ORIGINAL ARTICLE

IMPROVEMENT IN XEROSTOMIA RELATED QUALITY OF LIFE OF ORAL CAVITY AND OROPHARYNGEAL SQUAMOUS CELL CARCINOMA PATIENTS TREATED WITH IMRT COMPARED TO CONVENTIONAL RT

Aseem Rai bhatnagar[1], Rameshwaram Sharma[2], Prashant Kumbhaj[1]

Authors' Affiliation: [1]Resident; [2]Associate Professor, Department of Radiotherapy & Oncology, SMS Medical College, Jaipur
Correspondence: Dr. Prashant kumbhaj, Email: drprashantkumbhaj@yahoo.com

ABSTRACT

Background: The incidence of head and neck squamous cell cancer is quite high in India as compared to the developed countries. Conventional RT for the majority of head and neck cancers is delivered using two parallel opposed radiation beams and parotid glands receive a significant radiation dose (>50 Gy) resulting in permanent xerostomia.

Materials and Methods: For this study, we evaluated 64 patients with oral cavity and oropharyngeal squamous cell carcinomas, treated by IMRT / Conventional RT for xerostomia related quality of life (QoL). We used EORTC H&N35 QLQ for analysis of data & divided the questions into xerostomia experienced at rest and during meals.

Results: Patients treated with IMRT reported significantly less difficulty in transporting and swallowing their food and needed less water for a dry mouth during day, night and meals. Within the IMRT group the xerostomia scores were better for those patients with mean parotid dose to the "spared" parotid < 26 Gy.

Discussion: The parotids are responsible for the saliva output during meals whereas the oral cavity and submandibular glands lubricate the mouth at rest. Our results showed that patients receiving IMRT had a better xerostomia related QoL than patients who received bilateral opposed radiation fields. Xerostomia at rest and during meals was used as the endpoint in our analysis.

Conclusion: Parotid gland sparing IMRT improves xerostomia related QoL.

Keywords: Head and Neck Cancer, Xerostomia, IMRT, QoL

INTRODUCTION

The incidence of head and neck squamous cell cancer is exceptionally high in India (over 30%) as compared to western and other developed countries (around 5%). This is attributed to popular practice of chewing betel nut leaves rolled with lime and tobacco (a mixture known as "Pan") which results in prolonged carcinogen exposure to the oral mucosa. The practice of "Reverse Smoking" (smoking with the lighted end of the cigar in the mouth, also known as Chutta), peculiar to certain parts of India, is associated with increase in cancer of the hard palate. The oral cavity bears the brunt of the carcinogen and nearly 80,000 oral cancers are diagnosed every year in the country. Nearly two thirds of these are located in the gingivo-buccal complex (comprising the lower gingivum, buccal mucosa and retro-molar trigone), where the betel 'quid' is kept for long periods [2].In head and neck cancer oral cavity comparises 9.4% of all cancers and oropharynx comparises 6.9% of all cancers in india.

The majority of cases are locoregionally advanced (Stage III & IV) at the time of diagnosis. Our centre being the largest Government Medical College in the largest State of India, has high number of such patients. Our centre has been accredited by ESMO (European Society of Medical Oncologists) as an Integrative Oncology and Palliative Care Centre.

Because of critical location of most of these neoplasms, they interfere with breathing, eating and phonation, thus affecting the quality of life. Surgery and/or chemoradiotherapy are the mainstay of the treatment of locally advanced head and neck cancers.

Radiotherapy as the primary treatment option allows for organ and function conservation. Unavailability of good quality surgical facilities at every centre; high expenses of surgery and newer IMRT techniques weighs heavily in treatment decisions, with more patients preferring conventional chemoradiotherapy. A large number of patients are referred for primary radiation therapy, irrespective of stage and probability of disease control.

Radiation-induced xerostomia (dry mouth) is one of the common complications of head and neck irradiation.(3) Radiation-induced salivary gland injury often occurs because most of the salivary glands are included in the general irradiation fields for head and neck malignancy and regional lymph nodes. Salivary gland radiation injury leads to salivary secretion dysfunction and induces several clinical symptoms such as dysphagia (swallowing difficulty) and xerostomia (with speech difficulty, sleep disturbance, intraoral infection, and dental caries(4) .There is reduction in salivary output and change in salivary composition.

