

# Abstracts - Mucositis

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## Photobiomodulation with low-level laser therapy reduces oral mucositis caused by head and neck radio-chemotherapy: prospective randomized controlled trial.

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### Abstract

The objective of this study was to assess the effectiveness of photobiomodulation with low-level laser therapy (LLLT) as a preventive and therapeutic procedure for the treatment of oral and oropharyngeal mucositis caused by radio-chemotherapy in patients diagnosed with oral squamous cell carcinoma (SCC). An experimental, prospective, double-blind, randomized controlled study was conducted involving patients diagnosed with oral SCC undergoing oncological treatment. The variables analyzed included grade, appearance, and remission of mucositis. A final sample of 26 patients was included: 11 (42.3%) in the study group and 15 (57.7%) in the control group; their average age was  $60.89 \pm 9.99$  years. Statistically significant differences between the groups were observed from week 5 of oncological treatment; 72.7% of the laser group showed normal mucosa (mucositis grade 0), while in the control group, 20.0% showed grade 0 mucositis and 40.0% showed grade 2 mucositis ( $P < 0.01$ ). No statistically significant difference between the groups was found regarding the application or use of medication throughout the study period ( $P > 0.05$ ). The tolerance evaluation did not show any statistically significant difference between the groups regarding the occurrence of side effects or adverse events during the trial ( $P > 0.05$ ). Photobiomodulation with LLLT reduces the incidence and severity of mucositis in patients treated with radiotherapy±chemotherapy.

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## **A systematic review and meta-analysis of the effect of low-level laser therapy (LLLT) on chemotherapy-induced oral mucositis in pediatric and young patients.**

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### **Abstract**

Oral mucositis is one of the most frequent complications after chemotherapy, occurring in approximately 52 to 80% of children receiving treatment for cancer. Recently, it has been suggested that the use of low-energy laser could reduce the grade of oral mucositis and alleviate the symptoms. In 2014, Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology has recommended low-level laser therapy in prevention of mucositis for hematopoietic stem cell transplantation patients because of its beneficial effects in majority of recent studies. However, the recommendation was made for adult patients, not pediatric patients. Data about the effect of low-level laser therapy in pediatric patients is limited. This study aims to synthesize the available clinical evidences on the effects of low-level laser therapy (LLLT) in the prevention and treatment of chemotherapy-induced oral mucositis (OM). A meta-analysis was performed using trials identified through the Cochrane Central Register of Controlled Trials, Embase, MEDLINE, Web of Science, China Biology Medicine (CBM), Wanfang Database, and China National Knowledge Infrastructure (CNKI). Data on occurrence, duration, and severity of oral mucositis were collected. All randomized controlled studies and clinical controlled studies comparing LLLT to routine qualified prevention or treatment during or after chemotherapy were critically appraised and analyzed. We found 8 qualified clinical trials with a total of 373 pediatric patients; the methodological quality was acceptable. After prophylactic LLLT, the odds ratio for developing OM was significantly lower compared with placebo (OR = 0.50, 95% CI 0.29 to 0.87, P = 0.01), the odds ratio for developing grade III OM or worse was statistically significantly lower compared with placebo (OR = 0.30, 95% CI (0.10, 0.90), P = 0.03), and the OM severity was statistically significantly lower compared with placebo (SMD = - 0.56, 95% CI (- 0.98, - 0.14), P = 0.009). For therapeutic LLLT, the OM severity was significantly reduced compared to routine care (SMD = - 1.18, 95% CI (- 1.52, - 0.84), P < 0.00001). Oral pain was also reduced after LLLT over routine care (MD = - 0.73, 95% CI (- 1.36, - 0.11), P = 0.02).

### **CONCLUSION:**

Prophylactic LLLT reduces mucositis and severe mucositis and decreases the average severity of oral mucositis in pediatric and young patients with cancer. Therapeutic LLLT also reduces the average severity of oral mucositis and oral pain. Further research should investigate the optimal parameter of LLLT in pediatric and young patients, and studies with higher methodological quality should be performed. What is known: • Low-level laser therapy (LLLT) was recommended by Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology; however, evidences about LLLT on oral mucositis in pediatric and young patients were insufficient and lack supportive synthesized data. • Recently, there have been several new RCTs or CCTs for pediatric patients or young adults.

