Cost-effectiveness of low-level laser therapy (LLLT) in head and neck cancer patients receiving concurrent chemoradiation.

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BACKGROUND: Oral mucositis is a major event increasing treatment costs of head and neck squamous cell carcinoma (HNSCC) patients treated with chemoradiation (CRT). This study was designed to estimate the cost-effectiveness of low-level laser therapy (LLLT) to prevent oral mucositis in HNSCC patients receiving CRT. METHODS: From June 2007 to December 2010, 94 patients with HNSCC of nasopharynx, oropharynx, and hypopharynx entered a prospective, randomized, double blind, placebo-controlled, phase III trial. CRT consisted of conventional radiotherapy (RT: 70.2Gy, 1.8Gy/d, 5times/wk) +concurrent cisplatin (100mg/m2) every 3weeks. An InGaAlP (660nm-100mW-4J/cm2) laser diode was used for LLLT. RESULTS: From the perspective of Brazil's public health care system (SUS), total costs were higher in Placebo Group (PG) than Laser Group (LG) for opioid use (LG=US$ 9.08, PG=US$ 44.28), gastrostomy feeding (LG=US$ 50.50, PG=US$ 129.86), and hospitalization (PG=US$ 77.03). In LG, the cost was higher for laser therapy only (US$ 1880.57). The total incremental cost associated with the use of LLLT was US$ 1689.00 per patient. The incremental cost-effectiveness ratio (ICER) was US$ 4961.37 per grade 3-4 OM case prevented compared to no treatment. CONCLUSIONS: Our results indicate that morbidity was lower in the Laser Group and that LLLT was more cost-effective than placebo up to a threshold of at least US$ 5000 per mucositis case prevented. CLINICAL TRIAL INFORMATION: NCT01439724.

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Pilot Study on the Efficacy of Combined Intraoral and Extraoral Low-Level Laser Therapy for Prevention of Oral Mucositis in Pediatric Patients Undergoing Hematopoietic Stem Cell Transplantation.

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OBJECTIVE AND BACKGROUND DATA: Studies suggest that intraoral low-level laser therapy (LLLT) can ameliorate oral mucositis in adult patients receiving high-dose chemotherapy. The objective 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). METHODS: Twelve children undergoing HSCT were treated four times a week with a combined protocol of intraoral and extraoral LLLT, for a mean duration of 22 days. Clinical and functional mucositis scores were assessed using the National Cancer Institute 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: Clinical mucositis scores were significantly lower in the LLLT group than in the control group ($p = 0.004$). Incidence of ulcerative oral mucositis was also significantly lower in the LLLT group ($p = 0.027$). Functional limitation associated with diet/swallowing was less severe in the LLLT group; however, this was not statistically significant. CONCLUSIONS: This study indicates that a combined protocol of intraoral and extraoral application of LLLT can reduce the severity of oral mucositis in pediatric patients undergoing HSCT. Randomized double-blind clinical trials with a larger number of subjects are needed to further test such combined protocols.

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Low-level laser therapy prevents severe oral mucositis in patients submitted to hematopoietic stem cell transplantation: a randomized clinical trial.

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PURPOSE: The purpose of this study is to evaluate the effectiveness of low-level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic stem cell transplantation. METHODS: This is a randomized, parallel, superiority trial including 35 patients divided into the following: laser (n = 17) and sham (n = 18). The variables assessed were oral mucositis (grade 2 of the World Health Organization oral toxicity scale), severe oral mucositis (grade 3 or 4), and pain (according to a visual analogue scale). In the laser group, a InGaAlP laser, wavelength of 650 nm, power 100 mW, energy per point of 2 J, time 20 s by point, extremity fiber optic 0.028 cm2, and energy density 70 J/cm2, was used, applied the first day of conditioning until D + 5, while the sham group received simulated laser over the same period. RESULTS: No statistically significant difference was found in the incidence of oral mucositis (p = 0.146). Severe mucositis was found in 40 % of the patients (14/35), 3 in the intervention group (17.65 %) and 11 in the sham group (61.11 %) (p = 0.015). The cumulative probability of survival with respect to the development of severe oral mucositis was >0.6 for the intervention group and 0 for the control group (p = 0.0397). On the day on which pain was considered the worst, patients in the sham group were more likely to classify their pain as severe compared to those in the laser group (p = 0.041). CONCLUSION: Low-level laser therapy proved effective for the prevention of severe oral mucositis and intense oral pain in patients submitted to hematopoietic stem cell transplantation.

