

EFFECTIVENESS OF LOW INTENSITY LASER THERAPY ON ORAL MUCOSITIS IN HEAD AND NECK CANCER PATIENTS

Efetividade da terapia com laser de baixa intensidade em mucosite oral de pacientes com câncer de cabeça e pescoço

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ABSTRACT

Introduction: About 870,000 new cases of malignant airway and digestive tract tumor are diagnosed annually worldwide. Patients undergoing radiotherapy (RT) for head and neck develop as side effects oral mucositis and other complications that can lead to discontinuation of anticancer treatment. **Aim:** This study was conducted to determine whether oral care can reduce the rates of discontinuation of anticancer treatment. **Method:** We selected patients with carcinoma of the head and neck radiotherapy with or without chemotherapy (CT) in the Hospital São Vicente de Paulo de Passo Fundo. A total of 187 patients were evaluated and divided into two groups: Group I (patients receiving dental treatment) and Group II (patients not receiving dental treatment). Group I - patients

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were submitted to daily assessments, receiving guidance, following a protocol for dental treatment and adjuvant application of low intensity laser throughout the period they performed RT. Group II - patients were evaluated and followed only, for not allowing the proposed treatment. **Results:** The interruption of radiation treatment was 2.4 % of the patients in Group I, and Group II 34.6%. **Conclusions:** prevention and early treatment of complications related to RT like oral mucositis can decrease the chance of the patient to abandon radiotherapy and consequently contribute for a better prognosis for cure and patient survival.

Key Words: Radiotherapy. Mucositis. Laser. Head and neck neoplasms.

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RESUMO

Introdução: Cerca de 870 mil novos casos de neoplasias malignas de vias aéreas e tumores do aparelho digestivo são diagnosticados anualmente em todo o mundo. Os pacientes submetidos à radioterapia (RT) de cabeça e pescoço desenvolvem efeitos colaterais como mucosite oral e outras complicações que podem levar à interrupção do tratamento anticâncer. **Objetivo:** Este estudo foi realizado para determinar se cuidados bucais podem reduzir as taxas de abandono do tratamento anticâncer. **Método:** Foram selecionados pacientes com carcinoma de cabeça e pescoço submetidos a radioterapia (RT), com ou sem quimioterapia (QT), no Hospital São Vicente de Paulo de Passo Fundo. Um total de 187 pacientes foram avaliados e divididos em dois grupos: Grupo I (pacientes que recebem tratamento dental) e Grupo II (pacientes que não receberam tratamento dental). Os pacientes do grupo I foram submetidos a cuidados diários, recebendo orientação, seguindo um protocolo de tratamento odontológico e aplicação adjuvante do laser de baixa intensidade durante todo o período que realizaram RT. Os pacientes do grupo II foram avaliados odontologicamente e acompanhados somente. **Resultados:** A interrupção do tratamento com radiação foi de 2,4% dos pacientes do Grupo I e no Grupo II 34,6%. **Conclusões:** a prevenção e o tratamento precoce das complicações relacionadas com a RT, como mucosite oral, podem diminuir a chance de o paciente abandonar a radioterapia e, conseqüentemente, contribuir para um melhor prognóstico de cura e sobrevida dos pacientes.

Palavras-chave: Radioterapia. Mucosite. Laser. Câncer de cabeça e pescoço.

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INTRODUCTION

Cancer is characterized by abnormal cells development and proliferation. Each year approximately 870,000 new cases of head and neck cancer (HNC) are diagnosed worldwide. The term head and neck cancer refers to a group of biologically similar cancers originating from the upper aerodigestive tract, including the lip, oral cavity, nasal cavity, paranasal sinuses, pharynx and larynx. The treatment of choice consists of surgery, radiation and combined surgery/radiation. Recently, chemotherapy (CT) has been used as a neoadjuvant treatment, as adjuvant treatment after definitive surgery and/or radiation, or concurrent with both definite and adjuvant radiotherapy (RT). Although RT plays an important role in the management of patients with HNC, it is also associated with several undesired side effects (KUHN, 2007; KUHN et al., 2008; KUHN-DALL'MAGRO and DALL'MAGRO, 2008).