What is new: • Prophylactic LLLT reduces the occurrence of mucositis and severe mucositis and decreases the average severity of oral mucositis in pediatric and young patients. • Therapeutic LLLT reduces the average severity of oral mucositis and oral pain.

### **KEYWORDS:**

Chemotherapy; Low-level laser therapy; Oral mucositis; Pediatric patients

## Photodynamic therapy for treatment of oral mucositis: Pilot study with pediatric patients undergoing chemotherapy.

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### Abstract

#### BACKGROUND:

Oral mucositis has become a major dose-limiting toxicity of antineoplastic treatment.

#### AIM:

The aim of this study was to evaluate the effect of photodynamic therapy (PDT) and low level laser therapy (LLLT) on the treatment of chemotherapy-induced mucositis in pediatric patients.

#### METHODS:

An open, controlled, and blind, randomized clinical trial was conducted with 29 patients, from 10 months to 18 years old, who were divided into two groups. Group A was submitted to photodynamic therapy (0.01% Methylene Blue and red laser,  $\lambda$ 660 nm) with 3J energy per point; and Group B submitted to low level laser therapy ( $\lambda$ 660 nm) with 1J energy per point. The results were evaluated by using the WHO and ChIMES mucositis scales. The Chi-square, Exact Fisher, Student's-t and Mann-Whitney tests, and the mixed linear regression model were used for comparison between the groups, with the maximum error admitted of 5%.

#### RESULTS:

There was no difference between the groups as regards the number of sessions necessary for clinical cure of the oral lesions ( $p = 0.954$ ) or reduction in pain reported by the patients ( $p = 0.258$ ;  $p = 0.486$ ). Within each group, however, there was significant reduction in pain ( $p = 0.032$ ;  $p = 0.003$ ). The number needed to treat (NNT) was 4.75.

#### CONCLUSIONS:

PDT or LLLT could be used for treatment of oral mucositis in children/young patients. Each were well tolerated and presented satisfactory results in reducing pain associated with the lesion.

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#### KEYWORDS:

Oral mucositis; Photochemotherapy; Photodynamic therapy; Phototherapy

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# Long-term survival of a randomized phase III trial of head and neck cancer patients receiving concurrent chemoradiation therapy with or without low-level laser therapy (LLLT) to prevent oral mucositis.

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## Abstract

### BACKGROUND:

The impact of low-level laser therapy (LLLT) to prevent oral mucositis in patients treated with exclusive chemoradiation therapy remains unknown. This study evaluated the overall, disease-free and progression-free survival of these patients.

### METHODS:

Overall, disease-free and progression-free survival of 94 patients diagnosed with oropharynx, nasopharynx, and hypopharynx cancer, who participated on a phase III study, was evaluated from 2007 to 2015. The patients were subjected to conventional radiotherapy plus cisplatin every 3weeks. LLLT was applied with an InGaAlP diode (660nm-100mW-1J-4J/cm<sup>2</sup>).

### RESULTS:

With a median follow-up of 41.3months (range 0.7-101.9), patients receiving LLLT had a statistically significant better complete response to treatment than those in the placebo group (LG=89.1%; PG=67.4%; p=0.013). Patients subjected to LLLT also displayed increase in progression-free survival than those in the placebo group (61.7% vs. 40.4%; p=0.030; HR:1.93; CI 95%: 1.07-3.5) and had a tendency for better overall survival (57.4% vs. 40.4%; p=0.90; HR:1.64; CI 95%: 0.92-2.91).

### CONCLUSION:

This is the first study to suggest that LLLT may improve survival of head and neck cancer patients treated with chemoradiotherapy. Further studies, with a larger sample, are necessary to confirm our findings.

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### KEYWORDS:

Chemotherapy; Disease-free survival; Head and neck cancer; Low-level laser therapy; Oral mucositis; Overall survival; Progression-free survival; Radiotherapy

## Effect of laser phototherapy in the prevention and treatment of chemo-induced mucositis in hamsters.

Lopez TC, Martins MD, Pavesi VC, Ferreira LS, Bussadori SK, Moreira MS, Marques MM.

### Source

Univ de São Paulo, School of Dentistry, Department of Restorative Dentistry, ,São Paulo,SP, Brazil.

