

## Evaluation of salivary flow in patients during head and neck radiotherapy

### *Análise do fluxo salivar em pacientes durante a radioterapia em cabeça e pescoço*

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**ABSTRACT:** Radiotherapy is frequently employed for the treatment of head and neck squamous cell carcinoma. Among the side effects, xerostomia is one of the most important. With the objective of evaluating the role of radiotherapy in salivary flow, we performed three salivary sample collections: at the beginning of, during, and immediately after radiotherapy. The results showed that the salivary flow values of the first collection were very similar to those of the control group. However, during treatment, there was a significant decrease of the salivary flow ( $p = 0.0008$ ), which continued low immediately after radiotherapy ( $p = 0.0009$ ). Our study showed that radiotherapy leads to an important reduction of salivary flow during and after radiotherapy.

**DESCRIPTORS:** Radiotherapy; Xerostomia; Squamous cell carcinoma.

**RESUMO:** A radioterapia é um tratamento comumente empregado em pacientes portadores de carcinomas espinocelulares em cabeça e pescoço. Entre os efeitos colaterais locais, a xerostomia é um dos mais importantes. Com o objetivo de avaliar o efeito da radioterapia sobre o fluxo salivar, foram feitas 3 coletas salivares: no início, em um período intermediário e posteriormente ao tratamento radioterápico. Os resultados obtidos demonstraram médias de fluxo salivar semelhantes entre a coleta inicial e o grupo controle. Com o decorrer da radioterapia, houve diminuição significativa do fluxo salivar na coleta intermediária ( $p = 0,0008$ ), que se manteve após o término da radioterapia ( $p = 0,0009$ ). Nosso estudo enfatiza que há redução significativa do fluxo salivar durante e após a radioterapia.

**DESCRIPTORIOS:** Radioterapia; Xerostomia; Carcinoma espinocelular.

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## INTRODUCTION

The most important therapies for treatment of head and neck squamous cell carcinomas (HNSCC) are surgery and radiotherapy. Chemotherapy is restricted for HNSCC, and is generally employed in advanced tumors<sup>2</sup>.

Although radiotherapy is effective to control HNSCC, side effects are undesirable and may aggravate the patient's health status<sup>19</sup>. Alterations found in irradiated sites occur mainly in skin, mucosa, bones, salivary glands and teeth<sup>10,11,18</sup>. As a consequence, different grades of dermatitis and mucositis, bone and teeth alterations are observed. In salivary glands, atrophy and acinar degeneration caused by radiotherapy commonly result in a decreased saliva production, which is a frequent complaint of head and neck irradiated patients<sup>6,9</sup>.

The severity of reduced salivary flow ranges from a little dryness complaint on a relatively normal mucosa to the total absence of saliva with severe mucosa burns<sup>6</sup>. With the reduction of salivary flow, which is observed at the beginning of treatment, other alterations may occur including an increase of salivary viscosity, pH, ions and immunoglobulins levels<sup>13</sup>. As a consequence, irradiated patients often present higher risk for the development of dental caries and difficulties to swallow, speak and eat<sup>1,4,7,12,17</sup>.

Although compensatory salivary production by non-affected salivary glands may exist, permanent salivary flow reduction is frequently found even one year after the end of the radiotherapeutic treatment. Reduction of salivary flow is strongly associated with the involvement of the parotid glands in the radiation field. The total dose is also

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important, and the greater harm is produced when doses reach over 44 grays (Gy)<sup>14</sup>.

The aim of this study was to evaluate salivary flow alterations during head and neck radiotherapy applied to patients with squamous cell carcinoma and to compare them with the values obtained for the control group.

## MATERIAL AND METHODS

This study included 47 patients divided in two groups. The research methodology was approved by the Ethical Research Committee, School of Dentistry of Piracicaba:

a) group I - (study group) - 22 patients attended at the Oral Diagnosis Clinic (OROCENTRO), School of Dentistry of Piracicaba, and at the

Radiotherapeutic Service, Sugar Cane Suppliers Hospital, Piracicaba, Brazil. The age of these patients ranged from 34 to 83 years, with an average of 58.5 years. There were 18 males (82%) and four females (18%). The majority of the patients (90.9%) were white, and 9.1% were black. These patients presented squamous cell carcinomas and were submitted to head and neck radiotherapeutic treatment, alone or combined with surgery. Three non-stimulated salivary collections were performed for 5 minutes each: at the beginning of, during, and at the end of radiotherapy (Table 1).

b) group II - (control group) - 25 healthful patients. Of these patients, 20 (80%) were males and 5 (20%) were females. The average age was 59.24 years, ranging from 42 to 78 years. The control

**TABLE 1** - Distribution of patients (group I) according to age, gender, skin color, tumor site, clinical stage and radiotherapeutic total dose (RTD).

