

Photobiomodulation (PBM) / Low Level laser Therapy (LLLT)

THOR Photomedicine Research Digest

www.thorlaser.com

Search criteria: Oral Mucositis

Search Date: 10 July 2018

Prepared for: THOR website

Prepared by: Dr. Patricia Burton

Notes: A selection of OM aspects improved by PBMT

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.

Antunes HS, Herchenhorn D, Small IA, Araújo CMM, Viégas CMP, de Assis Ramos G, Dias FL, Ferreira CG

Clinical Research Division, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil. Electronic address: hspindola@inca.gov.br. Head and Neck Oncology Group, Grupo de Oncologia D'Or, Brazil. Clinical Research Division, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil. Radiation Oncology Division, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil. Radiation Oncology Division, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil. Clinical Research Division, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil. Head and Neck Surgery Division, Instituto Nacional de Câncer (INCA), Rio de Janeiro, Brazil. D'Or Institute for Research and Education, Brazil.

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 3 weeks. LLLT was applied with an InGaAlP diode (660nm-100mW-1J-4J/cm²). **RESULTS:** With a median follow-up of 41.3 months (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.

Oral Oncol 2017 Aug 71 11-15

<http://www.ncbi.nlm.nih.gov/pubmed/?term=28688677>

Effect of low-level laser therapy on chemoradiotherapy-induced oral mucositis and salivary inflammatory mediators in head and neck cancer patients.

Oton-Leite AF, Silva GB, Morais MO, Silva TA, Leles CR, Valadares MC, Pinezi JC, Batista AC, Mendonca EF

Department of Oral Medicine (Oral Pathology), Dental School, Federal University of Goias, Goiania, Goias, 74605-220, Brazil.

BACKGROUND AND OBJECTIVE: Oral mucositis (OM) is considered a painful and debilitating side effect in patients receiving head and neck cancer treatment. Low-level laser therapy (LLLT) proved to be effective to prevent and treat chemoradiotherapy-induced OM. The aim of this study was to evaluate the effect of LLLT in the severity of OM in patients with head and neck cancer and on the release of salivary inflammatory mediators. Clinical (score of OM severity) and biochemical parameters (concentration of inflammatory mediators, growth factors, and enzymes in saliva) were used. **MATERIALS AND METHODS:** Thirty patients were randomized into two groups: control and laser. LLLT was performed three times a week in the laser group, while control group received sham irradiation. OM severity was assessed according to the World Health Organization (WHO) and National Cancer Institute (NCI) scales. Pro-inflammatory and anti-inflammatory cytokines (TNF-alpha, IL-6, IL-1beta, IL-10, TGF-beta), growth factors (EGF, FGF, VEGF), and metalloproteinases (MMP2/TIMP2, MMP9/TIMP2) concentrations were assessed using ELISA test. Saliva samples were collected on admission, and at the 7th, 21st, and 35th sessions of radiotherapy. **RESULTS:** The laser group showed a reduction in the severity of OM, which coursed with significantly diminished salivary concentration of EGF and VEGF in the 7th radiotherapy session and of IL-6 and FGF in the 35th. There was a trend for reduced levels of IL-1beta, TNF-alpha, IL-10, TGF-beta, MMP2/TIMP2, MMP9/TIMP2 in the laser group compared to the control, however, no statistically significant differences were found. **CONCLUSIONS:** These findings demonstrated that LLLT was effective in reducing the severity of chemoradiotherapy-induced OM and was associated with the reduction of inflammation and repair. *Lasers Surg. Med.* 47:296-305, 2015. (c) 2015 Wiley Periodicals, Inc.

Lasers Surg Med 2015 Apr 47(4) 296-305

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25824475>

Low level laser therapy against radiation induced oral mucositis in elderly head and neck cancer patients-a randomized placebo controlled trial.