### Abstract

The aim of this study was to investigate the effect of laser phototherapy (LPT) in the prevention and/or treatment of oral mucositis induced by 5-fluorouracil (5-FU; Eurofarma, São Paulo, Brazil) in hamsters. Ninety-six hamsters were divided into four groups (n = 24): Control (no treatment); Preventive [LPT from day (D) D-5 to D+5]; Therapeutic (LPT from D+5 to D+15); and Combined (preventive plus therapeutic LPT from D-5 to D+15). The animals received an intraperitoneal injection of 5-FU on Days 0 and 2. The pouch mucosa was scratched on Days 3 and 4.

The irradiation parameters were: indium-gallium-aluminum-phosphide (InGaAlP) diode laser (MM Optics, São Carlos, Brazil) (660 nm), beam area of 0.036 cm<sup>2</sup>, 40 mW, 1.11 W/cm<sup>2</sup>, 6.6 J/cm<sup>2</sup>, power density applied daily of 39.6 J/cm<sup>2</sup>, in punctual mode (six points and six seconds per point) and contact mode, one application per day.

The animals were sacrificed on Days 0, 5, 10 and 15 (n = 6) and weighed, and the pouch mucosa was removed for histopathological analysis. Clinical and corresponding histological scores were compared using ANOVA and Tukey's test (p ≤ 0.05). S

imilar weight losses ranging from 5% to 10% occurred in all groups. The therapeutic group had significantly lower clinical and histological scores than the other groups at Day 10.

This study showed that positive effects on oral mucositis management were obtained only when LPT was applied in the therapeutic protocol (from D+5 to D+15 after chemotherapy).

## **Effect of low-level laser therapy on patient reported measures of oral mucositis and quality of life in head and neck cancer patients receiving chemoradiotherapy--a randomized controlled trial.**

[Gautam AP](#), [Fernandes DJ](#), [Vidyasagar MS](#), [Maiya AG](#), [Nigudgi S](#).

### **Source**

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### **Abstract**

#### **PURPOSE:**

Chemoradiotherapy (CRT)-induced oral mucositis (OM) adversely affects a patient's oral functions and quality of life (QOL). Low-level laser therapy (LLLT) showed some preventive and curative effects against clinically reported objective measures of OM in few trials including our recently published study. There is dearth of evidence regarding the effects of LLLT on patient's subjective experience of OM and QOL. Hence, we did this study to evaluate the effects of LLLT on a patient's reported measures of OM and QOL in head and neck cancer (HNC) patients receiving CRT.

#### **METHODS:**

This triple blinded study randomized 220 HNC patients scheduled for CRT (three weekly Cisplatin + RT = 66 Gray (2 Gy/session), five fractions/week for 6.5 weeks, total 33 fractions) into laser (110) and placebo (110) groups. The laser group received LLLT (Technomed Electronics Advanced Laser Therapy 1000, He-Ne,  $\lambda = 632.8$  nm, power density = 24 mW/cm<sup>2</sup>, dosage = 3.0 J at each point, total dose/session = 36-40 J, spot size 1 cm<sup>2</sup>, irradiation time/point 125 s) before each radiation session, while the placebo group did not receive laser therapy. Methodology was similar to our recently published study (Gautam et al. *Radiother Oncol* 104:349-354, 2012). In this part of our study, a blinded assessor collected subjective outcomes of the patient's reported measures of OM using Oral Mucositis Weekly Questionnaire-Head and Neck (OMWQ-HN) and QOL using Functional Assessment of Cancer Treatment-Head and Neck (FACT-HN) Questionnaire. Data were analyzed using repeated measure ANOVA through general linear model. Statistical significance was kept at  $p < 0.05$ .

#### **RESULTS:**

Results analysis revealed that OMWQ-HN ( $F = 12.199$ ,  $df = 6, 1314$ ,  $p < 0.001$ ) and FACT-HN ( $p < 0.05$ ) scores were significantly lower in LLLT than placebo group patients. Also, a significant reduction ( $p < 0.001$ ) in incidence of severe OM, need for opioid analgesics, and total parenteral nutrition was observed.

#### **CONCLUSIONS:**

LLLT was effective in improving the patient's subjective experience of OM and QOL in HNC patients receiving CRT.

