

Salivary Flow Analysis of Head and Neck Irradiated Patients

Análise do Fluxo Salivar de Pacientes Irrradiados em Cabeça e Pescoço

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Abstract

This study aimed to analyze the salivary flow of irradiated patients for the head and neck cancer treatment after the conclusion of their treatment, and to compare it to the salivary flow of a group of non-irradiated patients. The salivary flow measurement was performed using the stimulated saliva analysis technique by masticatory action. The data collected were organized in planning using the Microsoft Excel program and then analyzed through the program IBM SPSS 20.0. The independent T-test was used to compare the median values between the groups that had normal distribution. 54 patients were evaluated, 18 from Group 1, of irradiated patients with an average time of ending radiotherapy of 11 months; and 36 patients from Group 2, with non-cancerous and non-irradiated patients. The mean salivary flow of Group 1 patients was 0.39 (± 0.85) and 100% of the patients expelled less than 3.5mL of saliva after stimulation for five minutes. Among the patients from Group 2, the mean salivary flow was 3.22 (± 2.65), and 77.78% of the patients had a salivary stimulation of less than 3.5 mL. This difference was statistically significant ($p = 0.004$). Through the methodology used, a high prevalence of hyposalivation was observed in patients irradiated in head and neck for cancer treatment even after months of the treatment conclusion and among patients without cancer and not submitted to radiotherapy. However, a deficiency in saliva production was statistically higher among patients irradiated in the head and neck.

Keywords: Neoplasms. Radiotherapy. Saliva. Xerostomia.

Resumo

Este estudo teve como objetivo analisar o fluxo salivar de pacientes irradiados no tratamento do câncer de cabeça e pescoço após a conclusão de seu tratamento, e compará-lo com o fluxo salivar de um grupo de pacientes não irradiados. A medição do fluxo salivar foi realizada utilizando a técnica de análise de saliva estimulada por ação mastigatória. Os dados coletados foram organizados no planejamento utilizando o programa Microsoft Excel e, em seguida, analisados através do programa IBM SPSS 20.0. O teste T independente foi utilizado para comparar os valores medianos entre os grupos que apresentaram distribuição normal. Foram avaliados 54 pacientes, 18 do Grupo 1, de pacientes irradiados com tempo médio de término da radioterapia de 11 meses; e 36 pacientes do Grupo 2, com pacientes não cancerosos e não irradiados. O fluxo salivar médio dos pacientes do Grupo 1 foi de 0,39 ($\pm 0,85$) e 100% dos pacientes expeliram menos de 3,5 mL de saliva após estimulação por cinco minutos. Entre os pacientes do Grupo 2, o fluxo salivar médio foi de 3,22 ($\pm 2,65$), e 77,78% dos pacientes apresentaram estimulação salivar inferior a 3,5 mL. Essa diferença foi estatisticamente significativa ($p = 0,004$). Por meio da metodologia utilizada, observou-se alta prevalência de hipossalivação em pacientes irradiados na cabeça e pescoço para tratamento de câncer mesmo após meses da conclusão do tratamento e entre pacientes sem câncer e não submetidos à radioterapia. No entanto, a deficiência na produção de saliva foi estatisticamente maior entre os pacientes irradiados na cabeça e pescoço.

Palavras-chave: Neoplasias. Radioterapia. Saliva. Xerostomia.

1 Introduction

Saliva has multiple functions, such as the food substances solubilization; it contributes to taste perception; the oral mucosa lubrication; facilitation of chewing, swallowing and phonation; acids neutralization; protection, coverage and defense of the oral mucosa against microorganisms¹.

However, some individuals may present changes in the quantity and quality of saliva produced, known as hyposalivation. This may affect the composition, buffer capacity and electrolytes concentration in saliva; the salivary microbiota composition and immunoprotein deficiency².

One of the causes of hyposalivation is the radiotherapy treatment of head and neck cancer, especially in patients whose

irradiation field includes the parotids and submandibular major salivary glands³.

