

The impact of low power laser in the treatment of conditioning-induced oral mucositis: A report of 11 clinical cases and their review

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CEP-20231-050

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Received: 19/05/2007

Accepted: 21/10/2007

Indexed in:

-Index Medicus / MEDLINE / PubMed
-EMBASE, Excerpta Medica
-SCOPUS
-Índice Médico Español
-IBECs

Antunes HS, Ferreira EM, Matos VD, Pinheiro CT, Ferreira CG. The Impact of low power laser in the treatment of conditioning-induced oral mucositis: A report of 11 clinical cases and their review. Med Oral Patol Oral Cir Bucal. 2008 Mar;13(3):E189-92.

© Medicina Oral S. L. C.I.F. B 96689336 - ISSN 1698-6946

<http://www.medicinaoral.com/medoralfree01/v13i3/medoralv13i3p189.pdf>

Abstract

We have investigated the clinical effects of low power laser therapy (LPLT) on the treatment of conditioning-induced oral mucositis (OM) in patients submitted to hematopoietic stem cell transplantation (HSCT). The evaluation of OM was done using the Oral Mucositis Assessment Scale (OMAS) and World Health Organization (WHO) scale.

In the context of a randomized placebo-controlled trial with 38 patients for the evaluation of preventive LPLT, eleven individuals were submitted to allogeneic (AL) HSCT and developed oral mucositis grade 4 (WHO) or a total area of OM of 12 cm (OMAS) and due to that were treated with LPLT with the purpose of symptom relief. The irradiation used was a diode InGaAlP, emitting light at 660 nm, 50 mW and 8 J/cm² measured at the end of fiber optic with 0.196cm² of section area during the treatment. The tip of the laser device touched the oral mucosa and patients recovered on average 6 days (3-12 days) from the beginning of the laser application. Our results have indicated that the use of LPLT in HSCT patients is a powerful instrument in the treatment of overt OM and is now a standard procedure in this group of patients in our hospital.

Key words: Low power laser therapy, hematopoietic stem cell transplantation, oral mucositis, radiotherapy, chemotherapy.

Introduction

Patients who undergo HSCT present OM, after conditioning regimens, that occur with a WHO-grade 3-4 incidence of 68.5 %, approaching 100% when all grades are considered (1). Oral mucositis is the most common and debilitating side effect reported and clinical presentation consists of mucosal burning, bleeding, erythema, edema and progresses to ulceration with or without pseudo-membrane formation, that develop most commonly on

the non-keratinized mucosa of the floor of the mouth, tongue, buccal mucosa, and soft palate and it occurs rapidly followed by the administration of chemotherapy (CT) or radiation (RT) in the head and neck. Besides morbidity and drop in quality of life the risks of fever and of serious infection are significantly increased in HSCT recipients with mucositis, compared with patients without mucositis (1-4). In 2004, the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer

and International Society of Oral Oncology (MASCC/ISOO) completed an evidence-based review of the literature for a variety of topics regarding the prevention and management of oral mucositis. The current management of such OM is focused on prevention, palliation, infection prevention and treatment (5-7).

It has been reported that low power laser therapy (LPLT) promotes wound healing and reduces pain and inflammation. Different effects appear to be related to laser characteristics and the particular type of tissue being treated (8,9). Helium-neon (He-Ne) laser (632.8 nm) and diode lasers treatment have been the most frequently studied form of LPLT for the prevention or treatment of oral mucositis and oral pain associated with cancer therapy including HSCT (1,7). Our group in a recent trial assessed the effectiveness of LPLT to prevent OM in HSCT patients. By using the WHO scale it was observed that patients receiving upfront LPLT presented less intense oral mucositis (63,2% WHO Grade 0-1) (1). Here we report the clinical effects of the InGaAlP (660 nm) laser on the reduction of the severity of conditioning-induced overt OM for HSCT patients. To illustrate the impact of the strategy we report one out of the 11 cases.

Case report

A 39 year-old white man, with Chronic myeloblastic leukemia (CML) and OM in the right and left side edge of the tongue beginning on April, 23th 2005, D +10 (Figure 1 and 2) and healing on April, 28th 2005, D + 15 (Figure 3 and 4) with 100 neutrophil in peripheral blood.

This case is part of eleven patients were subjected to allogeneic and autologous HSCT and his characteristics are summarized in Table 1. Dental care was performed by a dentist before admission of HSCT. The irradiation used was a 50-mW InGaAlP diode laser, emitting continuous light at 660 nm, with a real power output of 46.7 mW and energy density (ED) of 8 J/cm², measured at the fiber optic end with 0.196 cm² of section area during the experiment. It was applied in a punctual form, side by side of the very ulcerous area, touching the material, for 33.4 seconds per point. The evaluation of OM was performed using the OMAS (10) and WHO (11) scale. All the patients who reached grade 4 OM or a total area of OM of 12 cm, started receiving the LPLT with 8 J/cm² on the ulcerous areas until wound healing (healing time of ulcers was on average 6 days- Figure 1-4). They had carried out oral hygiene with extra-soft toothbrushes, dental paste with peroxides system and mouth rinses with an ethanol-free

Table 1. Patient characteristics.

