

Original Article

Xerostomia after Radiotherapy and its Effect on Quality of Life in Head and Neck Cancer Patients

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Abstract

Background: Xerostomia is one of the one complications following radiotherapy that can affect quality of life (QoL). This study aims to assess the severity of xerostomia in patients with head and neck cancers after radiotherapy and its effect on QoL.

Methods: In this longitudinal prospective study, the severity of xerostomia and related QoL was assessed in 63 head and neck cancer patients who referred to the Radiotherapy Ward. Patients completed a xerostomia questionnaire (XQ) at the beginning, and 2, 4, and 6 weeks after treatment over a period of 6 months. Additionally, unstimulated saliva was collected using the spitting method at all 4 visits.

Results: QoL significantly worsened with increased time ($P = 0.0001$); meanwhile, the severity of xerostomia increased significantly ($P = 0.0001$). However, there was no significant change in the amount of saliva at these 4 time points ($P = 0.23$). Regression analysis showed that with each milliliter decrease in saliva secretion, the QoL score decreased 2.25%. With one score increase in xerostomia, from the QoL mean score there was a 1.65% decrease.

Conclusion: The decrease in saliva and xerostomia that resulted from radiotherapy plays an important role in worsening QoL among patients who undergo radiotherapy for head and neck cancers. Although the amount of saliva has a significant association with QoL, the xerostomia score which shows subjects' general feeling also independently impacts QoL.

In future studies, we recommend patient assessments for periods longer than 6 months.

Keywords: Quality of life, radiotherapy, saliva flow, xerostomia

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Introduction

Oral cancers are among the most common cancers and 1 of the 10 most common causes of death, worldwide.¹ Multiple treatments exist for treating oral cancers that include surgery, radiotherapy, chemotherapy, and the combination of these 3 methods.² In radiotherapy, high energetic electromagnetic rays (X- or gamma rays) or particles with high levels of energy are used to destroy malignant cells. Ionizing rays lead to cellular death via preventing DNA synthesis and activity.² Although cells affected by radiotherapy either die or remain alive, they cease to divide.¹

Radiotherapy complications in the oral cavity are important with regards to oral diseases. Previous studies have shown that xerostomia is the most frequent complication among patients who receive radiotherapy. The prevalence of xerostomia has been reported to be from 73.5% to 93%.³⁻⁵ Other complications include viscous saliva, salivary gland dysfunction, mucositis, soft tissue necrosis, periodontal diseases, tasting disorders, decreased sense of taste, oral discomfort or jaw pain, tooth caries, mucosal pigmentation, limitations in opening the mouth, viral and fungal infections, and osteoradionecrosis.^{1,6-11} Although palliative treatments exist for

xerostomia, to date none are definite or curative. New techniques in radiotherapy can be effective in preventing xerostomia by decreasing salivary gland exposure.³

However, despite the tools to evaluate salivary gland function, xerostomia is only a subjective symptom.³ In addition to the treatment effect of radiotherapy on controlling tumor size and patients' survival; one must be concerned about short term and long term disabilities, and quality of life (QoL). Currently QoL is considered a health concern, whose measurement is essential in health research.^{7,9}

There are many published studies about the effects of radiotherapy on the mouth, of which xerostomia is the most frequent complaint from patients who receive radiotherapy.^{3,12,13} Numerous studies have researched post-radiation xerostomia in Iran.^{14,15} Although there is tremendous research in this area, few studies have simultaneously explored the associations of QoL, general feeling of subjects about xerostomia, and the amount of saliva during and after radiotherapy.

Previous studies have shown that objective signs are not accorded with subjective symptoms.⁵ Based on the above explanation, we aim to explore the associations of these three variables (QoL, xerostomia, and saliva quantity) in head and neck radiotherapy cases during and after treatment. The intent of this study is to evaluate xerostomia and its effect on QoL.

Materials and Methods

Patients and setting

In a longitudinal prospective study, 63 patients with head and

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neck cancers were followed for 6 weeks. The subjects were selected from the only radiotherapy referral center at Shafa Hospital, Kerman, Iran.