The modification in salivation caused by irradiation is permanent. The normal secretory function of the salivary glands is not restored even after a long period of follow-up⁴.

Thus, the objective of this study was to analyze the salivary flow of a group of irradiated patients for treatment of head and neck cancer months after the conclusion of their treatment, and to compare the salivary flow of a group of non-irradiated patients.

2 Material and Methods

This study is characterized as transversal with control

group and included patients submitted to radiotherapy for cancer treatment in the head and neck region at Mato Grosso Cancer Hospital (HCMT), in Cuiabá, MT, Brazil.

The criteria for inclusion of irradiated patients (Group 1) in the study were being older than 18 years; having already completed radiotherapy; the irradiated field should comprise the larger salivary glands and the total irradiation dose should be greater than 40 Gys.

Information related to age, sex, tumor location and total radiation dose were obtained from the patients' records.

For comparison purposes, a group of patients with similar socioeconomic profile was selected, but without cancer and not submitted to radiotherapy (Group 2) in the proportion of two to one. Patients were selected in the Dental Clinic of University of Cuiabá (UNIC) and in a center for the elderly in the same municipality. Exclusion criteria in this population were the continued use of medications and/or presence of systemic alterations that could interfere with salivation.

Measurement of salivary flow was performed by the analysis of saliva stimulated by masticatory action⁵ in which each patient chewed a paraffin wax slide for five minutes and continuously expelled the saliva in a disposable container. At the end of time, the foam was discarded and the contents measured with a graduated syringe.

The data collected were organized into spreadsheets using the Microsoft Excel program and then analyzed through the IBM SPSS 20.0 program. The independent T-test was used to compare the mean values between the groups whose distribution were normal. The level of significance (p-value) for all the analyzes was defined as $p < 0.05^6$.

All the patients were previously informed about the research characteristics and signed an informed consent form. The research project was approved by the Research Ethics Committee of UNIC under the protocol # 1.216.207 .

3 Results and Discussion

A total of 54 patients, 18 from Group 1 of irradiated patients and 36 from Group 2 of non-irradiated patients were evaluated. Among the patients in Group 1, 13 (72.22%) were male; while in Group 2, 24 (66.67%) were female. The mean age of Group 1 patients was 63.39 (± 11.78) and Group 2 patients 71.50 (± 7.85). The mean irradiation dose of Group 1 patients was 69.78 Gy (± 2.04). The average time elapsed from the end of radiotherapy among the Group 1 patients was 11 months.

The mean salivary flow of the irradiated patients was 0.39 (± 0.85) and 100% of these patients expelled less than 3.5mL of saliva after stimulation for five minutes. Among the patients in the control group, the mean salivary flow was 3.22 (± 2.65), and 77.78% of the patients had stimulated salivary flow below 3.5 mL. This difference was statistically significant ($p = 0.004$).

The possible correlation between the patient's age and the

salivary flow was also analyzed, but no correlation was found ($p = 0.220$).

Table 1 - Patients distribution by group according to sex, age, irradiation dose, time elapsed from the end of radiotherapy and salivary flow

Variables	Group 1	Group 2
Sex Male	13 (72.2%)	24 (66.7%)
Sex Female	5 (27.8%)	12 (33.3%)
Age (mean)	63.39 (± 11.78)	71.50 (± 7.85)
Irradiation dose (mean)	69.78 (± 2.04)	-
Time elapsed from the end of radiotherapy (mean in months)	11	-
Salivary flow (mean in mL)	0.39 (± 0.85)	3.22 (± 2.65)

Source: Research data.

Table 2 - Comparison of stimulated salivary flow among patients in Groups 1 and 2

Groups	Salivary Flow	Standard Deviation	P
Group 1	0.39	0.85	0.004
Group 2	3.22	2.65	

Source: Research data.