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Low-level laser therapy for treatment of chemotherapy-induced oral mucositis in childhood: a randomized double-blind controlled study.

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The aim of this study was to verify if low-level laser therapy could be useful to reduce chemotherapy-related oral mucositis grading and pain in childhood undergoing chemotherapy. A randomized double-blind clinical trial was carried out. Patients from 3 to 18 years of age undergoing cancer therapy and presenting OM grade 2 or more were eligible for this study. Patients were randomly divided in two groups: group A received laser therapy from the day of OM diagnosis and other 3 consecutive days (830 nm wavelength, power 150 mW, spot size 1 cm2, 30 s per cm2, energy density 4.5 J/cm2); group B received sham therapy (placebo) with the same timing. Two blind clinicians performed OM scoring and pain evaluation at day 1 (immediately before the beginning of laser treatment-T0), day 4 (after finishing laser therapy cycle-T1) and at day 7 (T2) as follow-up. A total of 123 patients were included in the study. Group A was composed of 62 children while group B is 61; in both groups, there was a progressive reduction in grade of OM, and at day 7, not every mucosal lesion disappeared. The difference in the decline of OM grading between the two groups resulted not statistically significant ($p = 0.07$). A statistically significant difference in pain reduction between two groups both at T1 and at T2 ($p < 0.005$) was observed. This study demonstrated the efficacy of LLLT in reducing pain due to chemotherapy-induced oral mucositis in children, while no significant benefit was noted in reducing OM grade.

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The Impact of Low-Level Laser Therapy on Oral Mucositis and Quality of Life in Patients Undergoing Hematopoietic Stem Cell Transplantation Using the Oral Health Impact Profile and the Functional Assessment of Cancer Therapy-Bone Marrow Transplantation Questionnaires.

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OBJECTIVE: The aim of this study was to assess the impact of low-level laser therapy (LLLT) on oral mucositis (OM) and quality of life (QoL) of hematopoietic stem cell transplantation (HSCT) patients. BACKGROUND DATA: OM related to high-dose chemotherapy is often associated with increased risk of mortality and impaired QoL in HSCT patients. LLLT has shown promising effects in the prevention and treatment of chemotherapy-induced OM. There is a dearth of literature focused on subjective aspects involving OM and QoL in patients receiving LLLT. METHODS: Thirty-nine patients were randomly assigned to two groups: control (n=19) and laser (n=20). LLLT was performed from the 1st day of the conditioning regimen until day 7 post-HSCT (D+7). OM severity was evaluated in all patients [World Health Organization (WHO) scale]. A blinded observer collected subjective outcomes from patients on admission (AD), D+7 and at discharge (DC). QoL was assessed using the Oral Health Impact Profile (OHIP-14) and the Functional Assessment of Cancer Therapy-Bone Marrow Transplantation (FACT-BMT) questionnaires. Statistical analyses included descriptive, bivariate and multivariate (generalized estimating equation) tests. RESULTS: The overall FACT-BMT (p=0.074) and OHIP-14 (p=0.749) scores were not associated with the use of laser therapy. Both instruments showed a deterioration in QoL for the whole sample on D+7. The laser group presented less severe OM than the control group (p<0.001). CONCLUSIONS: LLLT did not influence the oral and general health-related QoL of patients undergoing HSCT, although it was clinically effective in reducing the severity of chemotherapy-induced OM.

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Low level laser therapy may reduce risk of oral mucositis.

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Data sourcesMedline, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), CINHAL, Web of Science, Scopus, LILACS, Conference proceedings of the International Society of Paediatric Oncology, American Society of Clinical Oncology, American Society of Hematology, American Society of Pediatric Hematology and Oncology, and Multinational Association of Supportive Care in Cancer and the reference lists of identified studies.Study selectionTwo reviewers independently selected studies for inclusion with randomised controlled trials (RCTs) and quasi-RCTs being considered.Data extraction and synthesisData were extracted using a specifically developed form and study quality was assessed using the Cochrane risk of bias tool. Dichotomous outcomes data were synthesised using the risk ratio (RR) and 95% confidence interval (CI). Continuous outcomes measured using different scales were synthesised using the standardised mean difference (SMD) while those using the same scale were synthesised using the weighted mean difference (WMD).ResultsEighteen RCTs involving 1144 patients were included. Four trials were considered to be at low risk of bias across all domains. Prophylactic LLLT reduced the overall risk of severe mucositis (risk ratio (RR) 0.37, 95% confidence interval (CI) 0.20 to 0.67; P = 0.001). Compared to placebo/no therapy LLLT also reduced the following outcomes; severe mucositis at the time of anticipated maximal mucositis RR = 0.34, (95% CI; 0.20 to 0.59); overall mean grade of mucositis SMD -1.49, (95% CI; -2.02 to -0.95); duration of severe mucositis WMD -5.32, 95% (CI; -9.45 to -1.19) and incidence of severe pain (RR 0.26, 95% CI; 0.18 to 0.37).ConclusionsProphylactic LLLT reduced severe mucositis and pain in patients with cancer and HSCT recipients. Future research should identify the optimal characteristics of LLLT and determine feasibility in the clinical setting.

