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Impact of radiotherapy to the head and neck region on the oral condition

Impacto da radioterapia de cabeça e pescoço sobre a condição oral

Impacto de la radioterapia en la región de la cabeza y el cuello en la condición bucal

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Abstract

Investigations of the oral function of patients undergoing radiotherapy (RT) to the head and neck region are relevant for the overall quality of life. Considering the possible impact of the side-effects on nutrition, the recovery of these patients might be impaired. This study aimed at

investigating the oral condition of patients submitted to RT to the head and neck region. A single-center, cross-sectional mixed analysis assessing the oral conditions of patients before RT (group 1) and after 12-months of RT (group 2) was performed. Following inclusion and exclusion criteria consideration, fifty (n=25) patients were included in this study. A calibrated examiner conducted the oral examination, the following variables were assessed: a) DMF index: decayed, missing and filled teeth; b) xerostomia and dysgeusia, subjective assessment of salivary function and taste; c) simplified oral hygiene index – OHI-S, with plaque disclosing solution; d) unstimulated sialometry, assessment of salivary function. Statistical analysis compared the groups considering a significance level of 5%. The group evaluated after 12 months of RT showed high rate of dry mouth (92%) and dysgeusia complaint (72%) while no patient reported in group 1. Statistically significant difference was observed in the comparison of group 1 and 2 regarding DMF index (> 64%), OHI-S index (>38%), and unstimulated sialometry (<70%). Patients submitted to RT to the head and neck region for the treatment of cancer experience oral complications even at 12 months after the last session of RT.

Keywords: Radiotherapy; Oral Health; Head and Neck Neoplasm.

Resumo

Estudos sobre a condição oral de pacientes submetidos a radioterapia (RT) de cabeça e pescoço são relevantes na avaliação da qualidade de vida desses pacientes. Considerando o possível impacto dos efeitos adversos sobre a nutrição, a recuperação desses pacientes também pode ser comprometida. Este estudo teve como objetivo investigar a condição oral de pacientes submetidos a radioterapia de cabeça e pescoço. Uma análise transversal de paciente antes e após 12 meses da conclusão da RT foi realizada. Após consideração de critérios de inclusão e exclusão, 50 (n=25) pacientes foram incluídos no estudo. Um examinador calibrado conduziu o exame clínico oral e anamnese, as seguintes variáveis foram abordadas: a) CPOD, índice de dentes cariados perdidos e obturados; b) xerostomia e disgeusia, análise subjetiva da função salivar e paladar; c) IHOS- índice de higiene oral simplificado com evidenciador de placa bacteriana; d) sialometria não estimulada. A análise estatística para detectar diferença entre os grupos considerou um nível de significância de 5%. O grupo avaliado após 12 meses da RT apresentou alta taxa de queixa de xerostomia (92%) e disgeusia (72%), enquanto não houve relato de queixas no grupo 1. Diferenças estatísticas significantes foram observadas na comparação grupo 1 e 2 em relação ao índice CPOD (> 64%), IHO-S (>38%), e sialometria não estimulada. Pacientes submetidos a RT de cabeça e pescoço para o

tratamento de câncer apresentam complicações orais mesmo após 12 meses da última sessão de RT.

Palavras-chave: Radioterapia; Saúde bucal; Neoplasia de Cabeça e Pescoço.

Resumen

Estudios sobre la condición oral de pacientes sometidos a radioterapia (RT) de cabeza y cuello son relevantes en la análisis de la calidad de vida de ese tipo de pacientes, considerando el posible impacto de los efectos adversos sobre la nutrición, la recuperación de esos pacientes puede ser comprometida. El objetivo de este estudio fue investigar la condición oral de pacientes sometidos a RT de cabeza y cuello. Un análisis transversal de pacientes antes y después de 12 meses de la conclusión de RT fue realizada. Después de considerar los criterios de inclusión y exclusión, 50 (n=25) pacientes fueron incluidos en el estudio. Un examinador calibrado realizó el examen clínico oral y anamnesis, las siguientes variables fueron abordadas: a. CPOD, índice de dientes cariados perdidos y obturados; b. xerostomía y disgeusa, análisis subjetivo de la función salivar y sabor; c. IHOS – índice de higiene oral simplificado con evidenciador de placa bacteriana; d. sialometria no estimulada. El análisis estadístico para detectar diferencia entre los grupos consideró un nivel de significancia de 5%. El grupo analizado después de 12 meses de RT presentó una alta tasa de xerostomía (92%) e disgeusa (72%). El grupo 1 no presento ningún tipo de queja. Diferencias estadísticas significantes fueron encontradas en la comparación del grupo 1 y 2 en relación al CPOD (> 64%), IHO-S (>38%), y sialometria no estimulada. Pacientes sometidos a RT de cabeza y cuello para el tratamiento de cáncer presentan complicaciones orales mismo después de 12 meses de la última sesión de RT.

