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Original Article

Oncology Section

Toxicity Profile of IMRT Vs. 3D-CRT in Head and Neck Cancer: A Retrospective Study

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ABSTRACT

Introduction: Role of radiotherapy in comprehensive management of head and neck cancer for achieving tumour control and organ preservation is now well established and radiotherapy is routinely used in adjuvant setting after surgery, concurrently with chemotherapy or targeted agents and for palliation. Development of linear accelerator with Multileaf Collimator (MLC) have revolutionized radiation delivery techniques, allowing conformal and Intensity Modulated Radiotherapy (IMRT) to deliver highly conformal sculpted radiation dose to a very complex structure with improved sparing of adjoining critical structures like salivary glands, spinal cord, eyes, brainstem and larynx amounting to better therapeutic gain.

Aim: Aim of this retrospective study was to compare toxicity profile of IMRT with Three Dimensional Conformal Radiotherapy (3D CRT) in head and neck cancer.

Materials and Methods: Total of 80 patients from January 2013 to July 2015 with proven head and neck cancer who underwent radiotherapy on linac 2300 C/D machine were included in the study, IMRT group and 3D-CRT group comprised of 40 patients each. We have searched patient's radiotherapy details in record section of our institute and observations were noted down. Patients received 70Gy/35 fractions, Monday to Friday as radical treatment and 60 Gy/30 fractions as adjuvant treatment were included.

Results: The 3D-CRT group demonstrated significantly more acute toxic effects compared with the IMRT group in our analysis. Acute Grade 3 or greater toxic effects to the skin occurred in 5 of 40 (12.5%), patients in the 3D-CRT group compared with 3 of 40 (7.5%) patients in the IMRT group. Acute Grade 3 or greater toxic effects to the mucous membranes occurred in 23 of 40 (57.5%) patients in the 3D-CRT group and only 16 of 40 (40%) patients in the IMRT group. Statistically significant dysphagia developed in 34 of 40 (85%), patients in 3D-CRT group compared with 23 of 40 (57.5%) patients in IMRT group, while statistically significant xerostomia developed in 29 of 40 patients in 3D-CRT group (72.5%), compared with18 of 40 (45%) patients in IMRT group.

Conclusion: In our analysis, IMRT was associated with a significantly lower incidence of Grade 3 or greater xerostomia, acute toxic effects to skin and mucous membranes than 3D-CRT. In addition, compared to 3D-CRT, IMRT had lower rates of Grade 3 or greater mucositis and skin toxicity as well as less feeding tube use during radiotherapy. Our analysis showed potentially less toxicity in patients treated with IMRT in comparision to 3D-CRT.

Keywords: Acute toxicity, Late toxicity, Xerostomia

INTRODUCTION

Incidence of head and neck cancer is on rise in developing countries and in world it is the sixth leading cancer, 70% of them require radiotherapy as definitive or post operative radiation concurrently with chemotherapy or targeted agents and for palliation [1]. Advancement in imaging techniques, improved identification of target volume, 3D image reconstruction, computer optimized algorithms have led to evolution of radiation delivery from 2D Radiotherapy to Three Dimensional Conformal Radiotherapy (3D CRT) with geometric modulation of beam shape that conform as closely as possible to the target volume in terms of adequate dose to the tumour and minimal possible dose to normal tissue [2]. Further progress in conformal radiotherapy led to logical evolution of Intensity Modulated Radiation Therapy (IMRT) where simultaneous geometric and intensity modulation of radiation beams allows delivery of non-uniform fluence from any given position of the treatment beam to optimize the composite dose distribution [2]. Thus, with greater control on dose distribution within the target, IMRT allows much higher possibility to sculpt radiation dose thereby improving the therapeutic ratio [1,2]. Head and Neck is one of the ideal site for IMRT because of complex geometry of this area and substantial radiation related acute and late toxicities, usually distance between Clinical Target Volume (CTV) and critical structures such as salivary glands, optic apparatus, inner ear and brainstem is within few millimeter's. Xerostomia is by far the commonest late toxicity with impact on speech swallowing and may be contributory to mandibular osteoradionecrosis [2].

