Effect of Radiation on Saliva Flow Rate in Patients under Head and Neck Radiotherapy

Original Article

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Abstract

Introduction: The aim of this study was to evaluate the salivation flow rate objectively using Schirmer test; and mouth dryness and other consequences subjectively by distributing questionnaires to patients receiving head and neck radiotherapy.

Materials and Methods: In this descriptive study that was carried out at Imam Khomeini hospital, Tehran, Iran, the saliva flow rate of 33 patients receiving radiotherapy was evaluated in millimeter in 5 minutes using Schirmer test (with a filtered paper calibrated from 1 to 35mm) before treatment, two weeks and four weeks after and at the end of treatment thus having four groups of measurements. Mouth dryness and other consequences were recorded by questionnaire at final stage. Friedman test, chi-square, dependent and independent t-tests were applied to analyze the data.

Results: In all four groups, the mean of the saliva flow rate decrease during treatment was significant and followed a descending pattern. At the end of the treatment, the total received dosage and saliva flow rate had an inverse relationship, (P value=0.000). The mean salivation decrease in bilateral radiation was estimated more than unilateral one; though their relation was not statistically significant (P value=0.251). The mean salivation decrease in bilateral radiation of nasopharyngeal cancer was meaningfully greater than unilateral (P value 0.05).

Conclusion: During radiation, saliva flow rate depends on the total dosage and the radiation site. Increasing the total dosage of radiation and the field diameter would result in the decrease of salivation of the major salivary glands, particularly parotid ones.

Key words: •Radiotherapy •Salivary Glands •Xerostomia

Introduction

Radiotherapy is a reliable and common method in managing head and neck cancers. These malignancies are most frequent over 65 years of age and afflict 2-15 persons out of 100000 each year. Men are more susceptible to these cancers than women (3:1). The main causes are said to be nicotine, alcohol, viral infections, carcinogenic chemicals, radioactive and ultraviolet rays and poor oral hygiene.[1]Along with its therapeutic effects, radiotherapy of head and neck brings about unpleasant and undesirable effects on soft and hard oral tissues. Hypo salivation and Xerostomia are important and common consequences of radiotherapy. Saliva rate depends upon many factors such as age, gender, psychological conditions, daily biological rhythm, exposure to light and so on. Approximately, 70% of saliva is secreted in submandibular glands as mucus, 25% in parotid glands as serous, and the remaining 5% in sublingual and other minor glands. The normal saliva flow rates for adults between 18 to 70 years old is 0.25 -1 ml per minute. The amounts less than 0.1ml/min are considered mouth dryness.[2-5]

The salivation decrease caused by radiotherapy results in a change in saliva PH down to 5.5 and reduction of its buffering capability.[6] The mechanism of radiation damage to salivary glands is not fully understood yet. It seems that the inflammation created by the rays causes constriction of ducts, ductile cell death and their replacement by fibrin.[7-9] The salivation rate depends on the total dosage and dimensions of the irradiated field. The therapeutic dosage, in radiotherapy of head and neck, generally consists of 50 to 70 Gy for 5 to 7 weeks and daily doses of 1.8 to 2Gy. The changes will be irreversible when the dosage reaches 35-40 Gy[10] although some believe this value to be about 64 Gy for irreversible changes[11]. Some researchers have shown these effects of radiation. Mira et al. showed a decrease in saliva 24 hours after receiving doses up to 2.25Gy.[12] Bornstein et al. also proved mouth dryness as the most common complication of radiotherapy[13]; Baharudin et al. as well stated that salivary gland dysfunction is among the principal difficulties brought about by radiotherapy[14]; also Mc Milan et al. reached the same conclusion and found the relation between mouth dryness and the radiation dose significant.[15] Radiotherapy complications such as mucositis can sometimes stop the treatment for 4 to 5 weeks, and are so painful that make eating, drinking and brushing impossible for the patient.

The aim of this study was to evaluate the salivation flow rate objectively using Schirmer test; and mouth dryness and other consequences subjectively by distributing questionnaires to patients receiving head and neck radiotherapy.

Materials and Methods

This descriptive study was performed on 33 patients suffering from head and neck cancers who were treated in oncology and radiotherapy department of Imam Khomeini hospital, Tehran, Iran in 2009. Patients were asked to give their consent before registering their information and measuring the saliva flow rate. The patients' information registered in special forms included first name, surname, gender, age, history of systemic diseases, taking any medicine or addictive drug, and the type of cancer. The patients included in the study suffered from head and neck cancers, had not had received radiotherapy before, and had not had history of any disease affecting the salivary glands. Radiotherapy regimen which was scheduled for 6 weeks, consisted of daily exposure of 180-200cGy, five days per week. The saliva flow rate was measured four times: before treatment, two weeks and four weeks after treatment and at its completion, using Schirmer test paper [purchased from Chauvin pharmaceutical Ltd. (Ramford, Essex, UK)] in 5 minutes.

