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ORIGINAL ARTICLE

The Prevalence of Oral Complications in Patients undergoing head and Neck Radiotherapy

Simin Lesan,¹Somayeh Alirezaei^{*2},Mahdieh Aminnia³,Ali Kazemian⁴.

Oral and Maxillofacial Medicine Department, Islamic Azad University, Dental Branch, Tehran, Iran.
Oral and Maxillofacial Medicine Department, Islamic Azad University, Dental Branch, Tehran, Iran
DMD, Private office, Iran

4) Clinical Oncologist, Private Clinic, Iran

*Correspondence author's Email: Email:dr.somayehalirezaei@gmail.com

ABSTRACT

Radiotherapy is an important part of multimodality treatment of cancer, especially head and neck malignancies. It is – however– associated with various adverse effects. The aim of this study was to evaluate the oral side effects of radiotherapy in patients who were being treated for different malignancies of head and neck. Fifty patients were selected from the patients who were being treated at Imam Khomeini Hospital for different malignancies of head and neck. Total radiation dose was 60-70 Gy in 1.8-2Gy daily fractions, 5 days a week. The patients were evaluated on a weekly basis from one week before till one week after completion of the radiotherapy. The prevalence of adverse effects in participants and their correlation with various parameters was assessed using chi squared and Fisher's exact tests. Almost all patients undergoing radiotherapy to head and neck suffered from its complications to various extents, with xerostomia being the most common complication. Changes of taste were related to the amount of radiation exposure and receiving chemotherapy. Chemotherapy was also related to developing candidial infections. Female patients and the ones with stage 3 or 4 disease reported more pain and burning sensation during radiotherapy. Application of preventive measure in order to reduce the rate of above mentioned complications seems necessary. **Key words:** head and neck, radiotherapy, complications

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INTRODUCTION

Radiotherapy is an important part of multimodality treatment of cancer, including also surgery and chemotherapy [1]. It is –in many cases–considered as the main treatment modality for cancers of the head and neck. Head and neck malignancies are usually treated with high doses of radiotherapy, which is associated with various adverse effects [2]. The most common complication of radiation therapy of head and neck region include oral mucositis (pain, erythema, pseudomembrane formation, and ulcer), oral candidiasis, involvement of salivary glands (reduction in saliva production, changes in salivary content), xerostomia, trismus, dysgeusia, and periodontal complications [1].

The exact prevalence of these complications is not clear, as the prevalence depends on many different factors including radiation dosage and planning, as well as inherent response of tissues to high dose radiation.

In one study the reported prevalence of oral side effects were as follows: alterations in taste 64.3%, oral candidiasis 54.2%, xerostomia 95%, and mucositis 83% [3]. In another study, the prevalence of candidiasis has been reported as 30% [4-7].

Faramarzi *et al* [5] showed that incidence of some adverse effects such as nausea, xerostomia and constipation rose dramatically after the fifth weeks of radiation treatment. The aim of this study was to evaluate the oral side effects of radiotherapy in patients who were being treated for different malignancies of head and neck.

MATERIALS AND METHODS

Fifty patients, who were interested to participate, entered the study. The participants were selected from the patients who were being treated at Imam Khomeini Hospital for different malignancies of head and neck. Total radiation dose was 60-70 Gy in 1.8-2Gy daily fractions, 5 days a week. The patients were evaluated on a weekly basis from one week before till one week after completion of the radiotherapy. In each visit, the oral cavity of the patients was fully examined. The prevalence of adverse effects in participants and their correlation with various parameters was assessed using chi squared and Fisher's exact tests. The level of unstimulated saliva was measured by spitting technique, and xerostomia was defined as level of unstimulated saliva less than 0.1ml/min (1).Pain was evaluated using VAS score. Mucositis was defined based on National Cancer Institute's Common Toxicity Criteria (NCI-CTC) (2) as is shown in table.

Grades of mucositis due to radiation			
Grade	Description		
0	none		
1	erythema of the mucosa		
2	patchy pseudomembranous reaction (patches generally \leq 1.5 cm in diameter and non-contiguous)		
3	confluent pseudomembranous reaction (contiguous patches generally > 1.5 cm in diameter)		
4	necrosis or deep ulceration; may include bleeding not induced by minor trauma or abrasion		

Trismus was defined based on the criteria that follow [4]:

Grades of trismus			
Grade	Description		
1	Mouth opening 31-40 mm		
2	Mouth opening 25-30 mm		
3	Mouth opening less than 25 mm		

Alterations in taste were defined by asking about the changes in the basic tastes: sweetness, sourness, saltiness, and bitterness [4-8].