Patients	Age	Gender	Skin Color	Tumor site	Clinical stage	RTD (Gy)
1	58	M	B	Floor of the mouth	IV	81
2	61	M	W	Floor of the mouth	III	71
3	75	M	W	Tongue	III	70
4	58	M	W	Alveolar ridge	IV	82.6
5	74	M	W	Tongue	IV	70
6	83	M	W	Floor of the mouth	III	72
7	58	M	W	Tongue	III	71
8	62	M	W	Pyriiform sinus	IV	71
9	49	M	W	Cervical metastasis (unknown primary)	IV	60
10	52	M	W	Tongue	II	70
11	47	M	W	Pyriiform sinus	IV	80
12	56	F	W	Tonsil	IV	57
13	46	M	W	Tongue	IV	68.4
14	34	F	W	Retromolar	IV	58.8
15	46	M	W	Pyriiform sinus	III	70.4
16	64	M	W	Oropharynx	IV	70
17	69	M	W	Buccal mucosa	IV	68.4
18	63	F	B	Buccal mucosa	IV	70
19	53	F	W	Floor of the mouth	II	72.2
20	64	M	W	Oropharynx	IV	71
21	59	M	W	Hypopharynx	IV	60.4
22	54	M	W	Larynx	III	68

M - male, F - female, B - black, W - white, Gy - grays.

group was matched by age, skin color and gender. None of the patients had undergone radiotherapy or presented medication-related xerostomia. In the control group, only one salivary collection was performed (Table 2).

For the saliva collection, all patients were instructed to swallow the saliva present in their mouths, and after this step they were asked to put the total saliva produced in glass recipients. The saliva collected was identified and weighed. If patients were wearers of complete dentures or remov-

able partial dentures, they were informed to remove their prostheses during the collection.

The weight of each collection was measured and adjusted to flow in ml/min for each patient. To classify the salivary flows, values below 0.1 ml/min were indicative of xerostomia<sup>16</sup>. Two-tailed tests were used for evaluation of the salivary flow.

## RESULTS

The regions more affected by the squamous cell carcinomas were floor of the mouth (18.2%), buccal mucosa (9%) and pyriform sinus (13.6%). The more frequent clinical stages were stage IV (63.5%) and stage III (27.3%). The average dose of radiation used for the tumors was of 69.69 Gy. Radiotherapeutic fields involved the parotid glands in all patients, and total doses were higher than the minimum values for permanent xerostomia (Table 1).

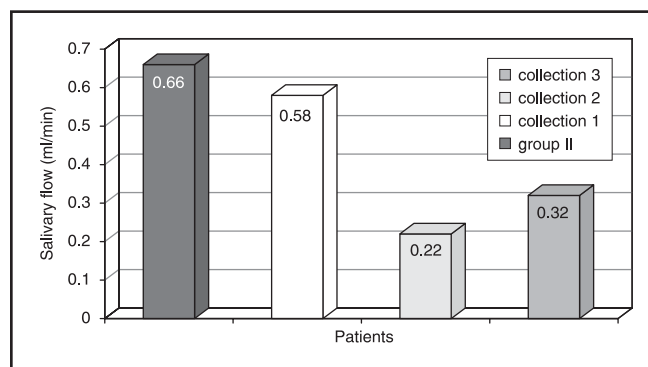
Regarding the salivary flow in the control group, the average was 0.6618 ml/min (Table 2). In irradiated patients, the average in the first collection was 0.5827 ml/min, being similar to that of the control group, with no statistical difference ( $p = 0.5366$ ). However, these patients presented a significant decrease between the initial collection and collection 2 ( $p = 0.0008$ ). In addition, this reduction persisted in collection 3. Statistical analysis did not show differences between collection 2 and 3 ( $p = 0.9822$ ). The data about the distribution of salivary flows (group I) are shown in Graph 1 and Table 3.