Oral Mucositis (OM) is a common toxicity associated with both chemotherapy, and head and neck radiotherapy (FEKRAZAD and CHINIFORUSH, 2014). Severe OM causes considerable pain and discomfort, leading to higher need for pain medication, parenteral nutrition, longer hospital stays and higher cost of care (DONNELLY et al., 2003). OM also may affect the efficacy of treatment plans by necessitating breaks in radiotherapy, reductions in dose intensity of chemotherapy and/or modifications in antineoplastic agents' schedules (FIGUEIREDO et al., 2013).

Despite its frequency and clinical significance, there is currently no effective way to prevent OM. For patients with established oral lesions, treatment has been limited to the use of palliative rinses, barrier protectants, topical antimicrobials and analgesics (SONIS et al., 2001; FEKRAZAD and CHINIFORUSH, 2014). The Multinational Association of Supportive Care in Cancer and the International Society for Oral Oncology published clinical practice guidelines for prevention and treatment of cancer therapy induced gastrointestinal and OM pointing the need for more studies in this area (NETO and WESTPHALEN, 2013).

The efficacy of low intensity laser therapy (LILT) on OM was showed by some studies that suggest stimulation of specific metabolic processes in healing wounds. Major changes include increased granulation tissue, early epithelialization, increased fibroblast proliferation and matrix synthesis, and enhanced neovascularization. Of note, daily treatment with LILT is required to provide the maximal benefit (BARASCH and PETERSON, 2003;

QUADRI et al., 2005; KUHN et al., 2005; AMORIN et al., 2006; KUHN et al., 2009; ANTUNES et al., 2014).

We decided therefore to conduct a study to evaluate the benefits of daily dental monitoring including LILT and their effects in the rates of discontinuation of anticancer treatment.

MATERIAL AND METHODS

This study was carried out at the Oncology Unit (OU) of the Hospital São Vicente de Paulo (HSVP). From 2010 to 2013 all consecutive cancer patients with HNC were eligible for this trial. The study was approved by Ethics Committees of Hospital São Vicente de Paulo de Passo Fundo.

Before starting radiotherapy all patients at the OU received a routine odontological assessment including removal of septic teeth and oral recommendations to brush teeth using a soft toothbrush and neutral toothpaste after every meal. In addition, patients were recommended to use a 0.12% chlorhexidine and 0.05% Sodium Fluoride (226 parts per million) mouth rinse twice a day (after breakfast and before going to bed at night). During chemo and/or radiotherapy patients received additional reminders and instructions to reinforce compliance to the initial recommendations on tooth brushing and mouth washing.

Groups:

Group I: Patients were submitted to daily assessments, receiving adjuvant LILT with a GaAlAs instrument by the Thera Lase made by Dental Manufactory Company (DMC) Equipment (São Carlos, SP, Brazil) with a continuous 830 nm wavelength, 100 mW power, dose 4 J/cm². The laser was operated by a trained dentist from the OU. International safety procedures for laser use were followed in this study and are considered an important routine in our department.

Group II: Patients were evaluated and followed only, for not allowing the proposed treatment with LILT.