Based on the definition of International Union Against Tuberculosis and Lung Disease, an individual was considered as a smoker if they have smoked at least 100 cigarettes in their lifetime and now smokes every day or some days [9].

RESULTS

Among 50 participants, 12 (24%) were female and 38 (76%) were male. Mean age of the patients was 59±15 years (range: 35 to 104).

Sixty four percent of the patients received 60Gy of radiation and 36% more than 60Gy. The duration of treatment was less than 6 weeks in 52% and more than that in 48% of patients. Regarding the staging based on TNM staging system, 10% of the patients had stage I disease, 30% stage II, 34% stage III, and 26% stage IV.

The type of the tumor was squamous cell carcinoma (SCC) in 92%, thyroid carcinoma in 4%, ameloblastoma in 2%, and mucoepidermoid carcinoma in 2%.Forty percent of the patients also received chemotherapy. On pre-treatment evaluation, none of the patients had any oral lesion. After the fifth weeks of treatment, all (100%) of the patients showed various degrees of oral mucositis. Among the studied patients, in 21 the treatment lasted more than 7 weeks. In this group, mucositis aggravated significantly by increasing the duration of treatment. All these patients suffered from changes in taste at the end of 7th week. Among all participants, 49 (98%) developed xerostomia. The prevalence of oral complications in each week of treatment has been shown on figure 1.



Fig 1: The prevalence of oral complications in each week of treatment.

As shown in the figure, the prevalence of oral complications rose dramatically after the third week of treatment, and peaked after the fifth week. Figure 2 shows the prevalence of different side effects based on the week of radiation treatment.







Table 1 shows the prevalence of mucositis based on various parameters.

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Table 1: the prevalence of mucositis based on various parameters.				
Parameter		Mucositis Neg (N=7)	Mucositis Pos (N=43)	P value
age	<59	2 (28.6%)	22 (51.2%)	0.2
	≥ 59	5 (71.4%)	21 (48.8%)	0.5
gondor	Male	6 (85.7%)	32 (74.4%)	0.5
genuer	Female	1 (14.3%)	11 (25.6%)	0.5
Systemic disease	No	5 (71.4%)	35 (81.4%)	0.5
systemic disease	Yes	2 (28.6%)	8 (18.6%)	0.5
Modication	No	6 (85.7%)	29 (67.4%)	0.4
Medication	Yes	2 (28.6%)	14 (32.6%)	0.4
Dadiation daga	60 Gy	5 (71.4%)	28 (65.1%)	0.7
Radiation dose	> 60 Gy	2 (28.6%)	15 (34.9%)	0.7
Treatment	6 weeks	4 (57.1%)	25 (58.1%)	0.0
duration	>6 weeks	3 (42.9%)	18 (41.9%)	0.9
Stago	I or II	2 (28.6%)	18 (41.9%)	0.5
Stage	III or IV	5 (71.4%)	25 (58.1%)	
	SCC	6 (85.7%)	40 (93%)	
Type of tumor	Thyroid carcinoma	0 (0%)	2 (4.65%)	0.4
Type of tumor	Mucoepidermoid	1 (14.3%)	0 (0%)	0.4
	Ameloblastoma	0 (0%)	1 (2.35%)	
Cara a la sar	No	4 (57.1%)	26 (60.5%)	0.0
SIIIOKEI	Yes	3 (42.9%)	17 (39.5%)	0.9
Alcohol	No	7 (100%)	36 (83.7%)	0.2
consumption	Yes	0 (0%)	7 (16.3%)	0.5
Chamatharany	No	6 (85.7%)	23 (53.5%)	0.2
chemotherapy	Yes	1 (14.3%)	20 (46.5%)	0.2

Table 2 shows the prevalence of change of taste based on various parameters.