Gautam AP, Fernandes DJ, Vidyasagar MS, Maiya AG, Guddattu V

Department of Radiotherapy and Oncology, Kasturba Medical College and Hospital, Manipal University, Manipal, Karnataka, India; Department of Physiotherapy, Manipal College of Allied Health Sciences, Manipal University, Manipal, Karnataka, India. Electronic address: ajayphysio@gmail.com. Department of Radiotherapy and Oncology, Kasturba Medical College and Hospital, Manipal University, Manipal, Karnataka, India. Electronic address: [donaaldjf@gmail.com](mailto:donaldjf@gmail.com). Department of Physiotherapy, Manipal College of Allied Health Sciences, Manipal University, Manipal, Karnataka, India. Electronic address: vsagar32@yahoo.com. Department of Physiotherapy, Manipal College of Allied Health Sciences, Manipal University, Manipal, Karnataka, India. Electronic address: ajmaiya@yahoo.com. Department of Biostatistics, Manipal University, Manipal, Karnataka, India. Electronic address: vasudev.guddattu@gmail.com.

OBJECTIVES: Radiotherapy (RT) is treatment of choice for Elderly Head and Neck Cancer (HNC) patients. Oral mucositis (OM) during RT affects patient's routine oral activities and overall health. Low Level Laser Therapy (LLLT) provided some promising results against cancer therapy induced OM in children and adults. No study specifically evaluated effects of LLLT against RT induced OM in elderly HNC patients until date, hence we did this study.

MATERIAL AND METHODS: This double blinded study randomized 46 elderly HNC patients scheduled for RT [Dosage=66 Gray (2 Gy/fraction), 5 fractions/week, total 33 fractions for 6.5 weeks], into laser (22) and placebo (24) groups. Laser group patients received LLLT [Helium-Neon, $\lambda=632.8$ nm, power density=0.024 W/cm²), dosage=3.0 J/point at six anatomical sites bilaterally i.e. 12 locations, total dose/session=36 J, beam aperture diameter=0.6 mm, beam spot size=1 cm²), irradiated area diameter=1 cm²), irradiation time/point=125 s, 5 sessions/week, non-contact method-distance between probe and irradiated tissues <1 cm, whereas placebo group did not receive laser. OM grades (RTOG/EORTC Scale), oral pain, weight loss, need for morphine analgesics and tube feeding, and RT break were recorded by a blinded assessor. Descriptive statistics and repeated measures ANOVA were used for analysis keeping $p<0.05$.

RESULTS: Significant reduction in the incidence and duration of severe OM ($p=0.016$) and severe pain ($p=0.023$) and weight loss ($p=0.004$) was observed in laser than placebo group. No difference was found for enteral feeding use ($p=0.667$) between two groups.

CONCLUSIONS: LLLT decreased the severity of OM and oral pain in elderly HNC patients. Also, lesser weight loss, morphine analgesic use and radiation break happened in laser group.

J Photochem Photobiol B 2015 Mar 144 51-6

<http://www.ncbi.nlm.nih.gov/pubmed/?term=25704314>

Phase III trial of low-level laser therapy to prevent oral mucositis in head and neck cancer patients treated with concurrent chemoradiation.

Antunes HS, Herchenhorn D, Small IA, Araujo CM, Viegas CM, Cabral E, Rampini MP, Rodrigues PC, Silva TG, Ferreira EM, Dias FL, Ferreira CG

Coordination of Clinical Research, Instituto Nacional de Cancer (INCA), Rio de Janeiro, Brazil. Electronic address: hspindola@inca.gov.br.
Brazil

