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Comparison of xerostomia and dysphagia as acute and chronic toxicity profiles among patients undergoing 3D conformal radiotherapy, intensity modulated radiotherapy and intensity guided modes of radiotherapy

B. Niveditha[1], Bounika Esvanth Rao[1], S. Angelinteen[2], D.K.S. Lakshminrusimhan[3], C.K. Vishnupriya[4], and Suvetha Veerasamy[1]

[1]*Department of Oral Medicine and Radiology, Madha Dental College and Hospital, Chennai, India.*

[2]*Department of Oral Medicine and Radiology Tagore Dental College & Hospital, Chennai, India*

[3]*Department of Oral Medicine and Radiology, R.V.S.Dental College and Hospital, Coimbatore, India.*

[4]*Department of Oral Medicine and Radiology, Ragas Dental college and Hospital, Chennai, India.*

Abstract

Oral Cancer is a health problem all over the world, being the fifth most common of all the cancers. In India, it is the commonest of all the cancers, out of which 90% - 95% are squamous cell carcinomas. Conventional radiotherapy is a standard approach for treatment of locoregionally advanced disease, however is associated with well-known acute and long-term toxicities. The advent of new technologies of beam shaping seems to bring hope, by drawing a positive impact in quality of life of patients. Some of the methods of radiation delivery include Three-dimensional conformal radiotherapy (3D CRT), Intensity Modulated Radiotherapy (IMRT), Image Guided Radiotherapy (IGRT), stereotactic body radiotherapy and proton beam therapy to name a few. The most noticeable clinical gain has been a distinct reduction in long-term morbidity in these patients. Aim is to assess and compare the toxicity profiles occurring due to radiotherapy in head and neck cancer patients undergoing 3D CRT, IMRT and IGRT modes. A total of 60 patients with a Kornofsky Performance Scale (KPS) more than 70 were included in the study. Of the 60 patients included in the study 20 were in the 3D CRT group, 20 were in the IMRT group and 20 were in the IGRT group. The patients were assessed for grade of xerostomia and dysphagia in an acute and chronic manner. The results showed that 3D CRT group demonstrated significantly more acute and chronic toxicities in relation to xerostomia and dysphagia when compared to IMRT and IGRT. However, on comparing the toxicities between IMRT and IGRT groups there were insignificant differences.

Keywords: Xerostomia, dysphagia, 3D CRT, IGRT and IMRT

Full length article **Corresponding Author*, e-mail: bounikarao@gmail.com

1. Introduction

Oral cancer is a broad term that includes various malignant diagnoses that presents in the oral tissues. The cancer and cancer therapy are associated with morbidities that may negatively affect the quality of life – from the time of diagnosis, during cancer therapy, in the immediate period after cancer treatment, and continue throughout the life of the patient [1]. Radiation therapy (RT) is an important and indispensable mode of treatment for head and neck cancers, given to up to 75% of all head and neck cancer patients [2]. Radiation therapy has evolved over the past 30 years from being based on two dimensional to three dimensional images, incorporating increasingly complex computer algorithms. The shape and intensity of the electron beam has to be collimated to attain the highest probability of tumor control or cure with the least amount of morbidity and toxicity to normal surrounding tissues [3]. In 3D CRT the radiation field conforms to the shape of the volume to be treated. The process of "virtual simulation "begins with each case, which lasts about 30 to 60 minutes and latter the CT images of the patient in the treatment position are transferred into the treatment planning computer. The volume of tumor to be treated is marked on each slice, highlighting the critical structures at risk [4].

Intensity modulated radiation therapy (IMRT) is available in many cancer centers and in dose distribution, IMRT has been shown to be superior to 3D CRT [5]. In IMRT, physician designates specific doses of radiation (constraints) that the tumor and normal surrounding tissues should receive [6]. The physician team then uses a sophisticated computer program to develop an individualized plan to meet the constraints. This process is termed "inverse treatment planning'. Some LINACs have an on-board Imager, an automated system that uses high-resolution X-rays to produce contrasting images of cancerous tumors and surrounding soft tissue, allowing physicians to target the cancerous tumor more precisely during treatment and decreasing radiation exposure of healthy tissues. Before the on-board imager, physicians would have to treat a larger area of the body near the cancerous tumor to compensate for any tumor movement, exposing healthy tissue to the radiation. This technique is called image guided radiotherapy (IGRT) [7]. Xerostomia and dysphagia are most important complications which occur as a side effect of radiotherapy. Radiation is found to cause a defect in cellular functioning and late damage occurs due to the classical cell killing of the progenitor and stem cells [8]. The cause of dysphagia in cancer patients is multifactorial, which may be related to old age, site of cancer, and treatment-related changes can all influence the resultant swallowing defects [9].

The purpose of the present study is to explore the acute and chronic toxicity profiles associated with 3D CRT, IMRT and IGRT in terms of mucositis and skin reactions. This would help us to further optimize the process and incorporate replanning strategies to obtain an even better locoregional control and thus produce a potential positive impact on the quality of the life of the patient.