	Age	Gender	Diagnostic	HSCT	Conditioning	OM grades	Healing time
1	56	Male	CML	Related Allogeneic	Regimen 3	3	6
2	36	Female	CML	Related Allogeneic	Regimen 3	4	6
3	38	Male	MS	Related Allogeneic	Regimen 3	4	8
4	39	Male	NHL	Autologous	Regimen 1	4	12
5	28	Male	CML	Related Allogeneic	Regimen 3	3	6
6	36	Female	CML	Unrelated Allogeneic	Regimen 2	4	3
7	21	Male	CML	Unrelated Allogeneic	Regimen 2	4	6
8	25	Female	MS	Related Allogeneic	Regimen 3	4	4
9	26	Female	HL	Autologous	Regimen 1	4	6
10	35	Male	MS	Related Allogeneic	Regimen 3	4	6
11	39	Male	CML	Related Allogeneic	Regimen 3	4	6

Regimen 1 Cyclophosphamide 1800 mg/m²/d, d - 6 and d - 3; carmustine 450 mg/m²/d, d - 2; etoposide 2400 mg/m², d - 7 (34 h).

Regimen 2 Cyclophosphamide 60 mg/kg/d, d - 3 and d - 2; TBI 22 Gy every 12 h, d - 7 to d - 5; antithymocyte globulin 15 mg/kg/d, d - 5 to d - 4.

Regimen 3 Cyclophosphamide 60 mg/kg/d, d - 3 and d - 2; busulfan 4 mg/kg/d, d - 7 to d - 4.

HSCT: Hematopoietic stem cell transplantation

CML: Chronic myeloblastic leukemia; MS: Myelodysplastic syndrome; NHL: Non-Hodgkin lymphoma; HL: Hodgkin lymphoma.

Healing time: In days



Fig. 1. Ulcerous lesion on the right side edge of the tongue, 10 days after HSCT.



Fig. 2. Ulcerous lesion on the left side edge of the tongue, 10 days after HSCT.



Fig. 3. Ulcerous lesion on the right side edge of the tongue, after LPLT Day 15.



Fig. 4. Ulcerous lesion on the left side edge of the tongue, after LPLT Day 15.

0.12 % chlorhexidine solution containing xylitol from D – 7 until neutrophil recovery.

Discussion

It has been noticed that OM begins on average D + 5 (5th day after HSCT) preferably in the buccal mucosa (85.4%), lateral tongue (79.1%) and ventral tongue (70.8%). This clinical picture has been quoted by many authors (2, 6, 7, 12). According to Karthaus et al (6) and Rubeinstein et al (7), in all patients these following signs and symptoms were found: erythema, burning, pain in the oral cavity, ulcers with and without pseudomembrane, bleeding making it difficult to speak and swallow, factors that increased death rates.

The current management of such OM is directed at prevention, palliation, infection prevention, and treatment (1,5,6). The Mucositis Study Group of the Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISOO) reports that for the treatment of mucositis it has been used topic and systemic agents such as: Clindamycin, Granulocyte–colony-stimulating factor, Granulocyte-macrophage–colony-stimulating factor, Gelclair, Nonsteroidal anti-inflammatory drugs, polymyxin E, tobramycin, and amphotericin, Prostaglandin E2 analogue, Prostaglandin inhibitor, Silver nitrate, Sodium alginate, Steroids, Tetrachlorodecaoxide, Traumeel S, Tretinoin cream (0.1%). However, it is vital to claim that by lack of scientific proof these products can neither be indicated or prohibited, making it necessary to perform new randomized placebo-controlled studies with control arrays that make use of evaluation scales of mucositis that are well known and easily applied (7).

In the last years, the laboratorial and clinical experiences have shown that LPLT promotes a tissue bio modulation followed by tissue recovery, which reduces the pain and inflammation. However, there is a lack of patterns and clarity in the scientific essays concerning the application standards from the laser (7-9). Rubeinstein et al (7) quote that LPLT must be used to reduce oral mucositis and also to diminish the patient's pain when they are submitted to chemotherapy of high dosages or conditioning of HSCT (level of evidence, II; grade of recommendation, B). The LPLT may also be used in order to prevent this matter in the patients submitted to HSCT with satisfactory results (1-3). Although, in patients that for any reason have no conditions to receive effective preventive treatment, therapeutic LPLT comes as a new treatment option for OM. The clinical case presented is part of a total amount of 11 patients that presented OM level 3-4 or 12 cm of affected area. We observed that these patients needed an average of 6 days (3-12 days) of LPLT which was enough to heal the ulcers, reducing bruises from the second day of application. But, we also observed that when LPLT is not used and other therapies or only analgesic therapies are applied, the length of OM may achieve 16 days (3).

