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EVALUATION OF LIFE QUALITY AFTER LASER THERAPY IN PATIENTS WITH ORAL MUCOSITIS INDUCED BY RADIOTHERAPY AND CHEMOTHERAPY

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ABSTRACT

Objective: The objective of this research is to evaluate the impact on the quality of life of patients with oral mucositis induced by radiotherapy and / or chemotherapy treated with laser therapy. **Materials and methods:** This is a prospective longitudinal analytic study approved by the Ethics Committee on Research numbered 1544272. Sixty-nine patients were evaluated through quality of life questionnaires from the University of Washington and the European Organization for Research and Treatment of Cancer applied after laser therapy in patients with oral mucositis. The laser therapy protocol was red laser (660 mm), 0.4J point, with equal distances of 1 centimeter throughout the lesion. The degree of mucositis was also analyzed using the scale of the World Health Organization. **Results:** Significant and progressive reduction in the severity of oral mucositis. According to the European quality of life questionnaire, there was worsening of trismus symptoms and consumption of analgesics. However, according to the University of Washington questionnaire, there was aggravation of pain and taste. **Conclusion:** Patients with oral mucositis submitted to the low-intensity laser therapy protocol presented reduction of mucosal lesion, with improvement of the quality of life in some of the aspects of the questionnaires analyzed.

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INTRODUCTION

Cancer, according to the World Health Organization (WHO) and the National Cancer Institute, is defined as a disordered, rapid, aggressive, and uncontrollable growth disorder of cells, spreading to organs and tissues of the body (Fregnani *et al*., 2016). It is regarded as a public health problem in developed and developing countries. Head and neck neoplasms are considered the sixth most frequent malignant disease in the world, with more than 400,000 new cases diagnosed annually (Morais-Faria *et al*., 2016). The most commonly used treatment for head and neck neoplasms is surgery combined with radiotherapy and / or chemotherapy (Albuquerque *et al*., 2007).

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Radiotherapy is the therapeutic use of ionizing radiation in the fight against cancer. Its purpose is to reach malignant cells, preventing their multiplication by mitosis, and / or producing cell death. However, chemotherapy compromises the protein synthesis and propagation of neoplastic cells, depressing the immune system and interfering with the cellular mechanism (Sawada *et al*., 2006). Although it has the advantage of preserving the tissue structure, when compared to the surgical treatment, radiotherapy and / or chemotherapy may cause adverse reactions in the oral cavity in patients with cancer in the head and neck region (Jham *et al*., 2006). The direct or indirect stomatotoxicity caused by chemotherapy and radiotherapy can cause side effects such as oral mucositis (OM), xerostomia, trismus, dental caries due to radiation, osteoradionecrosis (ORN), compromising patients' quality of

life (Faria *et al*., 2016; Hespanhol *et al*., 2010). OM is related as an inflammatory condition of the oral mucosa manifested through ulceration, edema, erythema, hemorrhage and pain. It can cause changes in treatment, until the interruption of chemotherapy and / or radiotherapy due to the impairment of quality of life (QoL). Approximately 100% of patients treated with radiotherapy develop this inflammation, and in about 40% of patients undergoing chemotherapy, in the treatment of head and neck cancer (Kelner *et al*., 2007). The low-power laser (LPL) has good clinical results for the treatment of OM, being indicated in the tissue repair process, because it has analgesic, anti-inflammatory and cicatrizing effects (Lins *et al*., 2010). LPL triggers epithelial and fibroblast proliferation, as well as cellular and vascular alterations stimulating cell growth directly through the regulation of genes related to cell proliferation (Reolon *et al*., 2017). The WHO defines QOL as "the individual's perception of their position in life, in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards and concerns." This definition includes psychological state, physical health, social relationship, environmental characteristics and spiritual pattern (Inouye *et al*., 2010). According to Filho *et al*. (2013) it is important to evaluate the QoL of patients with head and neck cancer who are undergoing radiotherapy and / or chemotherapy treatment to know the impacts of the disease and its treatment, thus improving the protocol of care with clinical, social support measures and rehabilitation. The objective of this study was to evaluate the QoL, through the questionnaires of the University of Washington and European Organization for Research and Treatment of Cancer of patients with OM induced by chemotherapy and / or radiotherapy and treated with laser therapy.