Figure1. The pack of Schirmer tear test

The Schirmer test that is usually used by ophthalmologists to measure the humidity of cornea contains a paper filter calibrated from 0 to 35 millimeters. It has a blue colored part that moves along with humidity to help read the wet number. Figure1 is a photograph of a typical Schirmer tear test used for measuring the saliva flow rate.

The patients should be sitting with their heads bend downward to eliminate the swallowing reflux. The saliva flow was measured in a quiet environment, with sufficient light, and in resting state. If the saliva is less than 7mm in 5min, it is a symptom of Xerostomia.[16]

Friedman test, Chi-square, dependent and independent t-test were applied to analyze the data. SPSS software was used in analytic processes. Mouth dryness and other complications as problem in speaking and swallowing, the subjective amount of saliva, dryness of lips, pharynx and tongue, and thirst were gathered using questionnaires.

Results

Among 33 subjects, 24 were males with average age of 62.8, and 9 were females with average of 53.7years. Table 1 shows the measured saliva flow rate in patients and their cancer sites and radiation doses.

Table1. Saliva flow rate in mm, total dosage of radiation in Gy and site of cancer

patient	Before treatment	2weeks after tr. †	4weeks after tr.	At the end	Radiation 1=uni ¥ 2=bilateral	Total dosage received	Site of cancer
1	30	12	0	0	2	70	Larynx
2	35	17	4	0	1	66	Left oral mucousa SCC
3	25	20	15	12	2	60	Jugular gullet
4	22	10	4	0	1	60	Parotid adenocarcinoma
5	10	7	0	0	2	60	Oropharynx
6	35	15	0	0	2	70	Nasopharynx
7	15	3	0	0	2	70	Lip,tongue,mandible,pharynx SCC
8	34	14	0	0	2	70	Nasopharynx
9	35	12	0	0	2	70	Nasopharynx
10	30	22	11	8	1	70	Left larynx
11	30	14	0	0	2	70	Nasophrynx
12	30	15	0	0	2	70	SCC tongue & mouth floor
13	25	15	0	0	2	60	2 sides of lips
14	35	20	6	0	2	70	Larynx& hypopharynx
15	32	17	9	6	2	60	Larynx bilateral
16	35	15	0	0	2	70	Nasopharynx
17	30	20	5	0	1	60	Right osteosarcoma
18	30	19	10	8	2	60	Neck
19	35	12	3	0	1	60	Jugular& mandible sarcoma
20	30	20	5	0	2	60	Mouth floor& neck
21	30	12	0	0	2	70	Tongue & mouth floor
22	35	12	0	0	2	70	Nasopharynx
23	30	20	10	7	1	60	Left tongue
24	30	10	3	0	1	70	Hypopharynx
25	30	16	5	0	1	66	Left oral mucousa
26	30	15	0	0	1	66	Tongue SCC with parotidectomy
27	30	14	6	0	1	70	Right parotid mass
28	35	15	0	0	2	70	Nasopharynx
29	35	19	10	8	1	50	Right parotid adenoma
30	35	22	12	9	2	60	Jugular adenocarsinoma
31	30	20	8	2	1	60	Left tongue
32	35	15	0	0	2	70	Nasopharynx
33	35	15	7	4	1	60	Lower lip

† tr: Treatment Yuni: unilateral

Friedman test was used to compare the average saliva rates before the treatment and at the completion of radiotherapy. The average before initiating the treatment until its completion reduced from 4 to 1.23 which indicates a decrease in salivation. The mean of saliva flow rate before treatment was 30.39±5.7mm that reduced to 1.93±0.35 until the end. The difference between four groups was significant (P value=0.000). The diagram of saliva flow rate during treatment demonstrates a descending path by time. Figure 2 shows mean of salivation at four measurement times. In order to investigate the total dosage and saliva flow rate at the end of the treatment, Pearson correlation coefficient test was used. Pearson correlation coefficient(r) equals -0.259 showing an indirect and incomplete relation between the two. That is an increase in the total dosage leads to a decrease in secreted saliva (P value=0.002), so there is a significant relation between the total received dosage and saliva flow rate. Figure 3 shows the relation between the saliva flow rate and total dosage.