These patients did not present gingivitis or other signals of oral infection. Negative blood cultures for *Streptococcus* were obtained. This result is probably related with the dental care preparation before the HSCT provided to our patients and previously reported by Barker (13) and NCI (14) and to the dental care during length of hospital stay. In order to prevent infection, we have chosen for an oral hygiene protocol with the usage of toothbrush and dental cream as well as rinsing with an ethanol-free 0.12 % chlorhexidine solution during the whole time of the hospitalization for the transplant. The option to prevent infection, even with good results, is not totally recommended by some authors as Rubeinstein et al (7) and Brenann et al (15) that agree to the previous preparation of the patient and the use of chlorhexidine for bacteria reduction flora but disagree on the use of chlorhexidine at 0.12% during the period that the patient presents ulcers in the oral cavity. Karthaus et al (6) say that chlorhexidine might be a good alternative for the patient that cannot brush their teeth due to OM.

It was not possible to evaluate if the laser application reduced the pain in the oral cavity as mentioned by Barasch et al (3) and Cowen et al (2) for the reason that when our patients presented OM they were already under the application of morphine chlorinate for pain control in the oropharyngeal which appeared previously. The analgesic therapy was applied with infusing bomb, with good results, procedure recommended by several authors (6, 7, 9, 16). Even though the number of cases presented is small, we may conclude that LPLT is efficient in the treatment of oral mucositis because even in patients with OM level 4 the healing time of ulcers was on average 6 days and the patients did not mention any uncomfortably sensation while the laser was being applied.

References

1. Antunes HS, De Azevedo AM, Da Silva Bouzas LF, Adão CA, Pinheiro CT, Mayhe R, et al. Low-power laser in the prevention of induced oral mucositis in bone marrow transplantation patients: a randomized trial. *Blood*. 2007 Mar 1;109(5):2250-5.
2. Cowen D, Tardieu C, Schubert M, Peterson D, Resbeut M, Faucher C, et al. Low energy Helium-Neon laser in the prevention of oral mucositis in patients undergoing bone marrow transplant: results of a double blind randomized trial. *Int J Radiat Oncol Biol Phys*. 1997 Jul 1;38(4):697-703.
3. Barasch A, Peterson DE, Tanzer JM, D'Ambrosio JA, Nuki K, Schubert MM, et al. Helium-neon laser effects on conditioning-induced oral mucositis in bone marrow transplantation patients. *Cancer*. 1995 Dec 15;76(12):2550-6.
4. Sonis ST. The pathobiology of mucositis. *Nat Rev Cancer*. 2004 Apr;4(4):277-84.
5. Köstler WJ, Hejna M, Wenzel C, Zielinski CC. Oral mucositis complicating chemotherapy and/or radiotherapy: options for prevention and treatment. *CA Cancer J Clin*. 2001 Sep-Oct;51(5):290-315.
6. Karthaus M, Rosenthal C, Ganser A. Prophylaxis and treatment of chemo- and radiotherapy-induced oral mucositis - are there new strategies. *Bone Marrow Transplant*. 1999 Nov;24(10):1095-108.
7. Rubenstein EB, Peterson DE, Schubert M, Keefe D, McGuire D, Epstein J, et al. Mucositis Study Section of the Multinational Association for Supportive Care in Cancer; International Society for Oral Oncology. Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer*. 2004 May 1;100(9 Suppl):2026-46.
8. Woodruff LD, Bounkeo JM, Brannon WM, Dawes KS, Barham CD, Waddell DL, et al. The efficacy of laser therapy in wound repair: a meta-analysis of the literature. *Photomed Laser Surg*. 2004 Jun;22(3):241-7.
9. Migliorati CA, Oberle-Edwards L, Schubert M. The role of alternative and natural agents, cryotherapy, and/or laser for management of alimentary mucositis. *Support Care Cancer*. 2006 Jun;14(6):533-40.
10. Sonis ST, Eilers JP, Epstein JB, LeVeque FG, Liggett WH Jr, Mulagha M, et al. Validation of a new scoring system for the assessment of clinical trial research of oral mucositis induced by radiation or chemotherapy. Mucositis Study Group. *Cancer*. 1999 May 15;85(10):2103-13.
11. Parulekar W, Mackenzie R, Bjarnason G, Jordan RC. Scoring oral mucositis. *Oral Oncol*. 1998 Jan;34(1):63-71.
12. Raber-Durlacher JE. Current practices for management of oral mucositis in cancer patients. *Support Care Cancer*. 1999 Mar;7(2):71-4.
13. Barker GJ. Current practices in the oral management of the patient undergoing chemotherapy or bone marrow transplantation. *Support Care Cancer*. 1999 Jan;7(1):17-20.
14. National Cancer Institute. Oral complications of chemotherapy and head and neck radiations. <http://www.cancer.gov/cancertopics/pdq/supportivecare/oralcomplications>. Accessed March 26, 2007.
15. Brennan MT, Von Bültzingslöwen I, Schubert MM, Keefe D. Alimentary mucositis: putting the guidelines into practice. *Support Care Cancer*. 2006 Jun;14(6):573-9.
16. McGuire DB, Correa ME, Johnson J, Wienandts P. The role of basic oral care and good clinical practice principles in the management of oral mucositis. *Support Care Cancer*. 2006 Jun;14(6):541-7.