MATERIALS AND METHODS

The research was approved by the Research Ethics Committee of the Faculdade Independente do Nordeste (CEP / FAINOR) in compliance with resolution 466/12, under number 1,544,272 and CAAE 553426.7.0000.5578. The research is of the longitudinal prospective type with samples of the intentional non-probabilistic type, respecting the inclusion and exclusion criteria. Inclusion criteria: patients of both sexes, over the age of 18 years, who were in radiotherapeutics and / or chemotherapy treatment for the treatment of cancer in the head and neck region, diagnosed with OM, in a host institution in a city in the Bahia's interior. Exclusion criteria were patients in which the OM site was located in the same region of the neoplastic lesion and patients who did not sign the informed consent form (ICF). All the patients who presented OM were submitted to laser therapy using the THERAPY XE (DMC, São Carlos, São Paulo, Brazil), with a wavelength of 660 nm (red laser) and 808 nm (infrared laser), combined with a power of 200mW, energy density 0.4J, for 4 seconds throughout the lesion, calculated for the device used with spot size of 0.028 cm2. The implantation of LPL with red light was done by the point technique, with intraoral irradiation and with equal distance of 1 cm at each point, perpendicular to the oral mucosa. The selected patients were initially given explanations about OM and diets, smoking and alcohol risks, oral hygiene instruction and motivation, chlorhexidine mouthwash 0.12%, as well as the mouthwash with chamomile tea and cryotherapy. Two dentists evaluated all patients initially selected for the presence of OM.

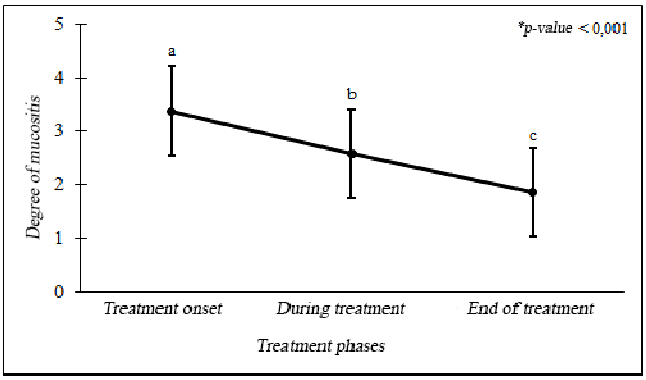
The oral clinical examination was performed with a flashlight (Missouri Led, São Paulo - SP, Brazil), dental wooden spatula (Santa Clara, São Paulo - SP, Brazil) and gauze (Cremer Max, São Paulo - SP, Brazil). Clinical data such as type of primary tumor, anatomical location of the tumor, total and fractional dose of radiation, drugs used in chemotherapy and radiotherapy, and epidemiological data such as: sex, age, occupation, city of origin were collected, information was added to a clinical form prepared for the research. The patients were evaluated three times a week, during all treatment of radiotherapy and / or chemotherapy, regarding the degree of mucositis using the WHO scale reference (Figueiredo *et al*., 2013), and respectively received the described treatment. A quality of life questionnaire from the University of Washington (QLQ-UW) was applied to the patients weekly, which is composed of twelve questions related to the characteristic functions of the head and neck region, as well as activity, recreation, pain, mood and anxiety. Each question has three to five response categories with a score varying from 0 (worst) to 100 (best), and a composite score, which is the mean of the twelve areas, is calculated (da Mota *et al*.,2003; Weymuller *et al*., 2001). The Questionnaire of European Organization for Research and Treatment of Cancer(EORTC QLQ – H&N35) is evaluated by seven areas. Pain (items 31, 32, 33, 34), swallowing (35, 36, 37, 38), senses (taste and smell, items 43 e 44), speech (46, 53, 54), social aspects of eating (49, 50, 51, 52), social contact (48, 55, 56, 57, 58), and sexuality (59, 60) are the areas mentioned. In addition, it has 11 specific items on dental problems (39), trismus(40), xerostomia (41), dry mouth(42), cough (45), malaise (47), analgesic consumption (61), nutritional supplements (62), feeding tube (63), and weight loss / gain (64, 65). Consists of 30 Likert's questions type with four possible answers of 4 points (ie: not at all - 1 point; a little - 2 point, moderate - 3 point, very much- 4 point) andfive questions with binary responses type yes - 2 points or no -1 point (Ringash andBeziak, 2001). Quality of life assessment was performed before the first LPL session for treatment of OM and at the end of therapy. The information obtained was tabulated. Descriptive statistics procedures were used to express the results as mean, standard deviation (SD) and frequencies (relative and absolute). The normality of the data was evaluated using the Shapiro-Wilk test. Intragroup differences in the degree of mucositis were verified by means of the Friedman test (with the comparisons between pairs being made by the Wilcoxon test). The Wilcoxon test was also used for comparisons between the initial and final quality of life scores. The significance level adopted was 5% ($\alpha = 0.05$) and the analysis were performed in IBM SPSS Statistics for Windows (IBM SPSS, 21.0, 2012, Armonk, NY: IBM Corp.).

