

# Oral mucositis PBM laser therapy for chemotherapy-induced, OM

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Low-level laser therapy: a standard in the supportive care of cancer therapy-induced oral mucositis in head and neck cancer patients?

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**Background and Objectives:** Oral mucositis (OM) remains a common and severe acute side effect of many oncological treatments, especially in patients being treated for head and neck cancer. It can affect quality of life, requires supportive care, and affects treatment planning and effectiveness. Low-level laser therapy (LLLT) appears to provide pain relief and reduce the incidence and severity of OM. It has been recommended as a treatment option for these patients without any consensus on the LLLT procedure. New recommendations and perspectives for clinical studies are to be discussed.

**Materials (topics) and methods:** The effectiveness of the soft laser in the treatment of iatrogenic oral mucositis was evaluated step by step over the past two decades. Its effectiveness and its level of recommendation got stronger over time. We will report and discuss some key findings and the latest recommendations published on the subject.

**Results:** The most important clinical results were reported and analyzed in a first meta-analysis last year 1). Eleven randomized placebo-controlled studies with a total of 415 patients who were treated with chemotherapy and / or radiation therapy for head and neck cancer were selected. The relative risk of developing OM was significantly reduced after LLLT, but only for a dose between 1 to 6 joules per point. Pain, severity and duration of the OM class  $\geq 2$  were also reduced with regard to possible side effects without any difference to placebo. Nine years after the positive results published for patients treated with radiation therapy only 2), a new French randomized, multicenter phase III study is currently underway for patients who treated with a new standard of care using LLLT as per the latest recommendations. Seven centers will be set up specifically for this study, which will enroll a hundred patients.

**Conclusions:** The very encouraging results of LLLT in the prevention and treatment of OM in patients treated with chemotherapy or radiation therapy for advanced head and neck cancer could soon be considered by the criteria of the multinational Association of Supportive care in Cancer (MASCC) proposed new standard of care. Modern lasers are less time consuming and extra-oral applicators for possible application by trained paramedical staff could be helpful to complete clinical practice. A preventive dose of 2 J / cm<sup>2</sup> and a curative dose of 4 J / cm<sup>2</sup> when using a red wavelength laser are now recommended.

Keywords: low-level laser therapy, oral mucositis, radiation therapy, chemotherapy

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## **Systematic review of photobiomodulation for the treatment of oral mucositis in cancer patients and guidelines for clinical practice**

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### Abstract

**Purpose** Systematic review of the literature and updating of the evidence-based clinical practice guidelines for the application of photobiomodulation (PBM), such as laser and other light therapies, for the prevention and / or treatment of oral mucositis (OM).

**METHODS** A systematic review was carried out by the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer / International Society for Oral Oncology (MASCC / ISOO) using PubMed and the Web of Science. We followed the MASCC methods for systematic review and development of guidelines. The rigorously evaluated evidence for each intervention in each cancer treatment was assigned a level of evidence (LoE). On the basis of the LoE, one of the following guidelines was defined: Recommendation, suggestion or no guideline possible. **Results** Recommendations are made for the prevention of OM and associated pain with PBM therapy in cancer patients treated with any of the following modalities: haematopoietic stem cell transplantation, Head and neck radiation therapy (without chemotherapy) and H&N radiation therapy with chemotherapy. For each of these modalities, we recommend 1-2 clinically effective protocols; the clinician should adhere to all parameters of the chosen protocol. Due to insufficient evidence, no guidelines are currently possible for the treatment of established OM or for the management of chemotherapy-related OM. The reported clinical settings were extremely variable, which limited data integration. Due to insufficient evidence, no guidelines are currently possible for the treatment of established OM or for the management of chemotherapy-related OM. The reported clinical settings were extremely variable, which limited data integration. Due to insufficient evidence, no guideline is currently possible for the treatment of established OM or for the management of chemotherapy-related OM. The reported clinical settings were extremely variable, which limited data integration.

**Conclusions** The evidence supports the use of specific settings of PBM therapy for the prevention of OM in certain patient groups. In these circumstances, PBM is

**Pilot study on the effectiveness of the combined intra- and extraoral low-level laser therapy for the prevention of oral mucositis in pediatric patients who are undergoing a hematopoietic stem cell transplant**

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short version

**Objective and background data:** Studies suggest that low-level intraoral laser therapy (LLLT) can relieve oral mucositis in adult patients receiving high-dose chemotherapy. The aim of this study was to evaluate the use of a combined protocol of intraoral and extraoral LLLT in children undergoing hematopoietic stem cell transplantation (HSCT).