The mean saliva decrease during the first two weeks was 15.57±5.6mm in bilateral radiation, and 14.50±4.5mm in unilateral one (P value=0.561). The mean of the saliva decrease after four weeks was 27.57±8.2mm in bilateral radiation, and 24.71±4.5mm in unilateral one (P value=0.251).

The mean of the saliva decrease in bilateral radiation was more than unilateral, yet due to small difference and because P value exceeds 0.05, it couldn't be considered statistically significant.

The mean of saliva decrease after four weeks in nasopharyngeal cancers (9 patients) was 31.55 mm for bilateral radiation, and 24.71mm for unilateral which was statistically significant (P value<0.05).

According to the questionnaires distributed among the patients in order to evaluate the subjective complications, it was declared that 84.8% of the patients suffered from dry mouth and lips, 87.8% from dry throat, and 81.8% from dry tongue. 20 patients had difficulty in speaking while 13 ones found easy; regarding the swallowing, the results were 28 versus 5, respectively. Table 2 contains the summary of other patients complications derived from questionnaires.

Table 2. Mouht dryness and other side effects derived from questionnaire

	Not too much	Very much
Mouth dryness	5	28
Throat dryness	4	29
Lip dryness	5	28
Tongue dryness	6	27
Thirst	22	11

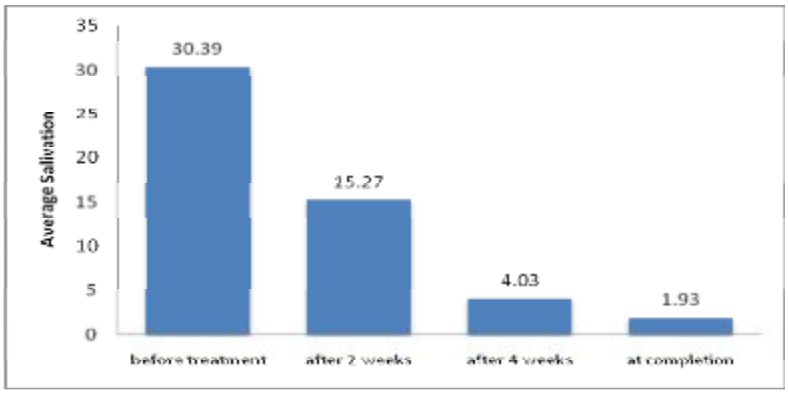

Figure 2.The mean of salivation in millimeters

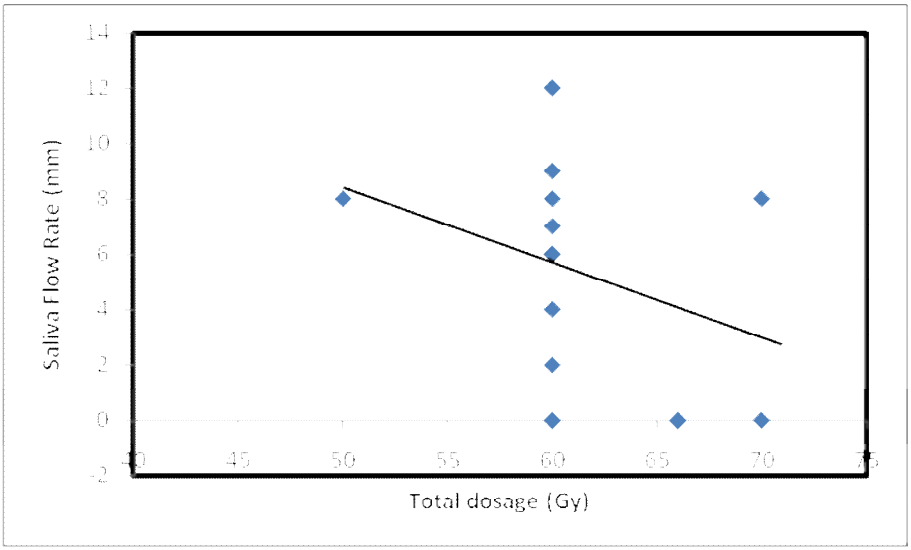

Figure 3. Saliva flow rate in mm and total dosage in Gy

Discussion

Head and neck cancers constitute about 4% of malignancies and are known as the second cause of mortality in developed countries. Approximately 90% of the cases appear after 45 years of age.[1] In this research the average age was 58.32 years.

In this study the saliva flow rate of 33 patients with head and neck cancers in Imam Khomeini hospital of Tehran were measured objectively through Schirmer test at the beginning of treatment, after two weeks, after four weeks, and at the completion of treatment. Dryness of mouth and other complication were investigated subjectively.