RESULTS

In the present study, data were analyzed of 69 individuals with ages ranging from 28 to 82 years (mean = 57.8, SD = 11.4). Table 1 shows the sociodemographic and behavioral characteristics of the research participants. Most of the patients were male, married, consumed alcoholic beverages and smokers. Table 2 shows the clinical profile of the patients evaluated. There was predominance of oropharynx and larynx cancer, a treatment that combined chemotherapy and radiotherapy and individuals who used nystatin. A minority were individuals who used dipyrone, codeine, paracetamol and diclofenac; no participant made use of tramadol. A similar frequency of patients with and without a family history of cancer was observed and who used analgesics or not.

Table 1. Sociodemographic and behavioral characteristics of study participants

Variable	% Answer	n	%
Sex	100,0		
Female		12	17,4
Male		57	82,6
Marital status	100,0		
Married		36	52,2
Single		29	27,5
Widower		13	18,8
Divorced		1	1,4
Consumption of alcoholic beverages	100,0		
Consume		35	50,7
Never consumed		17	24,6
Had already consumed but no longer consumed		17	24,6
Smoking	100,0		
Smoker		51	73,9
Non-smoker		10	14,5
Ex- smoker		8	11,6



The markers represent the means and the error bars represent the standard deviations. * Friedman's test: [a,b,c]distinct overwritten letters indicate a statistical difference between the treatment phases

Figure 1. Degree of mucositis of the study participants, according to the treatment phase

Table 2. Sociodemographic and behavioral characteristics of study participants

Variable	% Answer	n	%
Cancerlocation	100,0		
Oropharynxandlarynx		40	58,0
Mouth		7	10,1
Mandiblebody		4	5,8
Neck		14	20,3
Tongue		4	5,8
Family historyofcancer	81,2		
Yes		28	50,0
No		28	50,0
Treatment	100,0		
Chemotherapy		2	2,9
Radiotherapy		24	34,8
Chemotherapy + Radiotherapy		43	62,3
Use ofdipyrone	100,0		
Yes		15	21,7
No		54	78,3
Use ofcodeine	100,0		
Yes		18	26,1
No		51	73,9
Use ofparacetamol	100,0		
Yes		10	14,5
No		59	85,5
Use ofnystatin	100,0		
Yes		42	60,9
No		27	39,1
Use ofdiclofenac	100,0		
Yes		1	1,4
No		68	98,6
Use oftramadol	100		
Yes		0	0,0
No		69	100,0

The number of laser therapy sessions that each patient performed ranged from 3 to 20 (mean = 8; SD = 3). In Figure 1, the degree of OM of study participants is shown, according to the treatment phase. Significant and progressive reduction in the degree of severity of OM was observed at each stage of treatment. The results of the quality of life by the QLQ-H & N35 indicated that patients with head and neck cancer presented reduction of complaints related to swallowing, speech, social contact, dental problems and feeding tube after treatment with OM with LPL. On the other hand, worsening in the consumption of analgesics and in trismus symptoms were observed. No significant changes were observed in the areas of pain, senses, social eating, sexuality, xerostomia, dry mouth; cough, malaise, nutritional supplements, weight loss and weight gain (Table 3).

Table 3. Initial and final quality of life scores – QLQ-H&N35

Area	Initial	Final	*p-value
	Mean ± SD	Mean ± SD	
Pain	61,11 ± 25,79	52,08 ± 29,69	0,053
Swallowing	59,06 ± 36,32	49,28 ± 33,17	0,034
Senses	51,69 ± 30,27	44,69 ± 32,53	0,063
Speech	63,53 ± 23,97	43,09 ± 28,75	< 0,001
Social aspects of eating	50,12 ± 30,77	56,76 ± 26,09	0,068
Social contact	32,85 ± 27,66	25,12 ± 34,02	0,001
Sexuality	26,57 ± 32,38	25,60 ± 30,86	0,363
Dental problems	53,14 ± 42,90	45,41 ± 37,47	< 0,001
Trismus	43,96 ± 40,22	64,25 ± 36,30	0,002
Xerostomia	45,89 ± 40,46	53,62 ± 35,34	0,851
Dry mouth	71,01 ± 33,78	43,96 ± 37,26	0,247
Cough	51,69 ± 35,94	20,58 ± 23,92	0,749
Malaise	45,41 ± 33,32	31,40 ± 34,48	0,737
Analgesic consumption	59,42 ± 49,46	75,36 ± 43,41	0,008
Nutritional supplements	31,88 ± 46,94	31,88 ± 46,94	1,000
Feedingtube	60,87 ± 49,16	42,03 ± 49,72	0,007
Weightloss	81,16 ± 39,39	73,91 ± 44,23	0,225
Weightgain	24,64 ± 43,41	31,88 ± 46,94	0,166

QLQ-H&N35, Quality of Life Assessment Questionnaire - Head and Neck - European Organization for Research and Treatment of Cancer; SD, standard deviation. * Wilcoxon test.

