

Low-intensity Laser Therapy in the Treatment of Mucositis Induced by Chemotherapy and Radiotherapy

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Purpose: The aim of this article was to develop a protocol for the treatment of oral mucositis induced by chemotherapy and radiotherapy. A pilot trial was conducted with low-intensity laser therapy (GaAlAs/InGaAlP laser) to decrease the lesions' manifestation time and to promote pain control.

Materials and Methods: Fifty patients for whom chemotherapy or chemoradiotherapy was indicated were evaluated in this study. Fifteen patients developed mucositis (30%) and were divided into 3 groups of 5, receiving low-intensity laser therapy 3 times a week, with a specific dosage in each group. Group A: GaAlAs laser, wavelength 830 nm (infrared), power 70 mW, dose 5 J/cm²; group B: InGaAlP Laser, wavelength 685 nm (red), power 35 mW, dose 5 J/cm²; group C: placebo. The presence and severity of mucositis was clinically evaluated using the WHO scale, and pain was measured by using a visual analogue scale (VAS). The Kruskal-Wallis test was used to test differences among groups. Results were considered statically significant when $p < 0.05$.

Results: The infrared laser 830 nm (Group A) showed therapeutic superiority when compared with the red laser 685 nm (Group B) and the Group C (placebo). Group B showed intermediate results between groups A and C in terms of mucositis duration and the decrease of the lesion grade at 7 and 15 days. However, the pain level after 7 days of the treatment continued to be high compared to Group C (placebo).

Conclusions: Low-intensity laser therapy with a 830-nm (infrared) wavelength can be indicated for oral mucositis induced by chemoradiotherapy, due to its better therapy results compared to the red laser (685 nm) and the placebo group in the same application periods.

Keywords: low-intensity laser therapy, oral mucositis, chemotherapy, radiotherapy.

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Chemotherapy is described as a systemic treatment where some drugs act indiscriminately in the patient's cells, normal or cancer, promoting collateral effects characterized as disagreeable.¹ The cancer cells'

sensitivity and resistance to chemotherapy is determined by pharmacological and biochemical factors.² Chemotherapy is considered the treatment of choice for patients with malignant tumors, especially in ad-

vanced stages, and is currently incorporated in treatment programs associated with radiotherapy, surgery, and biological agents.³

Radiotherapy is frequently used as an alternative treatment or cojoint with surgery or chemotherapy in malignant lesions with a localized aspect. The ionized radiation damages both the tumor cells and the healthy surrounding tissue. The radiosensitivity grades can be classified according to the mitotic capacity of cells. The tumor cells are more susceptible to the ionized radiation due to their higher mitotic capacity; DNA damage and cell death are promoted.⁴

The most effective antineoplastic agents act especially on cell division, provoking damage specifically in tissues with rapidly dividing cells, such as bone marrow, lymphoblasts, mucosae, skin, and gonads. Suppressing proliferation of the epithelial cells can cause alopecia and sometimes skin lesions; suppressing mucosal cell division causes mucositis.⁵

Scully and Epstein⁶ describe mucositis as the most stressing lesion during chemoradiotherapy. This fact can be explained by the interference of the chemotherapy drugs in different stages of the cellular cycle, interacting with both the cancer and healthy cells. Epstein and Schubert⁷ reported that high doses of chemotherapy directly affect epithelial cell proliferation, resulting in loss and atrophy of oral mucosa protection.

The WHO⁸ (World Health Organization) classifies mucositis into 5 grades:

- Zero: slight modification of the normal aspect
- Grade I: erythema
- Grade II: erythema and ulcers; patient can eat solids
- Grade III: confluent ulcers; patient requires liquid diet
- Grade IV: oral alimentation not possible, hemorrhage

In a review of possibilities of mucositis treatment in bone marrow transplant patients, Torres-Pereira⁹ mentions a reduction of the mucositis grades in patients that received treatment with He-Ne (helium neonium) laser when compared to the control group without laser application, confirming the results of Plevova¹⁰ and Bensadoun et al.¹¹ According to Migliorati et al,¹² the GaAlAs (arsenate of galion and aluminum) laser was considered effective in pain control after bone marrow transplant in patients who underwent pre-transplant chemotherapy. However, mucositis development cannot be avoided.

The aim of this study was to establish a treatment method for oral mucositis induced by chemoradiother-

apy. A pilot study was begun with low-intensity laser, with the purpose of decreasing lesion duration and providing pain relief.

MATERIALS AND METHODS

This study included 50 patients of the Santa Casa of Porto Alegre Hospital that were submitted to chemoradiotherapy between May and September 2003 in accordance with the ethical norms of this institution (document number 195-02). Informed consent was obtained from all participating patients. The patients were evaluated before, during, and after chemotherapy and/or chemoradiotherapy, and received oral hygiene instructions and information on the risks of developing oral mucositis during antineoplastic treatment.

Before chemoradiotherapy, patients were instructed to use a 0.12% chlorhexidine mouthrinse twice a day, and a neutral toothpaste with a soft toothbrush. Septic teeth were removed. Information was provided about the risk of developing oral mucositis during antineoplastic therapy. During chemoradiotherapy, lesions were evaluated and treated. All patients were treated according to group and observed for a total of 8 weeks from the beginning of antineoplastic therapy. Patients who developed recidivous lesions after the study period of 8 weeks were treated but were not mentioned in this study.