The proposal of this study was approved under the ethical code of EC/KNRC/87-6 by the Neuroscience Research Center, Kerman University of Medical Sciences.

The sample size was calculated to estimate a Pearson correlation of 0.4 or more with 95% confidence interval between the three main variables of QoL, amount of saliva and xerostomia score.

The method of our sampling was sequential. Patients older than 18 years whose bilateral major salivary glands were exposed to radiotherapy at doses of at least 2500–3000 cGy were recruited to participate.³ Patients were included in this study if they presented with nasopharyngeal, laryngeal, parotid, or hypopharyngeal cancers, or any other tumors in the oral cavity. The type of radiation was conventional X-ray with a linear energy of 9 mv photons. Some patients who received radiotherapy were also administered chemotherapy (cisplatin), which was dependent upon pathologic status, particularly in cases of nasopharynx and hypopharynx carcinomas. Patients were excluded from the study if they had other known systemic disorders such as Sjögren syndrome, diabetes, connective tissue diseases (rheumatoid arthritis or systematic lupus erythematosus), or if they were taking any type of medication that effected saliva secretion.

Assessments

Patients were initially interviewed prior to the start of their radiotherapy; follow up visits were conducted 2, 4, and 6 weeks later.

Having explained the objectives of the study and its methodology, eligible subjects were asked to sign a consent form at the first visit. In all 4 sessions, subjects were asked to complete a questionnaire related to their xerostomia (XQ) and a QoL questionnaire. In addition, during all 4 visits, the amount of their saliva was measured by collecting unstimulated whole saliva in milliliters per minute for a total time of ten minutes.

Data was collected using XQ and QoL questionnaires. The XQ included eight questions evaluated by the Likert scale (1: not at all; 2: a little; 3: moderately; 4: quite a lot; and 5: very much). Hence, according to the XQ, the more the patient had a feeling of xerostomia, the higher the xerostomia score would be, which ranged between 8 and 40.¹⁶ For QoL, we used the QoL part of the XQ published by Dirix et al.³ In that study, 15 questions evaluated QoL with the Likert scale, as follows: 5: not at all; 4: a little; 3: moderately; 2: quite a lot; and 1: very much. The worse the patient's QoL was, the lower its score would be. This score ranged between 15 and 75. In addition to these questions, demographic information of age, sex, educational and marital status, lesion location, and the type of treatment were gathered.

In order to validate the questionnaires, we used the standard forward-backward translation by two independent translators to ensure that the Persian versions of the questionnaires were comparable with their English versions.

In the next step, the content of the questionnaires were verified based on feedback received from 20 people of varying literacy levels. In addition, the internal consistency of the questionnaire was computed using Chronbach's alpha, which ranged between 0.67 and 0.92 at four times of data collection. Using re-test with a 5-day gap, the intra-class correlation (ICC) in response to xerostomia and QoL questions were 0.31 and 0.37, respectively; both

were statistically significant ($P < 0.001$). Subjects received no interventions during those 5 days.

In order to collect patients' saliva, they had to refrain from eating, drinking, smoking, and brushing teeth 90 minutes prior to sample collection. In order to prevent the circadian pattern of saliva secretion bias, sample collection was conducted between 10 and 12 am. Saliva was collected using the spitting method.¹⁷ Each patient was asked to rest for a few minutes, close his/her mouth and not to swallow his saliva. Then the patient was asked to lay his head obliquely on a plate, which its weight was already registered on its outer side. After each three minutes, patients spitted their saliva in the plates and such an action was repeated for ten minutes. Considering that the normal amount of saliva in healthy individuals is 0.1 to 0.8 mL/min, the amount less than 0.1 mL/min accounted for insufficient saliva.¹

Statistical analysis

Data were analyzed using SPSS version 11.5; we compared the xerostomia and QoL scores and the amount of saliva in four measurements by repeated ANOVA. In order to assess the differences among four measurements, we compared double groups using paired *t*-test with Bonferroni correction. In addition, we assessed the association of these scores with the amount of saliva by Pearson correlation coefficients and multivariate linear regression models.