## **Amelioration of oral mucositis pain by NASA near-infrared light-emitting diodes in bone marrow transplant patients.**

Hodgson BD, Margolis DM, Salzman DE, Eastwood D, Tarima S, Williams LD, Sande JE, Vaughan WP, Whelan HT.

### **Source**

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### **Abstract**

#### **PURPOSE:**

This study seeks to investigate the use of extra-orally applied near-infrared phototherapy for the reduction of oral pain secondary to chemotherapy- and radiation therapy-induced mucositis in adult and pediatric hematopoietic stem cell transplant (HSCT) patients.

#### **METHODS:**

Eighty HSCT patients were divided into regular (R) and low (L) risk groups, then to experimental (E) and placebo (P) groups, resulting in four groups (ER, EL, PR, PL). Experimental subjects received 670 ( $\pm 10$ ) nm gallium-aluminum-arsenide light-emitting diode device for 80 s at  $\sim 50$  mW/cm<sup>2</sup> energy density and power exposure of 4 J/cm<sup>2</sup>. Placebo patients received the same procedures, but with a placebo phototherapy (identical device but  $<5$  mW/cm<sup>2</sup> energy density). Patients received their respective light therapy once per day starting on the day of the HSCT (day 0) and continued through day +14. Blinded evaluators examined the patients three times per week and scored their oral tissues and patient-reported pain assessments at each evaluation utilizing the WHO, NCI-CTCAE, and OMAS scales.

#### **RESULTS:**

Analysis of the mean scores at each observation demonstrate that the extra-oral application of phototherapy resulted in a significant reduction in patient-reported pain between the ER and PR patients ( $p < 0.05$ ) at day +14 when graded via the WHO criteria. The ER and EL patients were improved in almost all other categories and assessment scales, but the differences were not statistically significant.

#### **CONCLUSION:**

Phototherapy demonstrated a significant reduction in patient-reported pain as measured by the WHO criteria in this patient population included in this study. Improvement trends were noted in most other assessment measurements.

## **Efficacy of He-Ne Laser in the prevention and treatment of radiotherapy-induced oral mucositis in oral cancer patients.**

[Arora H](#), [Pai KM](#), [Maiya A](#), [Vidyasagar MS](#), [Rajeev A](#).

### **Source**

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### **Abstract**

#### **OBJECTIVE:**

The objective of this study was to evaluate the efficacy of low-level lasers for the prevention and treatment of radiotherapy-induced oral mucositis in oral cancer patients.

#### **MATERIAL AND METHODS:**

Twenty-four hospitalized patients with oral cancer, scheduled to undergo radiotherapy at KMC, Manipal, were enrolled in the present study and assigned to laser (Group I)/control group (Group II). They were treated using He-Ne laser ( $\lambda = 632.8\text{nm}$ , output = 10 mW and energy density = 1.8 J/cm<sup>2</sup>). Patients were subjected to treatment using laser scanner for 8 days and subsequently were treated using laser probe at 6 anatomic sites in the oral cavity for 5 minutes each. The patients were evaluated on each day of treatment for pain severity (NRS), functional impairment (FIS), and oral mucositis (RTOG) and were followed until the end of cancer treatment. Statistical analysis was done using SPSS version 10.

#### **RESULTS:**

Laser therapy applied prophylactically during radiotherapy can reduce the severity of oral mucositis, severity of pain, and functional impairment.

PMID:18230388 [PubMed - indexed for MEDLINE]

## **Effect of low level helium-neon (He-Ne) laser therapy in the prevention & treatment of radiation induced mucositis in head & neck cancer patients.**

[Arun Maiya G](#), [Sagar MS](#), [Fernandes D](#).

### **Source**

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### **Abstract**

#### **BACKGROUND & OBJECTIVES:**

Oral mucositis is a common debilitating complication of radiotherapy occurring in about 60 per cent of cancer patients. Considerable buccal toxicity of radiotherapy or chemotherapy in cancer patients to become discouraged and can affect their quality of life. In addition, such toxicity can alter the treatment plan. At present, there is no clinically appropriate prophylaxis efficacious antidote for mucositis. The low level laser (LEL) appears to be a simple, non-traumatic technique for the prevention and treatment of radiation induced mucositis. Therefore the present study was carried out to find out the effect of low-level helium-neon (He-Ne) laser in the prevention and treatment of radiation induced mucositis in head and neck cancer patients.