2. Materials and methods

A prospective study was conducted to assess the acute and chronic toxicity profiles between the time period of January 2017 to November 2017 (a period of 11 months). The sample size consisted of a total of 60 patients with histopathologically proven squamous cell carcinoma of head and neck. There were 20 patients each in the 3D CRT, IMRT and IGRT groups respectively. Patients were of the age groups 25 – 65 years from either sex,

All patients were treated on LINAC 2300C/D machine, with immobilization in supine position using a customized thermoplastic device. Treatment planning involved Computerized Tomography Scan of the area of interest, followed by delineation of various target volumes like Gross tumor Volume (GTV), Clinical Target Volume (CTV), Planning Target Volumes and Organs at Risk volumes. The delineation of various volumes was done as per consensus guidelines. After a cycle of radiotherapy was delivered, the toxicity pattern (grades of mucositis, skin reactions), developing within 90 days from the beginning of RT (acute toxicity) are assessed according to Radiation Therapy Oncology Group (RTOG) and European Organization for the Research and Treatment of Cancer (EORTC) criteria. RT toxicity developing after 90 days (chronic/late toxicity) is graded with the same scale for late sequelae.

2.1. Study design

Ethical clearance was obtained from the Institutional Review Board of Ragas Dental College and Hospital, Chennai and informed consent was obtained from each of the patients.

2.2. Statistical analysis

SPSS for Windows 13.0 (Statistical Package for the Social Sciences, Chicago, IL) was used. The statistical methods used include ANOVA, Turkey HSD and Post Hoc methods.

3. Results and Discussions

The results are tabulated and summarized as follows: Table 1 (comparison of xerostomia & dysphagia post RT and 90 days post RT among 3d CRT and IMRT groups) shows the significance between the groups. On comparing the grades of xerostomia between 3D CRT and IMRT groups immediately after radiotherapy, the P value was found to be 1.000 which was statistically insignificant. On comparing the grades of xerostomia between 3D CRT and IMRT groups, 90 days after radiotherapy, the P value was found to be 0.000 which was statistically highly significant. On comparing the grades of dysphagia between 3DCRT and IMRT groups immediately after radiotherapy, the P value was found to be 0.000 which was statistically highly significant. On comparing the grades of dysphagia between 3DCRT and IMRT groups, 90 days after radiotherapy, the P value was found to be 0.001 which was statistically highly significant. Table 2 (comparison of xerostomia and dysphagia post RT and 90 days post RT among 3D CRT and IGRT group of patients) shows the significance between the groups. On comparing the grades of xerostomia post RT among 3DCRT and IGRT group of patients, it was found that the P value was found to be 0.532 which was statistically highly insignificant. On comparing the grades of xerostomia 90 days post RT, among the 3D CRT and IGRT groups of patients, the P value was found to be 0.000 which was statistically significant. On comparing the grades of dysphagia post RT among 3DCRT and IGRT group of patients, it was found that the P value was found to be 0.000 which was statistically highly significant. On comparing the grades of dysphagia 90 days post RT, among the 3D CRT and IGRT groups of patients, the P value was found to be 0.000 which was statistically highly significant.

Table 3 (comparison of xerostomia and dysphagia post RT and 90 days post RT among IMRT and IGRT group of patients) shows the significance between the groups. On comparing the grades of xerostomia post RT among IMRT and IGRT group of patients, it was found that the P value was found to be 0.532 which was statistically insignificant. On comparing the grades of xerostomia 90 days post RT, among the IMRT and IGRT groups of patients, the P value was found to be 0.497 which was statistically insignificant.

Table 1: Comparison of xerostomia and dysphagia and in 3dcrt vs imrt group post rt and 90 days post rt

	Post Radiotherapy						**90 days post Radiotherapy**					
Characteristic	**3DCRT Vs IMRT**					**P value**	**3DCRT Vs IMRT**					**P value**
Xerostomia	Grade	No pts	%	No pts	%		Grade	No pts	%	No pts	%	
	I	15	75%	13	65 %		I	15	75%	17	85%	
	II	3	15%	3	15 %	**1.000**	II	5	25%	2	10%	**0.000**
	III	-	-	-	-		III	-	-	-	-	
	IV	-	-	-	-		IV	-	-	-	-	
Dysphagia	Grade	No pts	%	No pts	%	**P value**	Grade	No pts	%	No pts	%	**P value**
	I	11	55%	19	95 %		I	13	65%	10	50%	
	II	7	35%	1	5%	**0.000**	II	7	35%	1	5%	**0.001**
	III	2	10%	-	-		III	-	-	-	-	
	IV	-	-	-	-		IV	-	-	-	-	

Table 2: comparison of xerostomia and dysphagia and in 3dcrt vs igrt group post rt and 90 days post rt