**The Methods:** Twelve children who had to undergo HSCT were treated four times a week with a combined protocol of intra- and extraoral LLLT for an average of 22 days. Clinical and functional mucositis scores were assessed using the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI-CTCAE). These scores were compared with a matched retrospective control group of 12 children who did not receive LLLT during HSCT. **Results:** The clinical mucositis scores were significantly lower in the LLLT group than in the control group ( $p = 0.004$ ). The incidence of ulcerative oral mucositis was also significantly lower in the LLLT group ( $p = 0.027$ ). The functional impairment associated with diet / swallowing was less severe in the LLLT group; however, this was not statistically significant.

**Conclusions:** This study suggests that a combined protocol of intraoral and extraoral use of LLLT can reduce the severity of oral mucositis in pediatric patients with HSCT. Further testing of such combined protocols requires randomized, double-blind clinical trials with a larger number of subjects.

**Low-Level Lasers in the Prevention and Treatment of Oral Mucositis in Pediatric Patients with Acute Lymphoblastic Leukemia**

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**Objective:** The aim of this study was to examine the influence of low- To investigate level laser therapy (LLLT) for the prevention and treatment of oral mucositis (OM) in pediatric cancer patients taking methotrexate.

**Background data:** OM is a very common, potentially serious side effect caused by treatment with radiation therapy and chemotherapy for cancer.

**The Methods:** Forty patients with acute lymphoblastic leukemia who received high doses of methotrexate were divided into two groups. Group A (preventive group) consisted of patients who received a preventive laser (red subgroup A1 or infrared subgroup A2) for 5 days starting with the 1st day of the infusion. Group B (treatment group) consisted of patients who received laser treatment only if they developed mucositis after chemotherapy (red subgroup B1 or infrared subgroup B2). The laser was operated at a wavelength of 660 nm or 830 nm with a power of 100 mW, a power density of 3.57 W / cm<sup>2</sup>, a spot size of 0.028 cm<sup>2</sup>, an energy of 1 J, which led to an energy density of 35 J / cm<sup>2</sup> for 10 sec in the prophylactic group,

**Results:** The percentage of patients who did not develop OM was higher in group A (60% vs. 25%). In Group B, 3/20 patients developed Grade IV OM (15%), and a significant difference was noted between the two subgroups at the end of treatment ( $p = 0.019$ ).

**Conclusion:** The prophylactic laser performed better than when the patients did not receive preventive intervention, and the red laser (660 nm) was better than the infrared laser (830 nm) in the prevention and treatment of OM.

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## Prevention of Induced Oral Mucositis with Low-Level Laser

Therapy in Bone Marrow Transplant **Patients: A Randomized Clinical Trial** Geisa Badauy Lauria Silva, DDS, M.Sc., 1 Elismauro Francisco Mendonça, DDS, M.Sc., Ph.D ., 2, Cesar Bariani, MD, 1 Heliton Spindola Antunes, DDS, M.Sc., 3 and Maria Alves Garcia Silva, DDS, M.Sc., Ph.D.2

### Abstract

**Background data and objective:** Patients who have received high doses of chemotherapy, either alone or in combination with whole-body radiation, often report oral mucositis (OM) as the weakest side effect. The aim of this study was to investigate the clinical effects of low-level laser therapy (LLLT) on the prevention of conditioning-induced OM in hematopoietic stem cell transplantation (HSCT).

The methods: We randomized 42 patients who underwent autologous or allogeneic HSCT. A low-level InGaAlP diode laser was used, which emitted light at 660 nm, 40 mW and 4 J / cm<sup>2</sup>. An assessment of OM was carried out using the World Health Organization scale. Results and Conclusion: In the LLLT group, 57.1% of the patients had an OM grade 0, 9.6% a grade 1 and 33.3% a grade 2, while in the control group only 4.8% of the patients were free of OM (grade 0).

Results: Our results suggest that preventive use of LLLT in patients who have undergone HSCT is an effective tool in reducing the incidence of OM.

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### **Oral Mucositis Severity in Patients Undergoing Hematopoietic Cell Transplantation and Oral Laser Phototherapy Protocol: A Survey of 30 Patients**

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#### **Abstract**

background data and objective: The oral Mucositis (OM) is one of the worst cytotoxic effects of chemotherapy and radiation therapy in patients undergoing hematopoietic cell transplantation (HCT), and it causes severe morbidity.

Laser phototherapy has been considered as an alternative therapy for the prevention and treatment of OM. The aim of this study was to describe the incidence and severity of OM in HCT patients undergoing laser phototherapy and to discuss its effect on the oral mucosa.