BACKGROUND: Oral mucositis (OM) is a complication of chemoradiotherapy treatment of head and neck squamous cell carcinoma (HNSCC) patients with no effective therapy. This study was designed to assess the efficacy of preventive low-level laser therapy (LLLT) in reducing the incidence of grade 3-4 OM. **MATERIAL AND METHODS:** From June 2007 to December 2010, 94 HNSCC patients entered a prospective, randomized, double-blind, placebo-controlled phase III trial. Chemoradiotherapy consisted of conventional radiotherapy plus concurrent cisplatin every 3 weeks. A diode InGaAlP (660nm-100mW-1J-4J/cm²) was used. OM evaluation was performed by WHO and OMAS scales and quality of life by EORTC questionnaires (QLQ). **RESULTS:** A six-fold decrease in the incidence of grades 3-4 OM was detected in the LLLT group compared to the placebo; (6.4% versus 40.5%). LLLT impacted the incidence of grades 3-4 OM to a relative risk ratio of 0.158 (CI 95% 0.050 -0.498). After treatment QLQ-C30 showed, differences favoring LLLT in physical, emotional functioning, fatigue, and pain; while the QLQ-H&N35 showed improvements in LLLT arm for pain, swallowing, and trouble with social eating. **CONCLUSION:** Preventive LLLT in HNSCC patients receiving chemoradiotherapy is an effective tool for reducing the incidence of grade 3-4 OM. Efficacy data were corroborated by **improvements seen in quality of life.**

Radiother Oncol 2013 Sep 14

<http://www.ncbi.nlm.nih.gov/pubmed/?term=24044799>

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

Department of Radiotherapy and Oncology, Kasturba Medical College and Hospital, Manipal University, Manipal, Karnataka 576104, India, ajayphysio@gmail.com.
India

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/cm², dosage = 3.0 J at each point, total dose/session = 36-40 J, spot size 1 cm², 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.

Support Care Cancer 2012 Dec 8

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23224689>

Low-power laser in the prevention of induced oral mucositis in bone marrow transplantation patients: a randomized trial.

Antunes HS, de Azevedo AM, da Silva Bouzas LF, Adao CA, Pinheiro CT, Mayhe R, Pinheiro LH, Azevedo R, D'Aiuto de Matos V, Rodrigues PC, Small IA, Zangaro RA, Ferreira CG.

Section of Dentistry, Instituto Nacional de Cancer (INCA), Rio de Janeiro.
Brazil

We investigated the clinical effects of low-power laser therapy (LPLT) on prevention and reduction of severity of conditioning-induced oral mucositis (OM) for hematopoietic stem cell transplantation (HSCT). We randomized 38 patients who underwent autologous (AT) or allogeneic (AL) HSCT. A diode InGaAlP was used, emitting light at 660 nm, 50 mW, and 4 J/cm², measured at the fiberoptic end with 0.196 cm² of section area. The evaluation of OM was done using the Oral Mucositis Assessment Scale (OMAS) and the World Health Organization (WHO) scale. In the LPLT group, 94.7% of patients had an OM grade (WHO) lower than or equal to grade 2, including 63.2% with grade 0 and 1, whereas in the controls group, 31.5% of patients had an OM grade lower than or equal to grade 2 ($P < .001$). Remarkably, the hazard ratio (HR) for grades 2, 3, and 4 OM was 0.41 (range, 0.22-0.75; $P = .002$) and for grades 3 and 4 it was 0.07 (range, 0.11-0.53; $P < .001$). Using OMAS by the calculation of ulcerous area, 5.3% of the laser group presented with ulcers of 9.1 cm² to 18 cm², whereas 73.6% of the control group presented with ulcers from 9.1 cm² to 18 cm² ($P = .003$). Our results indicate that the use of upfront LPLT in patients who have undergone HSCT is a powerful instrument in **reducing the incidence of OM** and **is now standard in our center.**

Blood 2007 Mar 109 (5) 2250-55

<http://www.ncbi.nlm.nih.gov/pubmed/?term=17053058>

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

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

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 ($p = \text{NS}$). **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.

Int J Radiat Oncol Biol Phys 1997 Jul 1 38(4) 697-703

<http://www.ncbi.nlm.nih.gov/pubmed/?term=9240635>

More information available online

Visit www.thorlaser.com

Visit blog.thorlaser.com

Visit www.novothor.com

[Watch video interviews](#)

[View training locations and dates](#)

[Sign up to our newsletter](#)

[Make a purchase enquiry](#)