Head and neck cancer includes a variety of malignant tumors with different characteristics. However, in about 95% of cases, the primary histological type observed is epidermoid carcinoma⁷.

Radiotherapy is adopted as the primary treatment in the early disease stages. However, in more advanced cases, radiotherapy is usually combined with chemotherapy, surgery, or both⁷.

The adverse radiotherapy effects in the oral cavity have a great impact on the patients' quality of life. These complications include viscous saliva, salivary gland dysfunction, mucositis, soft tissue necrosis, periodontal diseases, tasting disorders, decreased taste sensation, oral discomfort or mandibular pain, dental caries, mucosal pigmentation, Mouth opening limitation, viral and fungal infections and osteoradionecrosis. However, xerostomia and hyposalivation are the most frequent complications among these patients (between 73.5% and 96.4% of cases)⁸⁻⁹. In this study, 100% of the irradiated patients had hyposalivation and did not reach 3.5 mL after stimulation for five minutes.

Under normal conditions, spontaneous saliva secretion ranges from 0.25-0.35 mL/min, but may be increased by external stimulation, e.g. by chewing paraffin blocks, ranging between 1.0-3.0 mL/min. Values below 0.7 mL/min after masticatory stimulation are considered deficient, signaling the occurrence of hyposalivation in the individual¹⁰.

The salivary flow reduction also includes changes in its composition, buffer capacity, electrolyte concentration, flora composition and immunoprotein deficiency², not evaluated in this study.

In this study, the salivary flow of patients irradiated in the head and neck was significantly different from the non-

irradiated patients, even several months after the end of the treatment. The deficiency in the saliva production in irradiated patients occurs due to the parenchyma injury of the larger salivary glands, leading to fibrosis and secretory hypofunction³. The salivary glands hypofunction was not reestablished after the radiotherapeutic treatment conclusion, remaining in a chronic form⁴. Salivary acini are highly radiosensitive, in a way that radiotherapy can culminate in apoptosis, necrosis, impaired signaling between cell and receptor, inflammation, edema and vascular changes. Radiotherapy interferes with the signaling process of afferent and efferent fibers in the autonomic nervous system, which participate in the saliva production, affecting the salivary production¹¹. Thus, patients tend to present discomfort and difficulty performing basic functions (taste, chewing, swallowing, difficulty with speech)⁴.

This evidences the need to develop strategies to protect the larger salivary glands when they are within the field of cancer irradiation, without prejudice to the patient's treatment. In this sense, some alternatives have gained prominence and clinical interest. Among them, the surgical transposition of the major salivary glands, as well as the use of cytoprotective agents, acupuncture, and low-intensity laser therapy are noteworthy⁷.

This study also found a high prevalence of hyposalivation among non-irradiated patients. This is believed to have occurred because of their advanced age. It is known that age is also a factor that may contribute to the salivary flow reduction¹². In the elderly population xerostomia is a side effect that becomes more evident due to the medications intake for chronic diseases. With aging, there is also a degeneration process in the salivary glands that causes a decrease in viscosity and the amount of secreted saliva¹³.

Salivary flow reduction is also related to patients with systemic diseases, such as Sjögren's Syndrome, diabetes mellitus, rheumatoid arthritis and systemic lupus erythematosus or even the continuous use of systemic medicines, quite frequent in people of this age group¹². However, these were the sample exclusion criteria and did not interfere in the Group 2 patients' salivary flow.

Thus, it is suggested that patients irradiated in the head and neck, even after months of completion of their treatment, and elderly patients adopt measures that reduce the hyposalivation effects by lubricating the oral tissues through continuous wetting with water and commercial solutions, or using systemic action medications such as pilocarpine that acts stimulating the salivary glands³.

4 Conclusion

Through the methodology used, a high hyposalivation prevalence was observed in patients irradiated in the head and neck for cancer treatment even after several months of treatment completion and also among the elderly people. Thus, strategies must be formulated to reduce the adverse hyposalivation effects in these two specific groups of patients.

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