Table 4. Initial and final quality of life scores – UW-QOL

Area	Initial	Final	*p-value
	Média ± DP	Média ± DP	
Pain	45,65 ± 22,26	52,90 ± 23,30	0,020
Appearance	55,80 ± 28,81	48,55 ± 21,39	0,053
Physicalactivity	52,17 ± 30,84	58,33 ± 28,01	0,183
Recreation	64,12 ± 34,18	55,07 ± 32,25	0,135
Swallowing	48,30 ± 31,72	30,87 ± 31,54	0,001
Chewing	36,96 ± 36,07	26,09 ± 34,95	0,015
Speech	64,97 ± 22,83	73,06 ± 29,31	0,080
Shoulder	89,84 ± 22,44	89,91 ± 20,00	0,286
Taste	31,39 ± 32,86	43,54 ± 39,80	0,016
Saliva	56,00 ± 26,07	55,12 ± 29,19	0,757
Humor	72,46 ± 25,42	71,38 ± 23,59	0,833
Anxiety	66,72 ± 32,90	54,68 ± 38,82	0,030

UW-QOL, University of Washington – *Quality of Life Questionnaire*; SD, standard deviation. * Wilcoxon test.

Table 4 presents the initial and final quality of life scores, evaluated by the UW-QOL questionnaire. The data show that, after treatment of MO with LPL, individuals with head and neck cancer exhibited reduced complaints related to swallowing, chewing and anxiety. On the other hand, there was aggravation concerning pain and taste. No significant changes in the areas of appearance, activity, recreation, speech, shoulder, saliva, and mood were observed.

DISCUSSION

Cancer is part of a group of chronic diseases that has affected the population on a large scale, especially head and neck

cancer, which is directly related to smoking habits and alcoholism, according to Santos *et al*. (2012) and is proven in this study (Table 1). Among the different locations of cancer in the head and neck region, it is observed in the present studya prevalence for the oropharynx and larynx regions, corroborating with Bergamasco *et al*. (2008). In the head and neck region, cancer has a variety of treatments, such as surgery, radiotherapy and chemotherapy. In spite of the attempt to solve / reduce the disease itself, the toxicity of these treatments can affect the oral mucosa, being determinant in the clinical evolution of some conditions, such as OM. Oral mucositis has some stages that can interfere directly in the individual's QoL (Silva *et al*., 2012, Teixeira *et al*., 2016). Several points can be evidenced when this loss of QoL, such as swallowing, speech, social contact, dental problems and probe for feeding, as can be observed in Table 3 and 4. Some studies indicate that OM is diagnosed between 90 and 97% of the patients under treatment with radiotherapy and chemotherapy. This condition can manifest itself during treatment and post-treatment (Carvalho *et al*., 2011; Gautam *et al*., 2012; Florentino *et al*., 2015). Corroborating with this data, in Figure 1, a relationship between the manifestations of OM, in the various degrees of severity, is observed with the various phases of the treatment, evidencing that its manifestation can occur at any moment. The OM influences the QoL of the individual with cancer. In this sense, the literature points to the use of LPL as a solution for OM, being considered a non-invasive treatment, studied more than 20 years ago. The mechanism of action of this therapy is stimulation of the chromophores that induce the increase of the production of substances in the cells of the mucosa, resulting in the increase of the cellular metabolism (Bensadoun; Nair, 2012; Florentino *et al*., 2015). After laser therapy, participants' QoL was evaluated, in which it was possible to observe that individuals had a reduction in complaints related to swallowing, chewing and anxiety. These data can be observed in Table 4. Silva *et al*. (2012) observed the same in a study.

Despite the results found in this research, it is possible to notice some limitations, such as difficulty in controlling group parameters due to physiological differences of the body, genetic predisposition, and anatomical site affected, comorbidities prior to head and neck cancer. The methodology chosen was the application of a questionnaire. This has some advantages, as discussed by Vartanian *et al*. (2007): to be self-applied, and may be occasionally applied by others previously trained. The authors state that the application of a QOL questionnaire to an individual with cancer during treatment may serve as a screening tool for some possible situations, such as depression. Given the importance of this topic associated to a significant increase in OM cases, it is worth noting the need for further studies on the subject. Noting that in the current literature, there is little research that specifically addresses the QoL of this group of patients.

Conclusion

- Based on the presented results it is possible to conclude that:
- Pacientes com câncer de cabeça e pescoço submetidos a um protocolo de tratamento para OM com LPL apresentaram redução da lesão da mucosa bucal.
- After treatment with laser therapy, improvement was observed in some aspects of QoL such as swallowing, speech, social contact, dental problems, feeding tube, chewing and anxiety. On the other hand, aggravation was also observed in complaints related to trismus, consumption of analgesics, pain and taste.

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