Table 2: the prevalence of change of taste based on various parameters.					
Parameter		Change of taste	Change of taste	Dyalua	
		Neg (N=4)	Pos (N=46)	P value	
	<59	1 (25%)	23 (50%)	0.4	
age	≥ 59	3 (75%)	23 (50%)		
gandan	Male	4(100%)	35 (76.1%)	0.2	
gender	Female	0 (0%)	11 (23.9%)	0.5	
Swatamia diagona	No	4(100%)	36 (78.3%)	05	
Systemic disease	Yes	0 (0%)	10 (21.7%)	0.5	
Madiantian	No	4(100%)	32 (69.6%)	0.2	
Medication	Yes	0 (0%)	14 (32.6%)	0.2	
Dediction does	60 Gy	4(100%)	29 (63%)	0.2	
Radiation dose	> 60 Gy	0 (0%)	17 (37%)		
Treatment	6 weeks	4(100%)	25 (54.3%)	0.6	
duration	>6 weeks	0 (0%)	21 (45.7%)	0.6	
Stage	I or II	3 (75%)	18 (39.1%)	0.5	
Stage	III or IV	1 (25%)	28 (60.9%)		
	SCC	4(100%)	42 (91.3%)		
Type of types	Thyroid carcinoma	0 (0%)	2 (4.3%)	0.4	
Type of tumor	Mucoepidermoid	0 (0%)	1 (2.2%)		
	Ameloblastoma	0 (0%)	1 (2.2%)		
Smoker	No	3 (75%)	27 (58.7%)	0.9	
	Yes	1 (25%)	19 (41.3 %)		
Alcohol	No	7 (100%)	36 (83.7%)	0.2	
consumption	Yes	0 (0%)	7 (16.3%)	0.5	
Chamatharany	No	4(100%)	25 (54.3%)	0.6	
Chemotherapy	Yes	0 (0%)	21 (45.7%)		

Table 3: the prevalence of candidiasis based on various parameters.					
Parameter		Candidiasis	Candidiasis Pos	Dyalua	
		Neg (N=7)	(N=43)	P value	
Age	<59	3 (42.9%)	21 (48.8%)	0.9	
	≥ 59	4 (57.1%)	22 (51.2%)		
Condor	Male	6 (85.7%)	32 (74.4%)	0.2	
Gender	Female	1 (14.3%)	11 (25.6%)	0.3	
Cuatamia diagona	No	6 (85.7%)	34 (79.1%)	0.7	
Systemic disease	Yes	1 (14.3%)	9 (20.9%)	0.7	
Madiantian	No	7 (100%)	27(62.8%)	0.2	
Medication	Yes	0 (0%)	16(37.2%)	0.2	
Dediction does	60 Gy	6 (85.7%)	27(62.8%)	0.2	
Radiation dose	> 60 Gy	1 (14.3%)	16 (37.2%)		
Treatment	6 weeks	4 (57.1%)	25 (58.1%)	0.6	
duration	>6 weeks	3 (42.9%)	18 (41.9%)	0.6	
Store	I or II	5 (71.4%)	18 (41.9%)	0.4	
Stage	III or IV	2 (28.6%)	25 (58.1%)		
	SCC	6 (85.7%)	40 (93%)	0.5	
True of turner	Thyroid carcinoma	0 (0%)	2 (4.%65)		
Type of tumor	Mucoepidermoid	1 (14.3%)	0 (0%)		
	Ameloblastoma	0 (0%)	1 (2.35%)		
Crucolaere	No	7 (100%)	26 (60.5%)	0.0	
Smoker	Yes	0 (0%)	17 (39.5%)	0.9	
Alcohol	No	7 (100%)	36 (83.7%)	0.2	
consumption	Yes	0 (0%)	7 (16.3%)	0.3	
Chomothono	No	6 (85.7%)	23 (53.5%)	0.6	
Chemotherapy	Yes	1 (14.3%)	20 (46.5%)		

Table 3 shows the prevalence of candidiasis based on various parameters.

Table 4 shows the prevalence of pain and burning sensation based on various parameters.

Table 4: the prevalence of pain and burning sensation based on various parameters.				
Parameter		pain Neg (N=21)	pain Pos (N=29)	P value
200	<59	6 (33.3%)	16 (55.2%)	0.9
age	≥ 59	14 (66.7%)	13 (44.8%)	
gondor	Male	20 (95.2%)	18 (62.1%)	0.2
gender	Female	1 (0.8%)	11 (37.9%)	0.5
Sustamia disaasa	No	17 (81%)	23 (79.3%)	0.7
systemic uisease	Yes	4 (19%)	6 (20.7%)	
Madiantian	No	15 (71.4%)	20 (69%)	0.2
Medication	Yes	6 (28.6%)	9 (31%)	
Dadiation daga	60 Gy	14 (66.7%)	18 (62.1%)	0.2
Radiation dose	> 60 Gy	7 (33.3%)	11 (37.9%)	
Treatment	6 weeks	13 (61.9%)	16 (55.2%)	0.6
duration	>6 weeks	8 (38.1%)	13 (44.8%)	0.0
Stago	I or II	11 (52.4%)	9 (31%)	0.4
Stage	III or IV	9 (47.6%)	20 (69%)	
	SCC	20 (95.2)	26 (89.6%)	0.5
Type of tumor	Thyroid carcinoma	0 (0%)	2 (7%)	
Type of tuffior	Mucoepidermoid	0 (0%)	1 (3.4%)	
	Ameloblastoma	1 (4.8%)	0 (0%)	
C I	No	11 (52.4%)	19 (65.5%)	0.9
SIIIOKEI	Yes	10 (47.6%)	10 (34.5%)	
Alcohol	No	7 (100%)	36 (83.7%)	0.2
consumption	Yes	0 (0%)	7 (16.3%)	0.5
Chamathanarr	No	14 (66.7%)	15 (51.7%)	0.6
chemotherapy	Yes	7 (33.3%)	17 (48.3%)	