Fifteen patients had mucositis and were treated with GaAlAs/InGaAlP (DMC Equipment, São Carlos, São Paulo, Brazil) laser when symptoms were manifest. International safety procedures for laser use were respected in this study, and are considered an important routine in our department. The patients were divided into 3 groups that received different treatments, 3 times a week for 15 days until the lesions disappeared:

Group A: Laser with 830 nm wavelength, infrared, power 70 mW, and dose 5J/cm².

Group B: Laser with 685 nm wavelength, visible red, power 35 mW, and dose 5J/cm².

Group C: Placebo application. Only the handpiece was used, the laser was not turned on. These patients received only conventional mucositis treatment and pain control.

The antineoplastic protocols used in these 50 patients were evaluated and a percentual analysis of mucositis development for each therapy type was performed. The 15 patients that developed mucositis were clinically evaluated using the WHO scale,⁸ and pain was measured by the visual analogue scale (VAS) adapted by Langley.¹³ The duration of mucositis and the grade

Table 1 Changes in the mucositis grade (WHO scale) and evaluation of pain (VAS) from baseline to 15 days

Patients/ Group	Pain (VAS)/ Mucositis grade (WHO) Initial	Pain (VAS)/ Mucositis grade (WHO) 7 days	Pain (VAS)/ Mucositis grade (WHO) 15 days
1/A	10 / IV	4 / II	2 / I
2/A	7 / IV	4 / II	0 / 0
3/A	8 / III	2 / I	0 / 0
4/A	9 / III	2 / I	0 / 0
5/A	8 / II	0 / 0	0 / 0
6/B	10 / III	8 / II	2 / I
7/B	10 / III	6 / II	3 / I
8/B	8 / II	7 / I	7 / I
9/B	9 / III	8 / III	5 / II
10/B	10 / III	7 / II	5 / I
11/C	8 / III	7 / III	6 / II
12/C	10 / IV	9 / III	10 / III
13/C	5 / II	4 / II	6 / III
14/C	10 / III	8 / III	8 / III
15/C	10 / IV	8 / III	7 / III

of lesions found in each patient, as well as the related pain scores, were recorded at the start of laser therapy and after 7 and 15 days. The Kruskal-Wallis test was used to test differences among groups. Results were considered statistically significant when $p < 0.05$.

RESULTS

The change in mucositis in patients receiving laser therapy is shown in Table 1. Group A (infrared laser 830 nm) (Figs 1 and 2) showed better results – shorter mucositis duration, reduced lesion grade, less pain – than group B (red laser 685 nm) and group C (placebo) (Figs 3 and 4). Mucositis duration differed significantly between groups A and C ($p = 0.0037$), as did the lesion grade after 7 days ($p = 0.008$) and 15 days ($p = 0.0006$), as well as the pain scores after 7 days ($p = 0.0072$) and 15 days ($p = 0.0009$). Group B showed results that were intermediate between groups A and C, but did not differ significantly from group A in terms of mucositis duration and lesion grade after 7 and 15 days.

DISCUSSION

Undesirable side effects can be associated with chemo- or radiotherapy of cancer, depending on the antineoplastic protocol used. It can promote tissue alterations, or even interrupt the patient's therapy, thus worsening the healing prognosis.^{2,14} The emotional and medical support of multidisciplinary staff is of unquestionable importance for the effective monitoring and treatment of the associated complications.¹⁵ According to the obtained results, the greatest extent of mucositis was associated with methotexate, cisplatin plus radiotherapy, 5 fluorouracil and adriamicin, confirming the results achieved by McCarthy et al¹⁶ and Parulekan et al.¹⁷

Our study was designed to evaluate the benefits of curative laser therapy in the management of oral mucositis, regarding patient acceptance of and compliance with this technique, with an emphasis on pain reduction and attenuation of mucositis severity. There are many uncontrolled reports of potential benefits of low-energy lasers, but only a few controlled studies have been published. Despite the small size and heterogeneous characteristics of our sample, it is evident that laser therapy is a noninvasive technique that seems to promote pain relief and reduce the severity of oral mucositis; for this reason, patients present a high acceptance of and compliance with this therapy.



Fig 1a Extensive oral mucositis lesion on tongue and lower lip. Grade IV (WHO), pain 10 (VAS).



Fig 1b Cheek mucosae in same patient.



Fig 2a Patient after 10 days (group A). He received low intensity laser therapy 3 times per week. Observe the healing process.



Fig 2b Healing process in the cheek mucosae after 10 days of laser treatment.



Fig 3 Oral mucositis of cheek mucosae, grade IV (WHO), pain 10 (VAS), group C (placebo, no laser treatment).



Fig 4 Same patient as Fig 3, poor healing after 10 days. Continual high pain level (8 on VAS).

CONCLUSION

Low-intensity laser therapy (GaAIIAs) with 830 nm wavelength (infrared), power 70 mW, energy density 5 J/cm², with 3 applications a week for 15 days, can be indicated for treatment of mucositis induced by chemoradiotherapy because it reduces mucositis duration and provides analgesia of lesions when compared to visible red laser (685 nm, power 35 mW, energy density 5J/cm²) and placebo over the same application time. Thus, laser therapy can be suggested as a means of improving the care of such patients, promoting faster healing of the mucositis while also reducing pain and the interruptions of antineoplastic treatment. Further randomized controlled trials with homogeneous samples and different laser application schedules should be conducted with the objective of developing effective protocols to treat and prevent such debilitating complications as oral mucositis.

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