	Post Radiotherapy						**90 days post Radiotherapy**					
Characteristic	**3DCRT Vs IMRT**					**P value**	**3DCRT Vs IMRT**					**P value**
Xerostomia	Grade	No pts	%	No pts	%		Grade	No pts	%	No pts	%	
	I	15	75%	14	70 %		I	15	75%	16	80%	
	II	3	15%	3	15 %	**0.532**	II	5	25%	1	5%	**0.000**
	III	-	-	-	-		III	-	-	-	-	
	IV	-	-	-	-		IV	-	-	-	-	
Dysphagia	Grade	No pts	%	No pts	%	**P value**	Grade	No pts	%	No pts	%	**P value**
	I	11	55%	19	95 %		I	13	65%	9	45%	
	II	7	35%	1	5%	**0.000**	II	7	35%	3	15%	**0.000**
	III	2	10%	-	-		III	-	-	-	-	
	IV	-	-	-	-		IV	-	-	-	-	

Table 3: comparison of xerostomia and dysphagia and in imrt vs igrt group post rt and 90 days post rt

	Post Radiotherapy						**90 days post Radiotherapy**					
Characteristic	**3DCRT Vs IMRT**					**P value**	**3DCRT Vs IMRT**					**P value**
Xerostomia	Grade	No pts	%	No pts	%		Grade	No pts	%	No pts	%	
	I	13	65%	14	70 %		I	17	85%	16	80%	
	II	3	15%	3	15 %	**0.532**	II	2	10%	1	5%	**0.497**
	III	-	-	-	-		III	-	-	-	-	
	IV	-	-	-	-		IV	-	-	-	-	
Dysphagia	Grade	No pts	%	No pts	%	**P value**	Grade	No pts	%	No pts	%	**P value**
	I	19	95%	19	95 %		I	10	50%	9	45%	
	II	1	5%	1	5%	**0.966**	II	1	5%	3	15%	**0.903**
	III	-	-	-	-		III	-	-	-	-	
	IV	-	-	-	-		IV	-	-	-	-	

On comparing the grades of dysphagia post RT among IMRT and IGRT group of patients, it was found that the P value was found to be 0.966 which was statistically insignificant. On comparing the grades of dysphagia 90 days post RT, among the IMRT and IGRT groups of patients, the P value was found to be 0.903 which was statistically highly insignificant. On comparing xerostomia occurring post RT between 3D CRT and IMRT groups the P value was 1.000 which was statistically insignificant. Among the 3D CRT and IGRT group the P value was 0.532 and among the IMRT and IGRT groups the P value was 0.532 both of which were statistically highly insignificant. The results of our study are in contradiction to the result of the studies conducted by Bramm et al (2006) [10], Tejpal Gupta et al (2012) [11], Gupta et al (2012) [12] and Gopa Gosh et al (2016) [13].This might be due to the fact as they have included patients where the planned RT has been given in site specific locations sparing the parotids, but in our study all the cancers of the oropharyngeal regions have been included, which could have had an effect on parotid secretions. On comparing xerostomia occurring 90 days post RT between 3D CRT, IMRT and IGRT groups, the P value was highly significant between 3D CRT and IMRT groups (0.000) and between 3D CRT and IGRT groups (0.000) and statistically insignificant between IMRT and IGRT groups (0.497). The results of our study are in accordance with the results obtained in the studies of Bramm et al (2006) [10], Nutting et al (2011) [14] and Ajay Singh Choudhary (2017) [15].

On comparing dysphagia occurring post RT between 3D CRT, IMRT and IGRT groups, the P value was statistically highly significant between 3D CRT and IMRT groups (0.000) and between 3D CRT and IGRT groups (0.000) and statistically insignificant between IMRT and IGRT groups (0.966). The results of our study are in accordance with the results obtained from the studies of Mann Trivedi et al (2015) [16], Gopa Gosh et al (2016) [13] and Ajay Singh Choudhary et al (2017) [15]. On comparing dysphagia 90 days post RT between 3D CRT, IMRT and IGRT groups, it was found that the P value was statistically significant between 3D CRT and IMRT groups (0.001) and between 3D CRT and IGRT groups (0.000) and statistically insignificant between IMRT and IGRT groups (0.903).The results of our study are in contradiction to the results of the study conducted by Tejpal Gupta et al (2012) [11] who conducted a study in a sample of 60 patients in the 3D CRT and IMRT groups and out of the 28 patients in 3D CRT group grade 3 dysphagia was demonstrated in none of the patients and out of the 32 patients in the IMRT group grade 3 dysphagia was demonstrated in 3 (9.5%) patients with a P value of 0.21 which was not statistically significant. Though statistically insignificant results were obtained from the study, the percentage of patients affected by grade 2 or greater dysphagia by 3D CRT is 71.5% and is greater compared to that of IMRT where the percentage of patients affected by grade 2 or more dysphagia is 59.3% and could be due to the differences in the midline protection contouring and the location of the primary tumor site.

Limitations: The small number of patients and relatively short follow-up remains the major limitations of the present study and further study with larger group and long-term follow-up is recommended.

4. Conclusions

The results of this study point to the fact that intensity of the side effects of radiotherapy depend not only on the dosage of the therapy, but also on the type of radiotherapy being to the patients. Within the limitations of our study, it is suggestive of IMRT being as effective as other treatment strategies for locally advanced head and neck cancer and provides better outcomes in terms of toxicity as compared to conventional techniques.

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