MATERIALS AND METHODS

A retrospective analysis of total 80 patients was done who underwent IMRT (40 patients) and 3D-CRT (40 patients) for head and neck squamous cell cancer in our institute between January 2013 to July 2015. The study used pre-existing medical records as obtaining informed consent of all patients would be impractical given the associated time and cost. Eligible patients were of primary oral cavity, squamous cell histology, no history of previous radiotherapy, Kornofsky Performance Scale (KPS) more than 70. Patients who excluded were histology suggestive of cancerother than squamous cell cancer, prior radiotherapy, Kornofsky Performance Scale (KPS) less than 70. We studied patient files in detail in our record section and important observations were noted down. Patients who received 70Gy in 35 fractions, 200cGy per fraction as radical radiotherapy and 60Gy in 30 fractions, 200cGy per fraction as adjuvant radiotherapy were included in this study. All patients were treated on linac 2300C/D machine, with immobilization in supine position using a customized thermoplastic

device. Treatment planning involved Contrast enhanced planning Computerized Tomography (CT) scan of the area of interest with 3mm slices on CT scan that is networked to the treatment planning system (ECLIPSE), followed by delineation of various target volumes like, Gross Tumour Volume (GTV), Clinical Target Volume (CTV), Planning Target Volume (PTV) and organ at risk volumes (spinal cord, both the parotids, eyes, brainstem) contoured on each slice. Other organs such as uninvolved oral mucosa and larynx were also contoured on each slice. An isometric margin of 5mm provided to the CTV for final PTV and 3mm to organs at risk for Planning Organ at Risk Volume (PORV). The GTV consisted only the primary and involved neck nodes. The delineation of the various volumes was done as per consensus guidelines. Toxicity pattern (grades of mucositis, skin reaction, xerostomia, dysphagia) of IMRT in 40 patients and 3D-CRT in 40 patients was noted down. Toxicity of Radio-Therapy (RT) developing within 90 days from the beginning of RT (acute toxicity) assessed according to Radiation Therapy Oncology Group (RTOG) and European Organisation 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. Chi-square test was used to find out the significance of results.

Characteristics	Number (%)	
	IMRT	3D-CRT
Age (Range)	31-65	21-77
Sex:		
Male	31(77.5)	29(72.5)
Female	9(22.5)	11(27.5)
Site:		
Buccal mucosa	26(65)	28(70)
Alveolus	14(35)	12(30)
T stage:		
T1	1(2.5]	2(5)
T2	13(32.5)	11(27.5)
T3	18(45)	20(50)
T4	8(20)	7(17.5)
N stage:		
N0	4(10)	6(15)
N1	21(52.5)	19(47.5)
N2	13(32.5)	12(30)
N3	2(5)	3(7.5)
Overall Stage:		
III	9(22.5)	12(30)
IVA	28(70)	25(62.5)
IVB	3(7.5)	3(7.5)

[Table/Fig-1]: Clinical characteristics of the patients.

Mucositis grade	IMRT	%	3D-CRT	%	p-value
I	40	100	40	100	NA
II	24	60	29	72.5	0.34
III	16	40	23	57.5	0.17
IV	-	-	3	7.5	NA

[Table/Fig-2]: Mucositis grading IMRT VS 3D-CRT.

Skin toxicity grade	IMRT	%	3D-CRT	%	p-value
I	40	100	40	100	NA
II	37	92.5	35	87.5	0.70
III	3	7.5	5	12.5	0.70
IV	0	-	0	-	-

[Table/Fig-3]: Mucositis grading IMRT VS 3D-CRT.

RESULTS

Majority of patients were males, and only nine females were in IMRT group and 11 in 3D-CRT group. Age group ranged between 31 to 65 in IMRT group and 21 to 77 in 3DCRT group.

Both groups comprised of buccal mucosa and alveolus cancer, former being the predominant one [Table/Fig-1]. Most of the patients had advanced stage at presentation and eligible patients underwent surgery with neck dissection prior to radiotherapy.

The 3D-CRT group demonstrated significantly more acute toxic effects compared with the IMRT group in our analysis. Acute grade 3 or greater toxic effects to the mucous membranes occurred in 23 of 40 (57.5%) patients in the 3D-CRT group and only 16 of 40 (40%) patients in the IMRT group [Table/Fig-2]. Acute Grade 3 or greater toxic effects to the skin occurred in 5 of 40 (12.5%) patients in the 3D-CRT group compared with 3 of 40 (7.5%) patients in the IMRT group [Table/Fig-3]. Statistically significant dysphagia developed in 34 of 40 (85%), patients in 3D-CRT group compared with 23 of 40 (57.5%) patients in IMRT group [Table/Fig-4], while statistically significant xerostomia developed in 29 of 40 patients

Dysphagia grade	IMRT	%	3D-CRT	%	p-value
I	40	100	40	100	NA
II	23	57.5	34	85	0.013
III	0	-	0	-	-
IV	0	-	0	-	-

[Table/Fig-4]: Dysphagia grading IMRT vs 3D-CRT.