Every day (monday to friday) after RT patients went to Department of Oral and Maxillofacial Surgery to be following. Some oral diseases were diagnosed and treated and were offer the opportunity to receive LILT to prevent OM according to below Figure 1:

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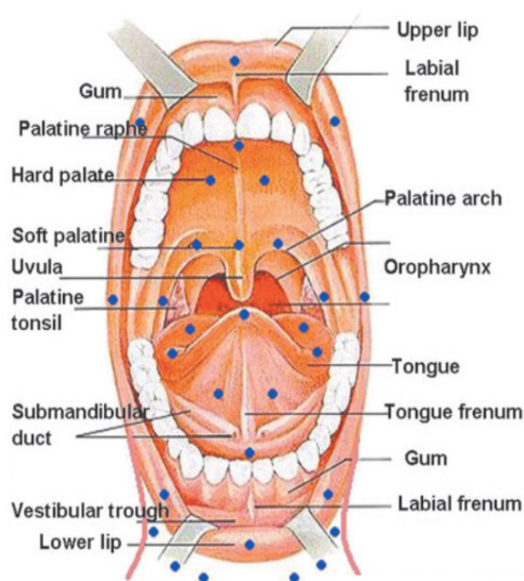


Figure 1 - LLLT intervention points (KUHN *et al.*, 2008)
Radiotherapy

Patients received a total dose of 75 Gy (Grays) at a rate of 1 fraction of 2 Gy/day, 5 days a week from a linear phothon accelerator, model Primus (Siemens-Germany), in according with the international Commission on Radiation Unit and Measurements without or with prior surgery or concomitant chemotherapy.

Oral evaluation

Oral evaluation protocol including: age, gender, type of cancer, type of treatment, OM World Health Organization – WHO (1979), pain (VAS) candidiasis, oral hygiene and laser application.

Statistical analysis

The statistical analysis was carried out using Student T test (concordance or differences between groups). A level of significance of 5% was used and data were analyzed using the SPSS program (2005). To compare the groups, we analyzed the date on gender and disease as frequencies and percentages.

RESULTS

A total of 187 patients were including in this study, 144 males (77%) e 43 females (23%). The mean age was 59.88 $\pm$ 12,95 (13 to 95 years). 125 patients were including into the Group I e 62 into the Group II. High scores of pain and OM were observed between patients of group II.

Intercurrences like: candidiasis and xerostomy were observed and treated in both groups.

Group I (125 patients) showed a RT interruption of 3 patients (2,4%) while in group II (62 patients), 20 (34,6%) had RT interruption induced by interurrences like pain, dehydration, severe OM, immunity and death ($p < 0,001$) (Figure 2).

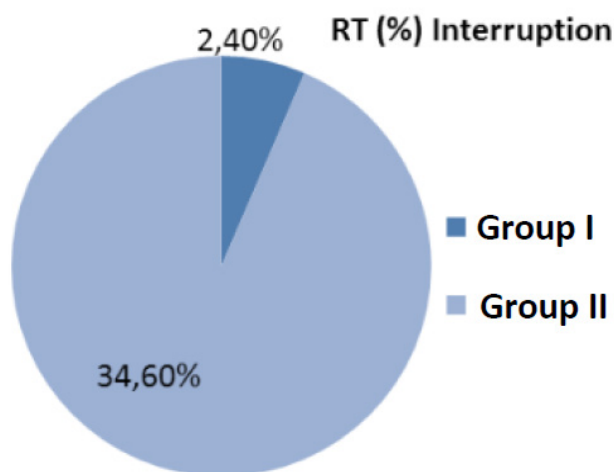


Figure 2 - RT (%) interruption between groups

The group that received LILT (group I) had minor scores of interruption of the antineoplastic treatment when compared with group 2 ($p < 0.001$).

RT sessions ranged between 20 and 42 (mean 32.36 $\pm$ 6.69). Into the group I: mean: 33.1 $\pm$ 6.8 and into the group 2: 31.59 $\pm$ 6. The total RT dose ranged between 36 e 75 Gy (mean: 58.25 $\pm$ 12.05).

There were not statistical differences when compared age, RT dose, antineoplastic treatment between groups I and II.