Palabras clave: Radioterapia; Salud Bucal; Neoplasias de Cabeza y Cuello.

1. Introduction

Malignant neoplasms of the lip and oral cavity is considered the fourth most common site and the sixth cause of cancer deaths in middle- and low-income countries (Ferlay, 2018). The 2018 worldwide estimation of deaths and new cases regarding the oral region were 177,384 and 354,864, respectively (Ferlay, 2018; Aamod, 2020). Although these sites attract more attention to potential oral complications, pharynx and larynx are also highly prevalent and associated with these concerns (PDQ Screening and Prevention Editorial Board, 2020),

this last is responsible for 8,000 new annual registrations and 3,000 deaths in Brazil (Victor, 2012).

Currently, primary treatment of oral cancer is surgical resection, which is frequently complemented by radiotherapy (RT). Chemotherapy, most often using cytotoxic, platin-based agents is also used in more advanced cases or in the treatment of recurrences (Rajesh, 2017). RT to the head and neck region involves high doses fractionated daily or weekly over 2-3 months (Pfister, 2015). Negative impacts on oral functions are related to the nature of the treatment of these cancers, not only to the mutilation aspect of resective surgeries, but also to the morbidity associated with localized radiation therapy (Rajesh, 2017), including dysphagia (Jacqui, 2020), gustatory disorder (José, 2019), oral mucositis (Karthika, 2015; Pierfrancesco, 2017), xerostomia (Punita, 2018; Kaae, 2019), osteoradionecrosis (Buglione, 2016), increased risk of dental caries (Janaine, 2014), and opportunistic fungal infections (Corvò, 2008; Spencer, 2004).

These complications are well-stablished as side-effects of RT in the oral cavity, some of them reverberate over 6 months from the start of RT (Rajesh, 2017). Investigations of the oral function of patients undergoing RT to the head and neck region are relevant for the overall quality of life and, considering the possible impact of these side-effects on nutrition, also for the recovery of these patients. This study aimed at investigating patients' oral condition before and after RT to the head and neck region.

2. Methodology

Study design and population

This is a single-center, cross-sectional mixed analysis assessing the oral conditions of head and neck cancer patients before and after radiotherapy to the head and neck region. The institutional review board at Lauro Wanderley University Hospital at the Federal University of Paraíba (Brazil) approved the study protocol and an informed consent was obtained from all volunteers (CAAE nº 55164516.5.0000.5188).

Patients scheduled for the treatment of cancer through radiotherapy to the head and neck region and patients who underwent the mentioned treatment 12 months before screening, at Napoleão Laureano Hospital, João Pessoa, Brazil, were eligible to participate in the study. This is a public hospital dedicated only to the treatment of cancer. Patients were invited to

participate in the study, as they appear for treatment at the hospital. If the patient volunteered to take part in the study, exclusion criteria were assessed. Exclusion criteria included the following: (1) patients with any type of syndrome; (2) patients with physical, sensory, behavioral, cognitive, or even emotional disability; (3) patients with less than 20 remaining teeth; (4) patients under 40 or over 70 years of age.

Data collection

Fifty participants were included in this study, this sample was divided in Group 1 (n = 25), patients who have not yet started RT treatment; Group 2 (n = 25), patients who had already completed RT treatment within 12 months after the last session. Patient were considered included in group 2 if radiotherapy conducted reached the dose of 70Gy. Data was collected during the period of June 2018 and April 2019 in a convenience sample.

Anamnesis and clinical oral examination were performed at the dental clinic of the faculty of dentistry in the same institution mentioned previously, both in the same day. All patients were examined during the same period of the day, middle morning. Only one examiner conducted the whole assessment, the following criteria were used: a) DMF index: decayed, missing and filled teeth, proposed by the World Health Organization (WHO); b) for xerostomia and dysgeusia, subjective assessment of salivary function and taste c) for the simplified oral hygiene index – OHI-S, the eviplac plaque disclosing solution (Biodynamics, Ibiporã, Paraná, Brazil) was used. d) unstimulated sialometry, assessment of salivary function. Baseline features, medical history, tumor characteristics and stage were assessed in the same opportunity. Examiner was calibrated and reliability was tested previous to patients assessment (κ = 0.87) (Landis, 1977). Distortion of the sense of taste and dry mouth perception were considered as present or absent, other variables were recorded as continuous data.