The methods: information about the age and gender of the patients, type of underlying disease, conditioning regimen, type of transplant, absence or presence of pain in the oral cavity, degree of OM, and side effects or unusual events were collected from 30 patients who developed HCT (allogeneic or autologous). These patients received daily oral laser phototherapy with an InGaAlP laser (660 nm and 40 mW). The data was recorded in tabular form and its frequency expressed as a percentage.

Results: When analyzing the OM patients, it was found that 33.4% of the patients had Grade I, 40% Grade II, 23.3% Grade III, and 3.3% Grade IV. On the most critical post-HCT days (D\_5 and D\_8) it was observed that 63.3% of patients had grade I disease and 33.3% had grade II disease; no patient had Grade III or IV disease during this period. This severity of OM was similar to other studies on laser phototherapy and OM.

Conclusion: The low levels of OM observed in this study demonstrate the beneficial effects of laser phototherapy, but randomized clinical trials are needed to confirm these findings.

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## **Low-Level Laser Therapy in the Treatment of Chemotherapy-Induced Oral Mucositis: Prophylaxis or Treatment?**

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**Objective:** Chemotherapy-induced oral mucositis (COM) is a common, debilitating complication of cancer therapy. The aim of this study was to investigate the effect of low-level laser therapy (LLLT) on the prevention of COM in patients with haematological malignancies.

**Background data:** OM is a very common, potentially serious side effect caused by treatment with radiation therapy and chemotherapy for cancer.

**The Methods:** Fifty-five patients undergoing chemotherapy at Imam Hospital were included in the study. These patients were divided into two groups. The patient's oral cavity was illuminated with a continuous laser beam using a GaAlAs laser device with a wavelength of 630 nm, an output power of 30 mW and a dose of 5 J / cm<sup>2</sup> for six days (LLLT group). The patients in the second group received placebo irradiation (zero power output) with the similar protocol. The severity of COM was clinically assessed based on the WHO rating scale. The patients' quality of life was assessed before and after the intervention using the EORTC QLQ-C30 questionnaire.

**The results:** The incidence of COM in the LLLT group (31%) was lower than in the placebo group (41%). The mean healing time for COM was 4.8 and 12 days in the LLLT and placebo groups ( $p = 0.03$ ). The xerostomia was significantly less severe in the LLLT group compared to the placebo group ( $p = 0.007$ ).

**Conclusion:** Our results showed that LLLT significantly reduced the incidence of WHO grades 3 and 4 oral mucositis, the weakest form of oral mucositis for which oral nutrition is impossible. In addition, LLLT was able to shorten the duration of oral mucositis, reduce the risk of secondary infection and accelerate the return to normal diet.

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## **Use of the 660 nm diode laser in the prevention and treatment of human oral mucositis induced by radiation and chemotherapy**

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**Aim:** The aim of this multidisciplinary study was to determine the effect of a 660 nm diode laser in

the prevention and treatment of human oral mucositis (OM) in patients with head and neck cancer who underwent radiation - and had undergone chemotherapy, quantitatively and qualitatively.

Background data: OM is a severe oral lesion that results from the toxic effects of treating cancer of the head and neck area. For the prevention and treatment of this oral complication, low-level laser therapy is indicated, which can be used alone or in conjunction with conventional drug treatment to provide pain relief and wound healing.

The methods: 72 patients with head and neck cancer who were treated in the cancer hospital in Mato-Grosso, Brazil, were included in this study and were divided into a control group (C; n=36) and a laser group (L; n=36). The laser therapy was carried out in combination with radiation therapy and chemotherapy twice a week with a diode laser (λ=660 nm, power=30mW, spot size=2 mm, energy=2 J per point).

Results: Statistically significant differences were observed between the two groups. Patients in Group L generally had no OM or pain, but all patients in Group C had OM ranging from Level I to III with pain. This difference was significant from week 1, increased through week 4, and remained stable through week 7.

Conclusion: Laser therapy was effective in preventing and treating oral effects induced by radiation and chemotherapy, thereby improving the patient's quality of life.

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### **Prevention of Induced Oral Mucositis with Low-Level Laser**

Therapy in Bone Marrow Transplant **Patients: A Randomized Clinical Trial** Geisa Badauy Lauria Silva, DDS, M.Sc., 1 Elismauro Francisco Mendonça, DDS, M.Sc., Ph.D., 2, Cesar Bariani, MD, 1 Heliton Spindola Antunes, DDS, M.Sc., 3 and Maria Alves Garcia Silva, DDS, M.Sc., Ph.D. 2

Background data and objective: Patients who have received high doses of chemotherapy, either alone or in combination with whole body radiation, often report oral mucositis (OM) as the weakest side effect. The aim of this study was to investigate the clinical effects of low-level laser therapy (LLLT) on the prevention of conditioning-induced OM in hematopoietic stem cell transplantation (HSCT).

