation radiotherapy in locally advanced oro-pharyngeal carcinoma.*

RESULTS: *Among the ARM A and ARM B TNM-stage group at presentation was stage III: 40% and 52% and stage IV: 60% and 48% respectively. Grade III mucositis was encountered in 60% of patients in arm A compared to 32% in arm B ($P < 0.01$). Grade III skin reactions was seen more in arm A than arm B (52% Vs 24%) ($P < 0.01$).*

CONCLUSION: *In altered fractionation radiotherapy, it was found that early boosting has an edge over the late boosting in terms of manageable acute toxicities and better compliance.*

INTRODUCTION

Head and neck carcinoma is the most common cancer in India with more than 70% of the cases presenting in advanced stages.^[1] The disease remains confined to the loco-regional site of origin in a significant proportion of patients and the most important cause of death is locoregional recurrence. Various studies have shown concurrent chemoradiation schedules to have better locoregional control (LRC) and improved the overall survival. Accelerated fractionation schedules have been studied effectively in head

and neck cancers. It is one method which tends to concentrate on shortening the overall treatment time and thus hampering tumor cell proliferation.^[2] Concomitant boost is one of the ways of acceleration wherein a second daily fraction is introduced during any phase of treatment, thus completing the treatment in 5-6 weeks. Mucositis and skin reactions are the most commonly encountered acute toxicity during the course of radiotherapy. This is found to be significantly higher in altered fractionation schedules.^[3]

AIM

To study the acute mucosal and skin reactions in altered fraction radiotherapy in locally advanced oro-pharyngeal carcinoma.

MATERIAL AND METHODS

Fifty previously untreated patients of oro-pharyngeal cancer (which include cancer of base of tongue, vallecula and lingual surface of epiglottis, tonsillar region, soft palate and uvula, and oropharyngeal walls), attending the Department of Radiotherapy, Regional Cancer Centre, Bikaner from January 2014 to December 2015 were included in the study fulfilling the following criteria: Biopsy proven cases of squamous cell carcinoma of oropharynx, Stage III, IV, ECOG status 0-1, N-status- upto N2, no commorbidities. Age- >18 - <70 years. The evaluation consisted of full medical history, physical examination, local examination and endoscopic assessment of site, nature and extent of the disease was done. Work-up consisted of complete hemogram, renal function test, random blood sugar, X ray chest PA view and X ray soft tissue neck (lateral view) and CT scan.

TREATMENT PLANNING AND DELIVERY

All the patients will be treated in a supine position and properly immobilized by the thermoplastic cast (ORFIT cast).

- Dose prescription and Treatment description:
- **ARM A:** 45 Gy/25fractions/5weeks, 1.8Gy/fraction/day, 5days/week was delivered to the large field comprising the primary disease with extension and the neck nodes. Simultaneously a boost of 22.5Gy/15fractions, 1.5Gy/fraction was delivered for the last 15 treatment days to the primary and involved nodal disease. The fractions were delivered 6 hours apart.
- **ARM B:** 45 Gy/25fractions/5weeks, 1.8Gy/fraction/day, 5days/week was delivered to the large field comprising the primary disease with extension and the

neck nodes. Simultaneously a boost of 22.5Gy/15fractions, 1.5Gy/fraction on alternate day from the 1st day of the treatment for 5weeks to the primary disease. The fractions were delivered 6 hours apart.

- All patients were planned and treatment was delivered on Cobalt-60 Bhabhatron. Off cord planning was done after delivering 45 Gy.
- The patients in both arms were assessed after every 5 fraction for treatment related acute toxicity.
- The treatment was stopped when the patient developed grade 4 mucosal or skin reactions reactions.

The **Biologically Effective Doses (BED)** for Tumor control and late adverse effects in each arm will be calculated using the linear quadratic equation. BEDs for both arm is as follows: 78.98 Gy for tumor control and 105.75 Gy for late reacting normal tissues complications. The **EQD₂** (equivalent dose for 1.8Gy per fraction+ 1.5Gy per fraction for boost) for both arms for tumor is 67.5 Gy. Thus the EQD₂ is the same in both the treatment arms.