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

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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.

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Guideline for the prevention of oral and oropharyngeal mucositis in children receiving treatment for cancer or undergoing haematopoietic stem cell transplantation.

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PURPOSE: To develop an evidence-based clinical practice guideline for the prevention of oral mucositis in children (0-18 years) receiving treatment for cancer or undergoing haematopoietic stem cell transplantation (HSCT). METHODS: The Mucositis Prevention Guideline Development Group was interdisciplinary and included internationally recognised experts in paediatric mucositis. For the evidence review, we included randomised controlled trials (RCTs) conducted in either children or adults evaluating the following interventions selected according to prespecified criteria: cryotherapy, low level light therapy (LLLT) and keratinocyte growth factor (KGF). We also examined RCTs of any intervention conducted in children. For all systematic reviews, we synthesised the occurrence of severe oral mucositis. The Grades of Recommendation, Assessment, Development and Evaluation approach was used to describe quality of evidence and strength of recommendations. RESULTS: We suggest cryotherapy or LLLT may be offered to cooperative children receiving chemotherapy or HSCT conditioning with regimens associated with a high rate of mucositis. We also suggest KGF may be offered to children receiving HSCT conditioning with regimens associated with a high rate of severe mucositis. However, KGF use merits caution as there is a lack of efficacy and toxicity data in children, and a lack of long-term follow-up data in paediatric cancers. No other interventions were recommended for oral mucositis prevention in children. CONCLUSIONS: All three specific interventions evaluated in this clinical practice guideline were associated with a weak recommendation for use. There may be important organisational and cost barriers to the adoption of LLLT and KGF. Considerations for implementation and key research gaps are highlighted.

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

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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/cm(2), 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 cm(2), irradiated area diameter=1 cm(2), 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.

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Effect of low-level laser therapy on inflammatory mediator release during chemotherapy-induced oral mucositis: a randomized preliminary study.

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Patients undergoing hematopoietic stem cell transplantation (HSCT) are submitted to a conditioning regimen of high-dose chemotherapy, with or without radiation therapy, which usually results in oral ulcerations and mucosal barrier breakdown. Oral mucositis (OM) is a common and debilitating toxicity side effect of autologous and allogeneic HSCT. The aim of this study was to evaluate the effect of low-level laser therapy (LLLT) on the severity of OM and inflammatory mediator (TNF-alpha, IL-6, IL-1beta, IL-10, TGF-beta, metalloproteinases, and growth factors) levels in saliva and blood of HSCT patients. Thirty patients were randomly assigned to two groups: control (n = 15) and laser (n = 15). LLLT was applied from the first day of the conditioning regimen until day 7 post-HSCT (D + 7). Saliva and blood were collected from patients on admission (AD), D-1, D + 3, D + 7, and on marrow engraftment day (ME). Clinical results showed less severe OM in the laser group ($p < 0.05$). The LLLT group showed increased matrix metalloproteinase 2 (MMP-2) levels in saliva on D + 7 ($p = 0.04$). Significant differences were also observed for IL-10 on D + 7 and on ME in blood plasma, when compared to the control group ($p < 0.05$). No significant differences were seen in saliva or blood for the other inflammatory mediators investigated. LLLT was clinically effective in reducing the severity of chemotherapy-induced OM in HSCT patients, and its mechanism of action does not seem to be completely linked to the modulation of pro- or anti-inflammatory cytokines, growth factors or matrix metalloproteinases.

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Efficacy of cryotherapy associated with laser therapy for decreasing severity of melphalan-induced oral mucositis during hematological stem-cell transplantation: a prospective clinical study.