Statistical Analysis

Baseline descriptive data (categorical and continuous) were presented in terms of absolute values, percentages, mean, and standard deviations (sd). Baseline differences were examined using unpaired t test (independent means) for continuous data, chi-squared and Fisher's exact-test for qualitative data. Groups differences regarding oral complications were tested by unpaired t test (independent means) and Fisher's exact-test. P values less than 0.05

were considered as statistically significant. GraphPad Prism 6.0 software was used for analysis of data.

3. Results

Social-demographic data were collected for all subjects at baseline and were presented on Table 1. Seven variables were studied across the two investigated groups – age, age groups, sex, education, marital status, employment status, and harmful habits, no significant difference in distribution of any of the variables between the groups was found. There was neither significant difference in distribution of any of the social-demographic variables between the two groups nor even in tumor characteristics and stage (all $p < 0.01$) (Table 2).

Table 1: Comparison of baseline features between two groups (n=50).

Features		Group 1	Group 2	p values
Age[#] (years; mean ± sd)		57.28 ± 4.84	56.8 ± 4.99	.7342
Age groups; n (%)[*]				.4732
	40-49	1(4)	2(8)	
	50-59	19(76)	15(60)	
	60-69	5(20)	8(32)	
Sex[*]				.7416
	Male	18 (72)	20 (80)	
	Female	7 (28)	5 (20)	
Education[*]				.7019
	Primary School	22(88)	20(80)	
	Secondary School	3(12)	5(20)	
Marital status[*]				.8865
	Single	1(4)	1(4)	
	Married	15(60)	13(52)	
	Divorced	3(12)	5(20)	
	Widowed	6(32)	6(24)	
Employment status[*]				.8174
	Retired	15(60)	12(48)	
	Unemployed	1(4)	1(4)	
	Self-employed	6(24)	9(36)	
	Service	3(12)	3(12)	
Harmful habits[*]				.9850
	Smoking	23(92)	15(60)	
	Drinking	15(60)	10(40)	
	Smoking and drinking	14(56)	10(40)	

[*]Chi-squared/Fisher's exact-test. [#] Independent *t* test; $P < 0.05$ considered as statistically significant.
Source: Authors.

Table 2: Tumor characteristics and stage (n=50).

Features		Group 1	Group 2	p values
Type n (%)				
	Squamous cell carcinoma	25 (100)	25 (100)	
Primary Site				.3805
	Oral cavity	7(28)	11(44)	
	Pharynx	12(48)	11(44)	
	Larynx	6(24)	3(12)	
Tumor Stage				.9094
	I	1 (4)	2 (8)	
	II	2 (8)	2 (8)	
	III	7(28)	8(32)	
	IV	15(60)	13(52)	
Surgery done				.5380
	Yes	16(64)	19(76)	
	No	9(36)	6(24)	

Chi-squared/Fisher's exact-test.
Source: Authors.

Data regarding dysgeusia and dry mouth sensation were obtained for both groups, revealing an increase of 72% and 92%, respectively, both differences were considered statically significant comparing to the group evaluated before RT. There was no report of dysgeusia and dry mouth sensation in patients screened before RT. Statistical difference was also noted in comparison of the groups in relation to teeth conditions and plaque disclosing. The mean unstimulated whole salivary flow for all subjects together declined significantly from 1.1 ml/min (SD .24) before RT to 0.32 ml/min (SD .08) after RT ($p < .0001$). Data on oral condition before and after RT are presented on Table 3.

Table 3: Oral condition before and after RT (n=50).

Oral complication	Group 1	Group 2	p values
Dry mouth; n (%)*	0	23 (92%)	<.0001
Dysgeusia*	0	18 (72%)	<.0001
DMF (mean ± sd)#	13.99(±2.23)	22.94(±4.31)	<.00001
OHI-S (mean ± sd) #	1.6(.26)	2.2(.35)	<.00001
Unstimulated sialometry (mL/min; mean ± sd) #	1.1(.24)	.32(.08)	<.00001

*Fisher's exact-test. # Independent *t* test; $P < 0.05$ considered as statistically significant.
Source: Authors.