Acute treatment related toxicity assessed and graded using common terminology criteria for adverse events (RTOG). The two arms were compared statistically using SPSS 20.0.

RESULTS

TABLE 1: SEX DISTRIBUTION

Sex	ARM A		ARM B	
	No. of patients	Percentage (%)	No. of patients	Percentage (%)
Male	24	96	23	92
Female	1	4	2	8

Table 1 shows the sex distribution of patients included in this study.

TABLE 2: TNM STAGE GROUP

TNM stage group	Study group		Control group	
	No.of patients	Percentage (%)	No.of patients	Percentage (%)
Stage III	10	40	13	52
Stage IV	15	60	12	48

Table 2 shows the distribution of patients according to TNM-stage group.

TABLE 3: TOXICITY PROFILE

Toxicity	Grade 0		Grade I		Grade II		Grade III		Grade IV		TOTAL
	ARM A	ARM B	ARM A	ARM B	ARM A	ARM B I	ARM A	ARM B	ARM A	ARM B	
Mucositis	0	0	1	0	7	17	15	8	2	0	50
Skin	0	0	2	3	9	16	13	6	1	0	50

Table 3 shows the incidence of acute toxicity in terms of grade. The P value of both the skin and mucosal reactions is <0.01

DISCUSSION

The treatment of loco regionally advanced head and neck cancers has undergone a paradigm shift over the past three decades, with management strategies changing from surgery or radiation therapy as single modality to combined modality treatment. A pragmatic approach is to evaluate alternative and viable radiation schedules that provide superior response rates than conventional radiation and yet maintain a favourable toxicity profile, unlike the chemo radiation regimens.

Concomitant boost radiotherapy technique has a strong radiobiological rationale, wherein the boost field is added to the ongoing radiotherapy portals

during any phase of radiation to counteract accelerated repopulation of the tumor clonogens.^[3,4] This basic premise enhances the chances of tumor control by using a larger dose per fraction in the area of gross tumor volume and at the same time maintains the beneficial effects of acceleration on the tumor and normal tissues. This seemed important not only to optimize the therapeutic ratio, but also the available resources, as this schedule leads to an abbreviation of the overall treatment time from 7 to 5 weeks.

Incidence of disease is more common in male in both arms. As per the literature the male to female ratio of head and neck cancers varies from 3-

5:1.^[5] Among the ARM A and ARM B Among the ARM A and ARM B TNM-stage group at presentation was stage III: 40% and 52% and stage IV: 60% and 48% respectively.

Mucositis is a major complication of any form of radiation therapy in head and neck cancers. It has a major impact on the overall quality of life during treatment, as well as after treatment. Trotti et al have reviewed the effect of mucositis on patients with head and neck cancers using conventional radiotherapy, accelerated radiotherapy [RT-AF] and chemoradiation [RT+CT]. The frequency of mucositis was highest in patients with RT-AF, affecting 100% of patients overall. Patients treated with RT-AF experienced the most severe mucositis, with more than half (57%) experiencing grade 3-4 mucositis.^[6]

Alteration of fractionation scheme has mucositis rate of 60% in various studies.^[7] In this study, grade III mucositis was encountered in 60% of patients in arm A compared to 32% in arm B ($p<0.01$). Severe skin reaction (grade III) was seen more in arm A than arm B (52% Vs 24%) ($p<0.01$). This could be explained by alternate day boost in arm B giving enough time for normal tissue recovery. All patients were started on soda bicarbonate and betadine gargles from first day of the treatment and were treated symptomatically with iv fluids and ryle's tube feeding whenever necessary.

CONCLUSION

In altered fractionation radiotherapy, it was found that early boosting has an edge over the late boosting in terms of manageable acute toxicities and better compliance. However, larger studies with longer follow-up are needed for standardization a protocol for such boost.

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