MATERIALS AND METHODS

Patients: All the patients had T 1-4, N 0-2, M 0 (Stage III/IV) oral cavity or oropharyngeal cancers (Table 2,3). The primary tumor (site) received a total dose of 70 Gy in 2 Gy daily fractions, 5 fractions a week, using Conventional or IMRT techniques. 30 patients were evaluated for xerostomia related quality of life - 15 each in IMRT and Conventional (Control) arms.

Data Collection tool: Assessment of xerostomia related quality of life

All patients completed the xerostomia related questionnaire of EORTC QLQ-H&N35 [5] where items are rated on a four-point scale. Higher scores represent worse symptoms. The questionnaire was translated for use in local language. This assessment took place twelve months after radiotherapy treatment.

We divided the QoL questions in 2 parts; the first part concerned with questions on xerostomia experienced at rest and the second part related to questions on xerostomia experienced during meals (Table 3,4).

Treatment: Irradiation was given on a linear accelerator (6 MV Siemens Oncor Expression) and all patients were immobilized using custom made masks. IMRT was delivered using the Linatech planning system; 95% of the Planning Target Volume (PTV) had to receive 95% of the prescribed dose. The aim was to reduce the mean dose to 26 Gy or less for at least one parotid gland (Fig. 1). Sparing of the submandibular glands or oral cavity was not attempted.

The Control group was irradiated with lateral – opposed photon beams (6 MV photons customized with MLC shieldings). The maximum dose allowed to the spinal cord was upto 50 Gy in both groups.

RESULTS

Patient characteristics: The mean dose to the primary tumor was 70 Gy in both IMRT and the control groups (Table 1, 2). The patients received platinum based chemotherapy concurrently. No salivary stimulating or protective agents such as pilocarpine or amifostine were allowed during the study.

Table 1: Patient Demographics

Age (years)	IMRT (%)	Control (%)
20 – 30	2 (6)	1 (3)
30 - 40	4 (13)	5 (16)
40 - 50	8 (25)	9 (28)
50 - 60	10 (31)	11 (34)
60– 70	8 (25)	6 (19)
Total	32	32

Table 2: Patient Characteristics

	IMRT (%)	Control (%)
Sex		
Males	25 (78)	27(84)
Females	7 (22)	5(16)
Tumour Site		
Oral Cavity	17 (53)	16(50)
Oropharynx	15 (47)	16(50)
T – stage		
T1	7 (22)	1 2(38)
T2	10 (31)	15(47)
T3	12 (38)	3(9)
T4	3 (9)	2(6)
N - stage		
N0	15 (47)	11(34)
N1	15 (47)	16(50)
N2	2 (6)	5(16)
Mean dose primary tumour (Gy)	70	70
Concomitant chemotherapy	Yes	Yes

Xerostomia in rest: Patients on IMRT were examined extensively regarding complaints related to xerostomia and almost all the complaints in the questionnaire were reported less frequently in the IMRT group (Table 3). Patients who received IMRT needed to drink water less often during the day. They did not experience a dry mouth as often and speaking was less impaired due to a dry mouth. No statistically significant difference in insomnia complaints was reported due to a dry mouth.

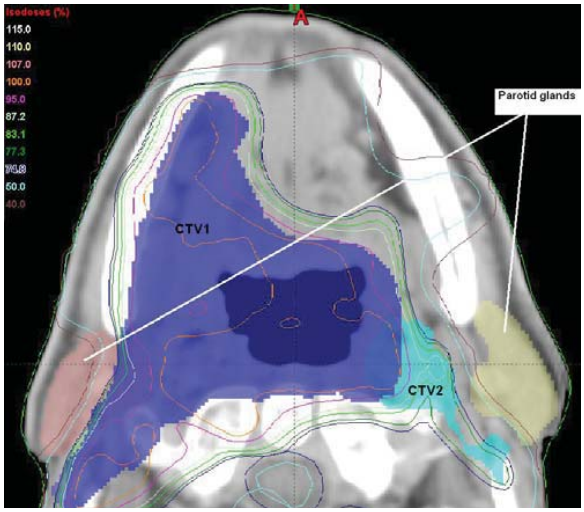

Figure 1: IMRT plan demonstrating left parotid gland sparing.
CTV1 - primary tumour and high risk nodes.
CTV2 – nodes at risk of micrometastases.
(CTV : Clinical Target Volume)