4. Discussion

The current analysis investigates oral complications expected to occur after RT to the head and neck region for the treatment of cancer, these include impact in salivary function, oral hygiene and tooth decayed/missed. Our results suggest that the impacts of RT reverberate over 1 year from the end of RT, providing additional insights about potential recovery of salivary flow rates at 12 months after RT to the preceding reports (Rajesh, 2017; Punita, 2018).

Xerostomia, or dry mouth sensation, develops at initial phase of RT due to irradiation damage of salivary glands (Ana, 2017). The reduced availability of saliva predisposes other oral complications such as distortion of the sense of taste, impaired swallowing, discomfort, increased microbial proliferation in view of the reduced buffer capacity in the oral environment, and consequently oral infections and dental caries (Bruno, 2006; Jensen, 2010). In our study, 92% of patients assessed after RT complain of dry mouth symptoms.

Reports suggest that xerostomia becomes present if radiation dose exceeds 40 Gy, which is usually the case of RT to the head and neck region, when total dose usually reaches around 70Gy and salivary flow might be impacted up to 80% (Dirix , 2010; Sciubba, 2006; Kaae, 2019). In our study unstimulated salivary flow rate was measured as 1.1 mL/min in patients before RT and .32 mL/min for those evaluated after RT, similar results were obtained in other studies (Rajesh, 2017; Punita, 2018). Punita and collaborators (2018) reported that salivary flow rates continue to decrease until 6 months after RT (.295 mL/min), and a minimal recovery is observed at 12 months (.362 mL/min). Stimulated saliva also appears to be affected proportionally, mean stimulated whole salivary flow declined from 1.09 to 0.47 mL/min at 6 months in other report (Rajesh, 2017). Salivary gland hypofunction after RT seriously affected the quality of life. A recent study found that in most cases the patient with xerostomia after RT had to find their own solution to overcome this problem due to the lack of information from professionals (Nan, 2018). Saliva substitutes, mainly based on carboxymethylcellulose, might be indicated (Jensen, 2010).

Modifications in salivary flow may also provoke gustatory disturbance (dysgeusia), but this side effect is rather related to taste buds damage during RT (Joel, 2019). Prevalence of taste disorder in patients who underwent RT was found to be around 66% (Epstein, 2016). There is no well-established curative therapy in this respect. Deficit is worse immediately after the end of RT and symptoms are attenuated during the follow up, difficulty in the identification of the sour taste is most detected in patients who had the oral cavity irradiated

(José, 2019). In our investigation, no patients complained of dysgeusia in the group 1, but in group 2, 18 patients (72%) mentioned dysgeusia symptoms.

Saliva composition changes increase the risk of dental caries and oral mucositis. Microbiome shift was reported to be associated to the increase of cariogenic cocci and yeast population (Elerson, 2018). Twenty bacteria genera were found to be positively related to radiation dose, and periodontal pathogenic bacteria was coincidently abundant when the onset of severe mucositis was noted, which were also associated with deterioration of hygiene (Jin, 2018). Oral hygiene and DMF index were significantly higher in group 2 comparing to group 1 for the present study.

This study does not investigate the prevalence of oral mucositis, mouth opening, and oral pain, what constitute a limitation of the study. Only a small sample was considered since exclusion criteria eliminates a lot of potential participants. However, the most relevant limitation of this study is the cross-sectional approaching of two independent groups, a longitudinal assessment could give more supportive data to the topic. It is important to consider the difficulty to carry out a 12-months follow up study with patients under RT to the head and neck region to treat cancer, a disease with a high fatality and mutilation rate. Then, our methods and results are enough to answer the raised question and give data on the impact of RT in the oral mouth in a first glance. Our research group has already designed a prospective cohort study (current under development) to further investigate the topic and eliminate the raised limitations.

There are many complications of the treatment of cancer in the head and neck region, as we see in the present study, most part of them are related to the oral cavity due to high radiotherapy dose. It is important to note that these oral complications directly affect patients' quality of life and systemic health. Health professionals, especially dental clinicians, must be informed of all risk factors and instructed about the oral management of these patients.

5. Conclusion

The present investigation demonstrates that patients submitted to RT in the head and neck region for the treatment of cancer experience oral complications even at 12 months after the last session of RT. These complications have a negative impact on oral function and quality of life, most part of them are developed at the expense of compromised salivary function.

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