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Melphalan followed by hematopoietic stem-cell transplantation (HSCT) is the standard treatment for multiple myeloma and other hematopoietic neoplasms. However, high doses of melphalan cause severe oral mucositis (OM). The objective was to verify the efficacy of cryotherapy plus laser therapy on reduction of OM severity. HSCT patients undergoing melphalan chemotherapy (n = 71) were randomly divided into two groups according to OM treatment: oral cryotherapy performed with ice chips for 1 h 35 min followed by low-level laser therapy (InGaAlP, 660 nm, 40 mW, 6 J/cm2) (n = 54) and laser therapy alone with the same protocol (n = 17). A control group (n = 33) was composed of HSCT patients treated with melphalan who received no specific treatment for OM. OM scores and clinical information were collected from D0 to D + 11. The cryotherapy/laser therapy group showed the lowest OM scores (maximum Grade I) and the lowest mean number of days (8 days) with OM in comparison with the other groups ($p < 0.001$). OM Grades III and IV were present with high frequency only in the control group. The association of cryotherapy with laser therapy was effective in reducing OM severity in HSCT patients who underwent melphalan conditioning.

Hematol Oncol 2014 Feb 11

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

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Background and aims: Oral mucositis (OM) is still a common and severe acute side-effect of many oncologic treatments, especially in patients treated for head and neck cancer. It may affect quality of life, require supportive care and impact treatment planning and its efficacy. Low-level laser therapy (LLLT) seems to promote pain relief and reduces OM incidence and its severity. It has been recommended for these patients as a treatment option but without any consensus in the LLLT procedure. New recommendations and perspectives for clinical trials will be discussed. Materials (Subjects) and Methods: Step by step, the efficacy of soft laser in the management of iatrogenic oral mucositis has been evaluated during the last two decades. Its effectiveness and level of recommendation got stronger with time. We will report and discuss some major results and the latest recommendations published on this topic. Results: The major clinical results have been reported and analysed last year in a first meta-analysis (1)). 11 randomized placebo-controlled trials were selected with a total of 415 patients treated with chemotherapy and/or radiotherapy for head and neck cancer. The relative risk for developing OM was significantly reduced after LLLT but only for a dose between 1 to 6 Joules per point. Pain, severity and duration of OM grade >/= 2 were also reduced without difference with placebo for possible side-effects. Nine years after the positive results published for patients treated by radiotherapy alone (2)), a new French randomized, multicentric, phase III trial for patients treated with new standard treatment, using LLLT in accordance to recent recommendations is ongoing. Seven centers are specifically established for this trial which should include a hundred patients. Conclusions: The very encouraging results of LLLT in the prevention and treatment of OM in patients treated by chemotherapy or radiotherapy for advanced head and neck cancer could soon be proposed as a new standard of care, according to the multinational Association of Supportive care in Cancer (MASCC) criteria. Modern lasers are less time consuming and extraoral applicators for a possible use by trained paramedical staff could be helpful to complete clinician practice. A preventive dose of 2 J/cm(2) and a curative dose of 4 J/cm(2) if using a red wavelength lasers are now recommended.

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Effect of low level laser therapy in the reduction of oral complications in patients with cancer of the head and neck submitted to radiotherapy.

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BrazilThe aim of this study was to assess the effect of low level laser therapy on reducing the occurrence and severity of oral complications in patients with head and neck cancer undergoing radiotherapy. Sixty head and neck cancer outpatients from a cancer hospital receiving radiotherapy were selected and randomly assigned into two groups. The laser group was irradiated with an InGaAlP laser and the control received sham laser. The assessment of complications (oral mucositis, pain) was carried out one week after starting radiotherapy, and at the fifteenth and thirtieth sessions of radiotherapy. All patients from both groups showed some degree of oral mucositis. Better outcomes were observed in the laser group when compared with the control in the follow-up sessions, indicating lower degrees of oral mucositis, pain and higher salivary flow ($p < .05$). These findings support the use of laser therapy as an adjuvant treatment for the control of oral complications.

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Laser therapy in the control of oral mucositis: a meta-analysis.