#### **METHODS:**

The patients with carcinoma of oral cavity with stages II-IV a being uniformly treated with curative total tumour dose of 66 Gy in 33 fractions over 6 wk were selected for the study. The patients were divided based on computer generated randomization into laser (study group) and control groups with 25 patients in each group. Both study and control groups were comparable in terms of site of the lesion, stage of the cancer and histology. The study group patients were treated with He-Ne laser (wavelength 632.8 nm and output of 10mW) and control group patients were given oral analgesics, local application of anaesthetics, 0.9 per cent saline and povidine wash during the course of radiotherapy.

#### **RESULTS:**

All patients tolerated the laser treatment without any adverse effect or reactions. The result showed a significant difference in pain and mucositis ( $P < 0.001$ ) between the two groups. At the end of radiotherapy (after 6 wk) mean pain score and mucositis grade were significantly lower ( $P < 0.001$ ) in the study group compared to control.

#### **INTERPRETATION & CONCLUSION:**

The low-level He-Ne laser therapy during the radiotherapy treatment was found to be effective in preventing and treating the mucositis in head and neck cancer patients. Further studies need to be done on a larger sample to find the mechanism.

Comment in: [Low level laser therapy \(LLLT\): a new paradigm in the management of cancer therapy-induced mucositis ?](#)

[*Indian J Med Res.* 2006]Low level laser therapy (LLLT): a new paradigm in the management of cancer therapy-induced mucositis ? *Bensadoun R.J. Indian J Med Res.* 2006 Oct; 124(4):375-8.

PMID: 17159259 [PubMed - indexed for MEDLINE]

## **Low energy Helium-Neon laser in the prevention of oral mucositis in patients undergoing bone marrow transplant: results of a double blind randomized trial.**

[Cowen D](#), [Tardieu C](#), [Schubert M](#), [Peterson D](#), [Resbeut M](#), [Faucher C](#), [Franquin JC](#).

### **Source**

Department of Radiotherapy, Institut Paoli-Calmettes, Cancer Center, Marseilles, France.

### **Abstract**

#### **PURPOSE:**

To evaluate the efficiency of Helium-Neon (He-Ne) laser in the prevention of oral mucositis induced by high dose chemoradiotherapy before autologous bone marrow transplantation (BMT).

#### **METHODS AND MATERIALS:**

Between 1993 and 1995, 30 consecutive patients receiving an autologous peripheral stem-cell or bone marrow transplant (BMT) after high dose chemoradiotherapy were randomized to possibly receive prophylactic laser to the oral mucosa after giving informed consent. Chemotherapy consisted of cyclophosphamide, 60 mg/kg intravenously (I.V.) on day (d)-5 and d-4 in 27 cases, or melphalan 140 mg/kg I.V. on d-4 in three cases. Total body irradiation (TBI) consisted of 12 Gy midplane dose in six fractions (4 Gy/day for three days). He-Ne laser (632.8 nm wavelength, power 60 mW) applications were performed daily from d-5 to d-1 on five anatomic sites of the oral mucosa. Oral examination was performed daily from d0 to d + 20. Mucositis was scored according to an oral exam guide with a 16 item scale of which four were assessed by the patients themselves. Mean daily self assessment scores for oral pain, ability to swallow and oral dryness were measured. A daily mucositis index (DMI) and a cumulative oral mucositis score (COMS) were established. Requirement for narcotics and parenteral nutrition was recorded.

#### **RESULTS:**

The COMS was significantly reduced among laser treated (L+) patients ( $p = 0.04$ ). The improvement of DMI in L+ patients was also statistically significant ( $p < 0.05$ ) from d + 2 to d + 7. Occurrence and duration of grade III oral mucositis were reduced in L+ patients ( $p = 0.01$ ). Laser applications reduced oral pain as assessed by patients ( $p = 0.05$ ) and L+ patients required less morphine ( $p = 0.05$ ). Xerostomia and ability to swallow were improved among the L+ patients ( $p = 0.005$  and  $p = 0.01$ , respectively). Requirement for parenteral nutrition was not reduced ( $p = NS$ ).

#### **CONCLUSION:**

Helium-Neon laser treatment was well tolerated, feasible in all cases, and reduced high dose chemoradiotherapy-induced oral mucositis. Optimal laser treatment schedules still needs to be defined.