Results

Out of 63 subjects, 43 (77.8%) were male. Their mean \pm SD age was 45.6 ± 15.6 years. Average received radiation doses was 5398 cGy during their radiotherapy. The most frequent carcinoma was of the larynx (31.7%). Demographic information, the diseases, and their treatment characteristic are presented in Table 1.

There was a significant difference among the xerostomia score at all 4 time points ($P = 0.0001$). The xerostomia score in the first session was significantly lower than the next 3 sessions ($P < 0.001$), but the differences among following sessions were not statistically significant. Around 20% of the samples dropped out during the follow-up period.

There was a significant difference among the QoL score in all 4 sessions ($P = 0.0001$). The score of the first session was significantly higher than in the next 3 sessions. In addition, the score in the second session was higher than the third session. The mean salivary flow in the first session was 0.29 mL. Although it was greater than seen at during follow up, the variation was not statistically significant ($P = 0.23$; Table 2). The percentage of xerostomia (saliva < 0.1 mL/min) was 11% in the first session whereas it was 25%, 14%, and 25% in the following sessions, which was not statistically significant ($P = 0.13$).

The correlation coefficient between saliva amount and QoL score before starting radiotherapy showed a weak negative association ($r = -0.15$, $P = 0.23$), while this association was positive in the next 3 sessions ($r = 0.30$, $P = 0.02$; $r = 0.1$, $P = 0.46$; and $r = 0.3$, $P = 0.04$, respectively). We observed a strong negative association between QoL and xerostomia scores in all four sessions (-0.76 , -0.67 , -0.66 , and -0.56 ; all values of $P < 0.0001$). There was no relationship between the amount of saliva secreted and xerostomia in all four session (-0.0002 , -0.17 , -0.012 , and -0.38); this association was significant only in the fourth session ($P = 0.01$; Table 3). The changes in salivary flow, QoL, and XQ-score

are shown in Figure 1.

In our regression model, we found that each mL/min decrease in the flow of saliva decreased the QoL score by 2.25%. Meanwhile, with a one score increase in xerostomia score, the QoL score decreased by 1.65%. However, in the adjusted model for demographic variables, only the xerostomia score was significantly associated with QoL, which meant that salivary secretion compared to xerostomia score, had a weaker direct association with the QoL score.

None of the demographic variables showed significant associations with saliva flow and xerostomia in our repeated measure ANOVA model.

In addition, no significant relationship was seen between the dose of received radiotherapy with total xerostomia and QoL scores ($P > 0.1$ for all values).