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DISCUSSION

OM is a frequent acute side effect of antineoplastic treatment in patients treated by radiotherapy and/or chemotherapy especially for head and neck cancer. Its prevalence has increased over the last 5 years due to more aggressive treatment protocols and combined modality regimens, reaching 36% to 100% of patients. This painful side effect reduces quality of life and often requires narcotic analgesia, enteral or parenteral nutrition with additional costs. Modifications of treatment planning may be necessary, leading to 19% of interruptions and possibly affect local control and finally survival (JADAUD and BENSADOUN, 2012).

OM is a common dose-limiting debilitating treatment-related complication in cancer treatment characterized by erythematous, atrophic, erosive, or ulcerative lesions. OM results from two major mechanisms: Direct toxicity on the mucosa and myelosuppression due to the treatment; and its pathophysiology includes four interdependent phases: An initial inflammatory/vascular phase, an epithelial phase, an ulcerative/bacteriological phase, and a healing phase. Conservative treatment methods include topical anesthetics, cocktail mixtures, and mucosal coating agents, and physical agents like cryotherapy and laser therapy. Cancer survivors who had CRT-induced OM had altered affective state with greater impairment in quality of life compared to those who did not (KUMAR et al., 2013).

OM is still a common and severe acute side-effect of many oncologic treatments, especially in patients treated for head and neck cancer. It may affect quality of life, require supportive care and impact treatment planning and its efficacy. LILT seems to promote pain relief and reduces OM incidence and its severity.

Bjordal et al. (2011) in their systematic review found 11 randomized placebo-controlled trials with a total of 415 patients; and found that the relative risk (RR) for developing OM was significantly reduced after LILT compared with placebo LILT, with greater effect for doses above 1 J. LILT also reduced the duration, oral mucositis severity, and had similar side effects versus placebo LILT.

Bensadoun and Nair (2012) in their 'state-of-the-art' review identified 33 relevant articles and a pooled meta-analysis showed that LILT reduced risk of oral mucositis, reduced duration, severity of oral mucositis and reduced number of days with oral mucositis. The authors recommended red or infrared LILT for prophylaxis (output between 10-100 mW, dose of 2-3 J/cm²) and for therapeutic effect-max 4 J/cm², application on single spot rather than scanning motion.

Chemotherapy-induced OM starts approximately one week after completion of the chemotherapy cycle and varies according to dosage and drugs combination; it usually heals in 1-3 weeks depending of the grade of OM. Radiation-induced OM starts 2-3 weeks later, persisting longer, usually for 3-5 weeks, but may last as long as for 7 weeks (COSTA et al., 2013). Our study has shown evidence that LILT in addition to oral care can decrease the duration of chemotherapy and radiotherapy induced OM and the index of interruption of oncology treatment to 2.4%. It should encourage clinicians to use this technique to improve quality of life of cancer patients during the oncology treatment.

In summary, LILT represents more than a promising agent to prevent or treat cancer—therapy induced OM. With diode and new technologies, laser is now less time-consuming and extra oral applicators with specific wavelength could be helpful to treat other sites of mucositis and skin toxicities. Also it may be used by trained paramedical staff like nurses who can complete clinician contribution. We can now use published recommendations for soft laser parameters. This is important for different clinician communities that are concerned with oral mucositis and for the homogeneity of laser procedure in future trials. According to the MASCC criteria, and the results of the meta-analysis, LILT could be soon proposed with a level I of evidence, as a possible new standard of care in respect to the last recommendations published if intraoral application is performed (JADAUD and BENSADOUN, 2012; NETO and WESTPHALEN, 2013).

CONCLUSION

The very encouraging results of LILT in the prevention and treatment of OM in patients treated by chemotherapy or radiotherapy for advanced head and neck cancer could soon be proposed as a new standard of care, according to the multinational Association of Supportive care in Cancer (MASCC) criteria. Modern lasers are less time consuming and extra oral applicators for a possible use by trained paramedical staff could be helpful to complete clinician practice.

Future studies should be designed to include clinically controlled documentation of the beneficial effect in terms of pain control, narcotic administration, food intake and length of hospital stay of patients who develop this RT complication.

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