Xerostomia during meals: Again almost all complaints were reported less frequently in the IMRT group(Table 4). Patients who received IMRT reported less difficulty in oral transport and swallowing of solid and grounded food. They choked less often when swallowing. Both groups of patients reported they needed to swallow more often than before radiotherapy. No statistically significant difference in swallowing liquid food was reported.

Table 3: Questions related to xerostomia at rest

	Not at all %	A little %	Quite a bit %	Very much %	p value
Change in saliva amount?					
IMRT	7	13	73	7	0.0083
Control	13	13	20	53	
Dry mouth?					
IMRT	20	47	20	13	<0.0001
Control	7	33	33	27	
Complain of sticky saliva?					
IMRT	27	47	13	13	<0.0018
Control	13	33	40	13	
Increased frequency of drinking water during the daytime?					
IMRT	27	47	20	7	0.0003
Control	20	33	33	13	
Sleeping disturbance due to a dry mouth?					
IMRT	53	27	13	7	0.3273
Control	47	27	20	7	

Table 4: Questions related to xerostomia at meals

	Not at all %	A little %	Quite a bit %	Very much %	p value
Problem in opening mouth?					
IMRT	60	26	7	7	0.0001
Control	33	33	20	16	
Problems in swallowing liquid food?					
IMRT	80	13	7	0	0.04
Control	67	20	13	0	
Problems in swallowing pureed food?					
IMRT	60	20	20	0	0.0019
Control	40	27	26	7	
Problems in swallowing solid food?					
IMRT	33	40	20	7	<0.0001
Control	14	26	33	27	
Choking when swallowing?					
IMRT	27	40	20	13	<0.0001
Control	6	27	27	40	

DISCUSSION

Permanent xerostomia is the most prevalent late consequence of irradiation of head and neck cancer and a major cause of reduced quality of life (QOL) [6]. In addition to perception of dryness, diminished salivary output has other effects, like making mastication and deglutition difficult, which may contribute to nutritional deficiencies, predisposing the patient to mucosal fissures and ulcerations, changing the composition of oral flora, promoting dental caries and contributing to osteoradionecrosis [7].

The prevalence of xerostomia after radiotherapy of head and neck cancer relates to the extreme radiosensitivity of the salivary glands, with salivary acinar cell apoptosis at low doses and necrosis at high doses [8].

In traditional (2-dimensional) radiotherapy of head and neck cancer, the placement of the radiation fields and their shapes are based on the bony anatomy acquired by the simulator diagnostic-quality films. These fields typically encompass large majority of all the salivary glands when advanced cancer is irradiated. Using IMRT, the desired target doses can be delivered with a high conformity, and dose limits to critical noninvolved organs are achieved at a higher degree than was previously possible. In treating advanced head and neck cancer with highly conformal RT, an important goal has been the sparing of the parotid glands to reduce xerostomia. IMRT reduces the radiation dose to the contralateral parotid gland to 32% compared to 93% for the standard plans.

The parotid glands are said to be largely responsible for the saliva output during meals whereas the oral cavity and submandibular glands are supposed to be mainly responsible for lubrication at rest [9].

In certain tumour sites like the base of tongue, it is essential to treat the parapharyngeal spaces bilaterally. In

these patients it is still possible to spare the superficial lobes of the parotid glands on both sides. The rationale behind this is that the parotid glands have their functional subunits organised in parallel ie. damage to a part of organ does not result in complete loss of function.

Earlier reports on QoL after salivary gland sparing IMRT, except for Jabbari et al, made no distinction in QoL during meals and during rest. In general: the differences between the conventional and the IMRT group emerged largest and most significant by the xerostomia during meals questions [10,11,12].