DISCUSSION

Each year worldwide, thousands of people are diagnosed with head and neck cancers, including cancers of nasopharynx, oropharynx, salivary glands and oral cavity. Radiotherapy-in majority of cases- is the principal treatment modality for these patients [3, 11]. In this study the prevalence of radiation-induced complications were evaluated in 50 patients who were treated for head and neck cancer. Similar to many other studies, xerostomia turned out to be one of the most common side effects of the patients. In Hashemifard *et al* study in Iranian patients, 95.2% of the patients developed xerostomia [3, 12].

It is believed that radiation therapy by interfering with cellular mitosis would result in a decline in the number of cells in the basal layer, which in turn leads to tissue atrophy. This complication then would induce pain and burning sensation [3]. In our study 29 patients (58%) developed xerostomia which was lower than that of Hashemipour study (71%). Our study also showed that women, who had stage 3 or 4 disease, complained more about the pain or burning sensation. Mucositis is another complication of treatment which can result in oral ulcers, bacterial viral or fungal infection, odynophagia, dysphagia, bleeding, and sometimes sepsis and death [13]. In our study, 33 patients (86%) experienced different grades of mucositis, which is similar to the findings of Jajaram *et al* [14] as well as Hashemipour *et al* [15] on Iranian patients. In the lattes study, more men compared to women suffered from mucositis, however, in our study the difference between the two genders was not significant. Farizad *et al* study on 80 patients also demonstrated that mucositis occurred in 65 (81.25%) of patients [10]. Candidiasis is the most common fungal infection of oropharynx and during radiotherapy and many patients show the clinical manifestation of this infection. Diminished saliva production further worsens the situation [1]. Forty three (86%) of our patients developed this infection as pseudomembranous candidiasis or angular cheilitis. This figure was lower at 64.3% and 52% in Hashemipour and Jham studies respectively [15]. To some extent, this difference might be due to diagnostic differences, as in many patients it might be difficult to differentiate simple mucositis from the superimposed candidial infection. We also found a significant relation between receiving chemotherapy and developing oral candidiasis.

Radiation therapy to the neck and head often cause taste changes because of damage to the taste buds and salivary glands. Doses greater than 30 Gy almost always impairs the individual's ability to detect basic tastes (sweetness, sourness, saltiness, and bitterness). Taste changes caused by radiation treatment usually begin to improve three weeks to two months after the end of treatment. Improvement may continue for about a year, but the sense of taste may not entirely return to the way it was before treatment, especially if there is damage to the salivary glands [1].

In our study, 46 patients (92%) developed changes in taste at the end of treatment, namely inability to detect one or more basic tastes of feeling of a bitter taste in the mouth. This figure was considerably lower at 52% in Hashemipour study, which might be due to differences in the measurements. We also found that the patients, who received concurrent chemotherapy, or whose treatment duration was more than 6 weeks, complained more about the changes in taste.

Reduced ability to open the mouth is related to the amount of radiation exposure to the external pterygoid muscle [1]. None of our patients developed trismus following the radiation therapy. This figure was much higher in Hashemipour's study [15], as more than 50% of their patients were reported to have at least grade 2 trismus [2]. We believe that this striking difference is due to much longer follow up periods of those patients [17].

Our study failed to show any relation between xerostomia or mucositis; and patient and treatment characteristics.

CONCLUSION

Our study showed that almost all patients undergoing radiotherapy to head and neck would suffer from its complications to various extents, with xerostomia being the most common complication. Changes of taste were related to the amount of radiation exposure and receiving chemotherapy. Chemotherapy was also related to developing candidial infections. Female patients and the ones with stage 3 or 4 disease reported more pain and burning sensation during radiotherapy. Application of preventive measure in order to reduce the rate of above mentioned complications seems necessary (17, 18).

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