Xerostomia grade	IMRT	%	3D-CRT	%	p-value
I	40	100	40	100	NA
II	18	45	29	72.5	0.023
III	-	-	-	-	-
IV	0	-	0	-	-

[Table/Fig-5]: Xerostomia grading IMRT vs 3D-CRT.

Late toxicity	Grade	IMRT		3D-CRT	
		No.	%	No.	%
Skin / subcutaneous thickening	1	3	7.5	5	12.5
	2	0	-	0	-
	3	0	-	0	-
	4	0	-	0	-
Mucositis	1	4	10	7	17.5
	2	0	-	0	-
	3	0	-	0	-
	4	0	-	0	-
Dysphagia	1	3	7.5	4	10
	2	0	-	0	-
	3	0	-	0	-
	4	0	-	0	-
Xerostomia	1	11	27.5	23	57.5
	2	2	5	7	17.5
	3	0	-	0	-
	4	0	-	0	-
Laryngeal oedema	1	0	-	0	-
	2	0	-	0	-
Temporal lobe Necrosis		0	-	0	-

[Table/Fig-6]: Late adverse effects of radiation therapy reported after 90 days after start of radiotherapy.

in 3D-CRT group (72.5%), compared with18 of 40 (45%) patients in IMRT group [Table/Fig-5]. Late Grade-I xerostomia developed in 11 of 40 (27.5%) IMRT group and 23 of 40 (57.5%) in 3D-CRT group [Table/Fig-6].

DISCUSSION

Radiotherapy has played a significant role in the treatment of head and neck cancers. More than two third of head and neck cancer patients need to undergo either definitive or post-operative radiation therapy [3]. Conventional radiotherapy is associated with significant acute and late toxicities and to overcome this, newer techniques have evolved with the aim of delivering cancericidal dose to tumour while delivering miminum dose to surrounding normal tissues. As compared to conventional radiotherapy, IMRT/3-D CRT technique offers better sparing of normal tissue thus minimising toxicity. The IMRT technique gives the ability to create treatment fields with varying beam intensity by using inverse planning and iterative optimization algorithms [4]. The radiation beam can be adjusted to the irregularly shaped target volumes with extremely high precision while reducing the radiation delivered to the surrounding healthy tissue and critical structures e.g., spinal cord, brain stem, parotid glands, eyes etc., in case of head and neck cancer [5,6].

The ability of delivering lower doses of radiation to normal tissue while maintaining or increasing the dose in the target volume makes IMRT the most appropriate treatment option compared to conventional radiotherapy [7-10].

S Clavel, et al., reported Grade 2 or greater acute mucositis of 75% with IMRT while it was 77% with 2-3D CRT [9] and we observed Grade 3 or > or greater mucositis in 57.5% 3D-CRT group and 40% in IMRT Group [9]. Nutting et al., reported xerostomia in 38% with IMRT and 74% with conventional therapy [10] which is comparable with our study, with statistically significant xerostomia in 29 of 40 patients in 3D-CRT group (72.5%), compared with 18 of 40 (45%) patients in IMRT group.

While Lambrecht et al., reported xerostomia in 23% with IMRT and 68% with 3D-CRT. Grade 3 or greater mucositis was 32% with IMRT while it is 44% with 3D-CRT [11] as compared to xerostomia of 45% and 72.5% and grade 3 or greater mucositis of 40% and 57.5% in our group respectively.

Thus, all the above study concluded that IMRT has a pivotal role in management of head and neck cancer and in reduction of radiation-induced toxicity [7-11].

In our analysis, compared to 3D-CRT, IMRT had lower rates of Grade 3 or greater mucositis and skin toxicity as well as less feeding tube use during radiotherapy. Incidence of xerostomia is also less in IMRT group as compared to 3D-CRT group. Late toxicity is also less in IMRT group as compared to 3D-CRT group. Late mucositis developed 10% in IMRT group and 17.5% in 3D-CRT group, late grade1 xerostomia developed in 27.5% in IMRT group and 57.5% in 3D-CRT group while grade 2 xerostomia was 5% and 17.5% respectively.

LIMITATION

The limitation of the study was its retrospective nature and small sample size.

CONCLUSION

Within the limitations of the current study, it is suggestive of IMRT being as effective as other treatment strategies for locally advanced head and neck cancer and provides better outcome in terms of toxicity as compared to conventional techniques.

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