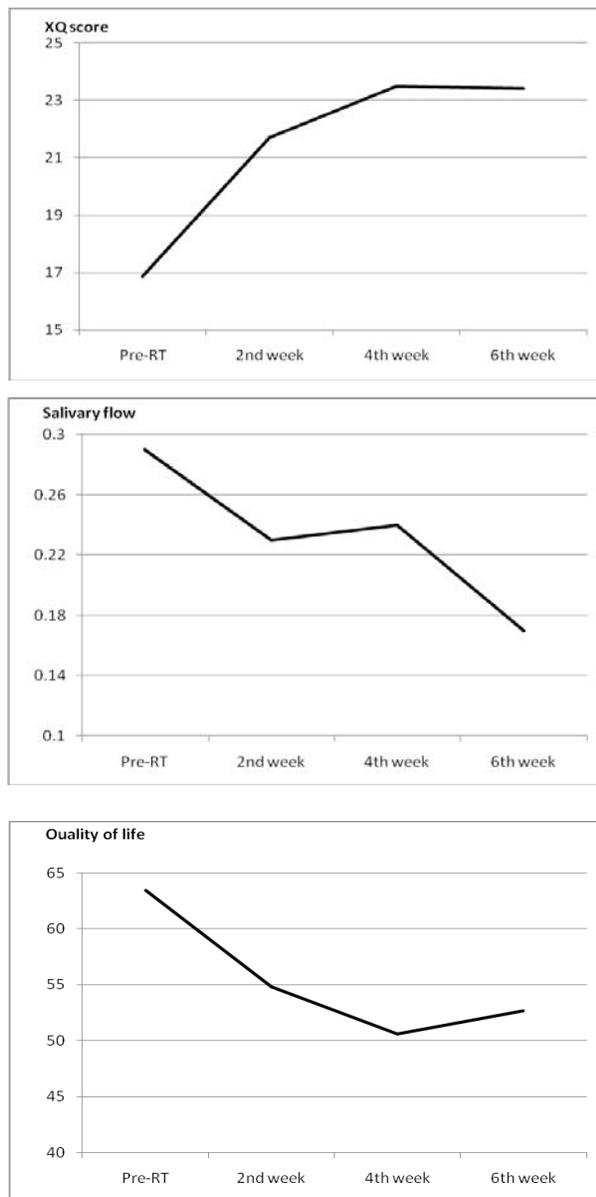


Figure 1. Changes in salivary flow, XQ score, and QoL during four intervals.

Discussion

The results of the present study revealed that the feeling of xerostomia more strongly affected QoL compared to actual salivary flow amongst patients undergoing radiotherapy. The amount of saliva secreted did not significantly change during therapy while patients began to suffer from xerostomia after the start of treatment. The later lead to a decrease in QoL during radiotherapy. The results also showed that QoL decreased in the first two weeks of radiotherapy, but afterward it was more or less constant.

Previous studies have demonstrated that xerostomia, which is caused by local permanent damage to the salivary glands in the radiation treatment zone, is a common and important complaint amongst patients who undergo head and neck radiotherapy.^{3,4,18-22} In a study conducted in 2006 by Pow et al., the effect of intensity modulated radiotherapy on the severity of xerostomia and QoL was assessed, which revealed that xerostomia was an important problem of patients after 2 months of radiotherapy.⁴ In the present study, it was revealed that the mean amount of saliva in the first session was more than the next 3 sessions. Such a finding was compatible with a study by Lin et al.¹⁷ As with the Dirix et al. and Lin et al. findings, we detected an increase in trend in the feeling of xerostomia during the first 6 weeks of radiotherapy.^{3,17}

We did not find any significant, strong association between the sensation of xerostomia and actual salivary flow. It seems that xerostomia is a subjective feeling and other factors may have more effect than the amount of saliva. This finding was also observed in a study by Viasanathan and Nix.²³

Generally, oral problems such as patients' facial appearance, swallowing, speaking, and a decreased level of activity could affect their oral health-related QoL by influencing psycho-social aspects.^{7,24-26}

In a study conducted by McMilan et al., it was shown that oral health-related QoL in patients who underwent radiotherapy due to nasopharyngeal cancer significantly improved over time.²⁶ It seemed that the psychological shock that patients may have at the time of diagnosis and in the beginning of treatment manifest as xerostomia even in the absence of a considerable decrease in saliva amount.

In the present study, the score of patients' QoL significantly decreased during the first 6 weeks after the treatment. Although a decrease in QoL and a simultaneous increase in xerostomia do not confirm a causal association, this issue could be due to initiation of radiotherapy. According to other studies, the effect of xerostomia on oral health and QoL is very important.^{3,17}

We only followed our subjects for 6 weeks; however, the long term trend of QoL might be different. Oates et al. followed their cases for 24 months and showed that QoL improved after the start of treatment.⁷ However, longer follow ups were conducted and the results showed QoL improved for an extended time after treatment, but xerostomia did not decrease.^{7,26}

Based on the above explanation, we believe the short period of follow up was the main limitation of our study. This was solely due to practical considerations, which have also been mentioned in similar studies.¹⁷ In addition, we did not assess other aspects of oral health such as pain and mucositis. We encountered numerous problems in our saliva collections mainly due to the severe health condition of our subjects and their low literacy rates, both of which increased our work and efforts in this study to convince subjects to cooperate accordingly.

Table 1. Demographic characteristics of the patients.