## DISCUSSION

The reduction of salivary flow is an important side effect of head and neck radiotherapy, causing difficulties to chew, swallow, speak and eat<sup>5,10,11</sup>. It

**TABLE 2** - Distribution of patients (group II) according to age, gender and salivary flow (ml/min).

Patients	Age	Gender	Salivary collection (ml/min)
1	69	M	1.9204
2	73	M	0.325
3	52	M	1.1072
4	42	M	0.643
5	45	M	0.397
6	68	M	0.5065
7	65	M	0.5662
8	66	M	0.4738
9	75	M	0.4752
10	78	M	0.4296
11	73	M	1.402
12	48	M	0.9786
13	47	M	0.1646
14	67	M	0.066
15	62	M	0.213
16	64	M	0.8546
17	43	M	1.66
18	46	M	0.108
19	61	F	0.5222
20	62	M	1.2612
21	74	F	0.278
22	56	M	0.5004
23	49	F	0.74432
24	42	F	0.4626
25	54	F	0.5366
Average	59.24	-	0.6618



**GRAPH 1** - Salivary flow averages (ml/min) in group I (three collections) and group II (control).

**TABLE 3** - Distribution of patients (group I) according to salivary collections (ml/min).

Patient	Collection 1	Collection 2	Collection 3
1	0.958	0.5908	0.3226
2	0.6508	0.4914	0.4024
3	0.6116	0.0956	0.0936
4	0.2434	0.201	0.1766
5	0.87	0.2848	0.5354
6	0.2676	0.2864	0.4412
7	0.3164	0.0586	0.089
8	1.329	0.1396	0.2164
9	0.8172	0.188	0.0566
10	0.6742	0.2716	0.1335
11	0.2422	0.3218	0.2692
12	0.0924	0.2272	0.0018
13	1.6884	0.1348	0.1986
14	0.2322	0.0158	0.749
15	1.1346	0.1868	0.2796
16	0.1736	0.3248	0.0616
17	0.3449	0.304	0.27
18	0.3756	0.0394	0.0694
19	0.2374	0.0232	0.1044
20	0.3528	0.22316	0.1826
21	0.6632	0.391	0.0988
22	0.544	0.2564	0.2796
Average	0.582705	0.229825	0.32260

also results in alterations in the oral microbiota as well as in an increase of the risk for the development of dental caries<sup>2,9,10,12</sup>. Patients submitted to radiotherapy present reduction of salivary flow in the first weeks of treatment. In many cases, this reduction becomes irreversible<sup>15</sup>. The sensation of mouth dryness called xerostomia is normally asso-

ciated with salivary flow. Normally, the level of salivary flow considered to be xerostomic in non-stimulated saliva is below 0.1 ml/min. In our study, 5 out of 22 evaluated patients (22.5%) were classified as xerostomic in collection 2 (during radiotherapy), and 7 patients (32%) were thus classified in collection 3 (end of radiotherapy).

In the first collection, patients from group I (irradiated) presented average salivary flows similar to those of patients from group II (control). Regarding the second collection of saliva, a significant reduction of saliva was observed. This reduction is in agreement with the fact that radiation applied to the head and neck promotes a decrease of saliva with doses of 20 Gy. It occurs particularly when parotid glands are included in the radiotherapeutic fields<sup>14,15</sup>. However, in our cases, salivary flow did not reach xerostomic levels, which could indicate that, in these cases, xerostomia is more a symptomatic phenomenon, or that the complaints of dry mouth and saliva viscosity are more relevant than the actual quantitative reduction of salivary flows.

In the third collection (end of treatment), salivary flows were low and similar to those of the second collection (during treatment). Some studies have also demonstrated that the salivary flow reduction is more significant in the first two weeks of radiotherapy, without important changes in the 13 following weeks<sup>3</sup>. However, others showed that there is a linear reduction of non-stimulated saliva<sup>8</sup>.

## CONCLUSION

To summarize, our study showed that radiotherapy leads to an important reduction of salivary flow during and after treatment.

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