The methods: We randomized 42 patients who underwent autologous or allogeneic HSCT. A low-level InGaAlP diode laser was used, which emitted light at 660 nm, 40 mW and 4 J / cm<sup>2</sup>. An assessment of OM was carried out using the World Health Organization scale.

The Results: Our results suggest that preventive use of LLLT in patients who have undergone HSCT is an effective tool in reducing the incidence of OM.

Conclusion: In the LLLT group 57.1% of the patients had an OM grade 0, 9.6% a grade 1 and 33.3% a grade 2, while in the control group only 4.8% of the patients were free from OM (Grade 0) were.

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**LEVEL LASER THERAPY IN THE PREVENTION AND TREATMENT OF ORAL MUCOSITIS INDUCED BY CANCER TREATMENTS: EVIDENCE-BASED DATA FROM RANDOMIZED STUDIES AND META-**

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**Abstract:** We discuss the promising status of photomedicine for preventive and therapeutic use in oral mucositis (OM) due to cancer therapy.

**Latest findings:** Photomedicine with LLLT or LED is very effective for intra- and extraoral devices in the treatment of OM, as shown by several reports including randomized controlled studies. A systematic review identified 33 relevant articles that were subjected to a meta-analysis, on the basis of which laser parameters are defined in routine practice. The meta-analysis showed that LLLT increased the risk of OM with a relative risk (RR) of 2.45 (CI 1.85-3.18), a shortened duration, the severity of the OM, and a reduced number of days with OM ( 4.38 days,  $p = 0.0009$ ) reduced. The relative risk was similar for the red (630-670 nm) and infrared (780-830 nm) LLLT. The pain-relieving effect on the Cohen scale was 1.22 (CI 0.19-2.25).

**Conclusion:** There is moderate to strong evidence in favor of photomedicine at optimal dosage as a safe, relatively inexpensive intervention for cancer therapy-induced OM. It is anticipated that photomedicine will soon become part of routine oral cancer support.

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PPE

**Objective:** The aim of this study was to demonstrate the utility of low-level laser therapy (LLLT) for the control of painful stomatitis in patients with hand, foot, and mouth disease ( HFMD).

**Background data:** LLLT has been used successfully in various painful conditions affecting the oral mucosa, although there have been few reports of LLLT in HFMD patients.

**The Methods:** In a randomized, double-blind, placebo-controlled study, the painful period of HFMD stomatitis was compared between the LLLT group ( $n = 11$ ) and the placebo LLLT group ( $n = 9$ ), who had a similar clinical background . The LLLT parameters provided were as follows: wavelength 830 nm, power of 30 mW, frequency of 30 Hz and energy output of 1.1 J / cm<sup>2</sup>. Treatment acceptability and safety were also assessed.

**Results:** The painful period was shorter in the LLLT group (4.0 +/- 1.3 days) than in the placebo LLT group (6.7 +/- 1.6 days) with a statistically significant difference (  $p < 0.005$ ). Treatment was judged acceptable in 90.0% (18 out of 20) of patients. In no case were adverse events observed.



Conclusion: The LLLT is a useful method to control HFMD stomatitis by shortening the painful period, with its high acceptance and the absence of adverse events.

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### **Laser phototherapy as topical prophylaxis against radiation-induced xerostomia**

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Jonas Alencar de Matos, DDS, 1 Patricia Moreira Freitas, DDS, MS, Ph.D., 2 and Jose Nicolau, DDS,  
Ph.D.1

**Abstract:** The common consequences of radiation therapy (RT) to the head and neck are oral mucositis, xerostomia, and severe pain. The aim of this study was to examine how laser phototherapy (LPT) used in oral mucositis can influence xerostomia symptoms and hyposalivation in patients undergoing RT. The patients were divided into two groups:

12 people who received three laser irradiations per week (G1) and 10 patients who received laser irradiation per week (G2). A diode laser (660 nm, 6 J = cm<sup>2</sup>, 0.24 J, 40 mW) was used until the lesions had completely healed or until the end of RT. During the first and last laser session, all resting and stimulated saliva was collected and questionnaires were given. According to a Wilcoxon and Student statistical test, the xerostomia in G1 was less than G2 ( $p < 0.05$ ) and the salivary flow rate was not different before and after RT, with the exception of the stimulated collection of G2 which was less ( $p < 0.05$ ).

Our results suggest that LPT can be beneficial as an auxiliary therapy for underactive salivary glands.

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