We did this study to find out whether extra expenditure on newer radiation delivery techniques like IMRT will result in favourable outcome with better quality if life especially in long term survivors. Our results showed that patients receiving IMRT had a better xerostomia related QoL than patients who received bilateral opposed conventional radiation fields. The aim of our treatment was to spare (one of) the parotid glands i.e. reducing the mean parotid dose to below 26 Gy. Sparing of the submandibular glands and oral cavity was not an objective since this could not be achieved together with irradiation of level II on both sides.

CONCLUSION

Compared to conventionally irradiated head and neck cancer patients, IMRT treated patients had improved xerostomia related QoL during meals and in rest. Within the

IMRT group the xerostomia scores were better for those patients with a mean parotid gland dose to the "spared" parotid gland below 26 Gy [13,14].

The findings suggest that the development of new radiation delivery techniques like IMRT can significantly improve these morbidities and thus the quality of life.

REFERENCES

1. National Cancer Registry Programme. Ten year consolidated report of the hospital based cancer registries.
2. Perez and Brady's Principles and Practice of Radiation Oncology,chapter 41,oral cavity cancers page no .893
3. Ship JA. Diagnosing, managing, and preventing salivary gland disorders. Oral Dis 2002;8:77–89
4. Vissink A, Burlage FR, Spijkervet FK, et al. Prevention and treatment of the consequences of head and neck radiotherapy. Crit Rev Oral Biol Med2003;14:213–25
5. Bjordal K, Ahlner-Elmqvist M, Tollesson E, Jensen AB, Razavi D, Maher EJ, Kaasa S: Development of a European Organization for Research and Treatment of Cancer (EORTC) questionnaire module to be used in quality of life assessments in head and neck cancer patients. EORTC Quality of Life Study Group. Acta Oncol 1994, 33:879-85.
6. Bjordal K, Kaasa S, Mastekaasa A: Quality of life in patients treated for head and neck cancer: A follow up study 7 to 11 years after radiotherapy. Int J Radiat Oncol Biol Phys 28 : 847 - 856, 1994
7. Balogh JM, Sutherland SE: Osteoradionecrosis of the mandible: A review. J Otolaryngol 18 : 245 -250, 1989
8. Stephens LC, Ang KK, Schultheiss TE, et al: Target cell and mode of radiation injury in rhesus salivary glands. Radiother Oncol 7 : 165 -174, 1986
9. Dawes C: Rhythms in salivary flow rate and composition. Int J Chronobiol 1974, 2:253-279
10. Parliament MB, Scrimger RA, Anderson SG, Kurien EC, Thompson HK, Field GC, Hanson J: Preservation of oral health-related quality of life and salivary flow rates after inverse-planned intensity-modulated radiotherapy (IMRT) for head-and-neck cancer. Int J Radiat Oncol Biol Phys 2004, 58:663-673.
11. Malouf JG, Aragon C, Henson BS, Eisbruch A, Ship JA: Influence of parotid-sparing radiotherapy on xerostomia in head and neck cancer patients. Cancer Detect Prev 2003, 27:305-310.
12. Jabbari S, Kim HM, Feng M, Lin A, Tsien C, Elshaikh M, Terrel JE, Murdoch- Kinch C, Eisbruch A: Matched case-control study of quality of life and xerostomia after intensity-modulated radiotherapy or standard radiotherapy for head-and-neck cancer: initial report. Int J Radiat Oncol Biol Phys 2005, 63:725-731
13. CM van Rij, WD Oughlane-Heemsbergen, AH Ackerstaff, EA Lamers, AJM Balm and CRN Rasch. Parotid gland sparing IMRT for head and neck cancer improves xerostomia related quality of life Radiation Oncology 2008, 3:41 doi:10.1186/1748-717X-3-41
14. Pètra M Braam, Judith M Roesink, Cornelis PJ Raaijmakers, Wim B Busschers and Chris HJ Terhaard. Quality of life and salivary output in patients with head-and-neck cancer five years after radiotherapy. Radiation Oncology 2007, 2:3 doi:10.1186/1748-717X-2-3.