	Characteristics	Number of patients (%)
sex	Male	49 (77.8%)
	Female	14 (22.2%)
Age	(mean \pm SD) years	45.6 \pm 15.6
Education	Uneducated	11 (17.5%)
	Diploma and less	50 (79.3%)
	University educated	2 (3.2%)
Married status	Married	58 (92.1%)
	Single	5 (7.9%)
Sight of lesion	Larynx	20 (31.7%)
	Oropharynx	17 (26.9%)
	Brain	11 (17.4%)
	Oral cavity	5 (7.9%)
	Lymphoma	4 (6.3%)
	Salivary gland cancer	7 (11.1%)
	Ear	1 (1.5%)
Treatment	RT	8 (12.7%)
	Chemotherapy & RT	55 (87.3%)
	Previous surgery	55 (87.3%)

Table 2. Saliva secretion, XQ-score, and QoL score in four sessions.

Time of measurement	Salivary flow (mL/min)		XQ score		QoL score	
	Mean \pm SD	Number	Mean \pm SD	Number	Mean \pm SD	Number
Before RT	63.45 \pm 10.55	62	16.87 \pm 7.42	62	0.29 \pm 0.2	60
Second week	54.81 \pm 9.81	54	21.72 \pm 5.94	54	0.23 \pm 0.17	54
Fourth week	50.57 \pm 8.91	53	23.51 \pm 4.60	54	0.24 \pm 0.25	54
Sixth week	52.64 \pm 6.27	47	23/42 \pm 4.6	49	0.17 \pm 0.22	43
P-value	0.0001		0.0001		0.23	

Table 3. The correlation among salivary flow, XQ score and QoL score in four sessions.

Time	Evaluation type	Salivary flow Correlation coefficient	XQ Correlation coefficient
Before treatment	QoL	-0.15	-0.76*
	XQ	-0.0002	—
Second week	QoL	0.30	-0.67*
	XQ	-0.17	—
Fourth week	QoL	0.104	-0.66*
	XQ	-0.012	—
Sixth week	QoL	0.31*	-0.56*
	XQ	-0.38*	—

*P \leq 0.05

According to the results of our study, it seems that low QoL amongst patients after head and neck radiotherapy can present an association with a sensation of dry mouth. It seems that xerostomia does not have a significant association with QoL and sensation of dry mouth.

References

- Epstein J, Van Der Waal I. Oral cancer. In: Greenberg MS, Glick M, Ship JA, eds. *Burket's Oral Medicine*. 11thed. Ontario, BC: Decker Inc., 2008; 153 – 190.
- Neeley M. Oral cancer and principle of radiotherapy. In: Prabhu SR, ed. *Text book of Oral Medicine*. 2nd ed. New Delhi: Jaypee Brothers; 2005: 187 – 196.
- Dirix P, Nuyts S, Vander Poorten V, Delaere P, Van den Bogaert W. The influence of xerostomia after radiotherapy on quality of life: results of a questionnaire in head and neck cancer. *Support Care Cancer*. 2008; **16**: 171 – 179.
- Pow EH, Kwong DL, McMillan AS, Wong MC, Sham JS, Leung LH, et al. Xerostomia and quality of life after intensity-modulated radiotherapy vs. conventional radiotherapy for early-stage nasopharyngeal carcinoma: initial report on a randomized controlled clinical trial. *Int J Radiat Oncol Biol Phys*. 2006; **66**: 981 – 991.
- Liu XK, Zeng ZY, Hong MH, Zhang AL, Cui NJ, Chen FJ. Clinical analysis of xerostomia in patients with nasopharyngeal carcinoma after radiation therapy [in Chinese]. *Ai Zheng*. 2004; **23**: 593 – 596.
- Brosky ME. The role of saliva in oral health: strategies for prevention and management of xerostomia. *J Support Oncol*. 2007; **5**: 228 – 229.
- Oates JE, Clark JR, Read J, Reeves N, Gao K, Jackson M, et al. Prospective evaluation of quality of life and nutrition before and after treatment for nasopharyngeal carcinoma. *Arch Otolaryngol head Neck Surg*. 2007; **133**: 533 – 540.
- Jham BC, da Silva Freire AR. Oral complications of radiotherapy in the head and neck. *Braz J Otorhinolaryngol*. 2006; **72**: 704 – 708.
- Carl W. Local radiation and systemic chemotherapy: preventing and managing the oral complications. *J Am Dent Assoc*. 1993; **124**: 119 – 123.
- Andrews N, Griffiths C. Dental complications of head and neck radiotherapy: Part 1. *Aust Dent J*. 2001; **46**: 88 – 94.
- Devita VT, Samuel JR, Rosenberg SA. Oral complications. In: Berger AM, Kilroy TJ, eds. *Cancer*. 6th ed. Philadelphia: Lippincott, Williams & Wilkins; 2001: 2881.
- Wu Y, Hu WH, Xia YF, Ma J, Liu MZ, Cui NJ. Quality of life of nasopharyngeal carcinoma survivors in Mainland China. *Qual Life Res*. 2007; **16**: 65 – 74.
- Guobis Z, Baseviciene N, Paipaliene P, Sabalys G, Kubilius R. Xero-