From these patients, 9 cases suffered from nasopharynx and oropharynx and larynx, 2 cases from neck cancers, and 17 from tongue, lip and other cancers.

The measured saliva flow during the first two weeks showed a 50% decrease which reached to 75% at the end of the fourth week. At the termination of treatment course, the measured saliva of 24 cases (comprising 75% of patients) reached to zero. In 28 persons (85% of patients) the measured saliva was less than or equal to 7mm. If the saliva rate measured by Schirmer test is less than 7mm, it is considered a symptom of mouth dryness; so one can consider xerostomia as one of the most common complications of radiotherapy. xerostomia has also been one of the most common complaints in the study of Duncun et al.[17]

McMillan et al. reported that the patients' most frequent complaint was mouth dryness and sticky saliva that had a significant correlation with dosage and field of radiation.[15] In the present study, there was a significant correlation, according to the cited statistics, between saliva decrease and the total dosage (P value=0.002).The increase in total dosage had resulted in a decrease in saliva flow rate. The mean of saliva decrease during the first two weeks of bilateral radiation was greater than unilateral; but it wasn't still a statistically significant (P value>0.05). The difference between the mean of saliva decrease after four weeks in bilateral radiation of nasopharynx and oropharynx cancers(on 9 patients) and unilateral cases was statistically significant (P value<0.05). This can be interpreted that in larynx and neck cancers, in spite of receiving bilateral radiation, the salivary glands were not situated in the radiated zone. At the other hand, in patients whose major salivary glands were in the radiation field and received bilateral radiotherapy (just like nasopharynx cancers), a much greater decrease was observed in comparison to the unilateral radiation. The fastest saliva decrease occurred in the first two weeks while the measured saliva flow rate after four weeks was equal to that of the completion time. Regarding the

total dose of approximately 65Gy and daily dose of 2Gy, the received dosage during the first two weeks was 20Gy. So the salivation shows a 50% decrease after receiving 20Gy. Vissink et al. showed that saliva decrease is meaningful in the first two weeks and there will be no noticeable change during the following 13 weeks after treatment.[18] The results obtained in this study were confirmed in another research conducted by Bonan et al.[19] where three groups were under investigation (pre-treatment, under treatment, treated) and it was declared that salivary flow rate had a remarkable decrease after receiving 20Gy.

According to the chart of mean saliva flow (Figure 2), although reduction of salivation keeps moving in a descending path, the "after-completion" group is, to a great extent, similar to the "after four weeks" group. In another study conducted by Henson et al. [20] it was demonstrated that salivation rate follows a linear and descending path until the completion of treatment; moreover, the received dosage and salivation have an inverse and incomplete correlation. This study showed that in cases where the major glands (parotid in particular) were in the radiated region, saliva flow rate decreased faster than other cases. This was more noticeable in nasopharynx cancers. In these cases saliva reduced by 60% during the first two weeks and reached to zero until the fourth week. According to the bilateral radiation and the great mass of radiated salivary glands, it can be concluded that position of radiation has a significant effect on the amount of saliva and dysfunctions of salivary glands. In Baharudin et al. ,in their study on radiotherapy patients, it was concluded that the amount of saliva (either in rest position or after stimulation) decreases after treatment.[14] Jbam et al. also stated that field of radiation has a significant role in the dysfunction of salivary glands.[21] Jbam et al. showed that saliva reduces down by 93% when the major salivary glands are in the radiated zone. Mouth dryness is more severe in bilateral radiations. However, if the radiation, as in larynx and thyroid cancers, does not include some parts of salivary glands, a less severe dryness will occur.[21]

The subjective feeling of mouth dryness (xerostomia) is not constantly in concordance with the objectively measured amount of saliva. In many cases the measured saliva was less than 0.1ml per minute which was compatible with dry mouth; but the patient did not have such a feeling.[20]

In the present research, the objectively measured xerostomia (85%) was in concordance with the patients' subjective feeling (84.4%).

Nowadays, treatment planning for tumors are done with the most possible preservation of sensitive tissues, considering aesthetic affaires, and minimizing the secondary complications and other factors that overshadow the patients' morale and quality of life.

Conclusion

During radiotherapy, saliva flow rate depends on the total dosage and the radiation site. With the major salivary glands (particularly parotid) being included in the radiation field, increasing the total dosage and radiation field diameter, the greater decrease of salivation will result. Cooperation between the physician and dentist is a prerequisite to raise the standards of patients' lives and preventing complica-tions caused by radiotherapy.

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