- stomia: clinic, etiology, diagnosis and treatment. *Medicina (Kaunas)*. 2006; **42**: 171 – 179.
14. Shahdad SA, Taylor C, Barclay SC, Steen IN, Preshaw PM. A double-blind, crossover study of Biotène Oralbalance and BioXtra systems as salivary substitutes in patients with post-radiotherapy xerostomia. *Eur J Cancer Care (Engl)*. 2005; **14**: 319 – 326.
 15. Sahba S, Ghadimi S, Taleeepour A-R, Hadad P, Zolfaghari E. The efficacy of Iranian made saliva substitute vs. VA-OraLube in improvement of oral health-related quality of life in radiotherapy-induced xerostomia. *J Dent Sch Shahid Beheshti Univ Med Sci*. 2009; **3**: 136 – 145.
 16. Eisbruch A, Kim HM, Terrell JE, Marsh LH, Dawson LA, Ship JA. Xerostomia and its predictors following parotid-sparing irradiation of head and neck cancer. *Int J Radiat Oncol Biol Phys*. 2001; **50**: 695 – 704.
 17. Lin SC, Jen YM, Chang YC, Lin CC. Assessment of xerostomia and its impact on quality of life in head and neck cancer patients undergoing radiotherapy, and validation of the Taiwanese version of the xerostomia questionnaire. *J Pain Symptom Manage*. 2008; **36**: 141 – 148.
 18. Momm F, Volegova-Neher NJ, Schulte-Mönting J, Guttenberger R. Different saliva substitutes for treatment of xerostomia following radiotherapy. A prospective crossover study. *Strahlenther Onkol*. 2005; **181**: 231 – 236.
 19. Guchelaar H, Vermes A, Meerwaldt J. Radiation-induced xerostomia: pathophysiology, clinical course and supportive treatment. *Support Care Cancer*. 1997; **5**: 281 – 288.
 20. Cassolato SF, Turnbull RS. Xerostomia: clinical aspects and treatment. *Gerodontology*. 2003; **20**: 64 – 77.
 21. Chambers MS, Rosenthal DI, Weber RS. Radiation-induced xerostomia. *Head Neck*. 2007; **29**: 58 – 63.
 22. Garg AK, Malo M. Manifestations and treatment of xerostomia and associated oral effects secondary to head and neck radiation therapy. *J Am Dent Assoc*. 1997; **128**: 1128 – 1133.
 23. Visvanathan V, Nix P. Managing the patient presenting with xerostomia: a review. *Int J Clin Pract*. 2010; **64**: 404 – 407.
 24. Shiboski CH, Hodgson TA, Ship JA, Schiodt M. Management of salivary hypofunction during and after radiotherapy. *Oral Surg Oral Med Pathol Oral Radiol Endod*. 2007; **103**: 1 – 19.
 25. Hahn TR, Kruskemper G. The impact of radiotherapy on quality of life – a survey of 1411 patient with oral cancer. *Mund Kiefer Gesichtschir*. 2007; **11**: 99 – 106.
 26. McMillan AS, Pow EH, Leung WK, Kwong DL, Wong MC. Oral health condition in southern Chinese after radiotherapy for nasopharyngeal carcinoma: Extent and nature of the problem. *Oral Dis*. 2003; **9**: 196 – 202.