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OBJECTIVE: To conduct a systematic review and meta-analysis of the effectiveness of Laser Therapy in the prevention of oral mucositis (OM) in patients undergoing oncotherapy. METHODS: To this systematic review and meta-analysis a search was performed in MEDLINE, LILACS and Cochrane using the keywords "laser therapy" and "Oral mucostitis." The case-control studies included were submitted to odds ratio (OR) analysis, which the cut-off point for statistic calculation was OM grade > 3. We carried out a meta-analysis by BioEstat 5.0, using the Random Effect DerSimonian-Laird statistical analysis. RESULTS: Twelve (studies were included in this systematic review, and the meta-analysis of seven of them showed that LT in patients undergoing oncotherapy is approximately nine times more effective in the prevention of OM grade > 3 than in patients without laser treatment (OR: 9,5281, confidence interval 95% 1,447 -52,0354, p=0,0093. CONCLUSION: These data demonstrated significant prophylatic effect of OM grade > 3 in patients undergoing LT. Further studies, with larger sample sizes, are needed for better evaluation of the prophylatic effect of OM grade > 3 by LT.

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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

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BrazilBACKGROUND: 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 3weeks. 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

Evaluation of the effect of low level laser on prevention of chemotherapy-induced mucositis.

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IranRadiotherapy in the head and neck region and chemotherapy might give rise to oral mucositis which is a severe and painful inflammation. There is no known definite cure for mucositis. A number of studies have attempted to evaluate the effect of low-power laser on radiotherapy- and chemotherapy-induced mucositis. The present study was undertaken to evaluate the effect of low-power laser on the prevention of mucositis, xerostomia and pain as a result of chemotherapy. The subjects in this double-blind randomized controlled study were 24 adult patients who underwent chemotherapy during 2009-2010. The results showed that low-power laser was able to decrease the effect of chemotherapy on oral mucositis, xerostomia and pain in a variety of malignancies ($P<0.05$). It can be concluded that low-power laser might decrease the intensity of mucositis.

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http://www.ncbi.nlm.nih.gov/pubmed/?term=23605599

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.

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IndiaPURPOSE: 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(2), dosage = 3.0 J at each point, total dose/session = 36 -40 J, spot size 1 cm(2), 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.

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Low level laser therapy for concurrent chemoradiotherapy induced oral mucositis in head and neck cancer patients - A triple blinded randomized controlled trial.

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IndiaBACKGROUND AND PURPOSE: Oral mucositis (OM) is most cumbersome acute side effect of concurrent chemoradiotherapy (CCRT) for head and neck cancer (HNC). OM associated pain affects oral functions and nutrition of the patient that may result in discontinuity of treatment. Several modalities have been tried to prevent and treat OM, but none proved completely successful until date. We used prophylactic low level laser therapy (LLLT) for the prevention and treatment of CCRT induced OM. MATERIALS AND METHODS: In this triple blinded study, 221 HNC patients scheduled to undergo CCRT (Cisplatin (1, 22, 43day)+RT=66 Grays (2Gy/fraction), 33 fractions, 5 fractions/week, for 45days) were block randomized into laser (n=111) and placebo (n=110) group. Laser group received LLLT (HeNe, lambda=632.8nm, power-density=24mW, dosage=3.0J/point, total dosage/session=36-40J, spot-size=1cm(2), 5 sessions/week) while placebo received sham treatment daily prior to radiation. OM (RTOG/EORTC Scale), oral pain (VAS), dysphagia (FIS), weight loss and CCRT break were assessed. Data were analyzed using frequencies and percentage, generalized estimating equations (GEE) and odds ratio. RESULTS: There was significant reduction in incidence of severe OM ($F=16.64$, $df=8876$, $p<0.0001$) and its associated pain ($F=25.06$, $df=8876$, $p<0.0001$), dysphagia ($F=20.17$, $df=8876$, $p<0.0001$) and opioid analgesics use ($p<0.0001$) in laser than placebo group patients. CONCLUSIONS: LLLT decreased the incidence of CCRT induced severe OM and its associated pain, dysphagia and opioid analgesics use.

Radiother Oncol 2012 Aug 9

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Low Level Helium Neon Laser therapy for chemoradiotherapy induced oral mucositis in oral cancer patients - A randomized controlled trial.

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IndiaBACKGROUND: Patients receiving chemoradiotherapy (CRT) for oral cancer (OC) often develop oral mucositis (OM). OM associated pain severely affects oral functions and nutrition of the patient, resulting in narcotic analgesic use and CRT interruption. Laser therapy has shown some promising results in preventing and treating OM caused by cancer therapies. So in this trial we used prophylactic Low Level Helium Neon (He-Ne) Laser for the prevention and treatment of CRT induced OM in OC patients. MATERIALS AND METHODS: This double blinded trial block randomized 121primary OC patients scheduled to undergo CRT [RT dosage=66Gray/33fractions for 5days/week and chemotherapy (3 weekly Cisplatin)] into laser (n=60) and placebo (n=61) group. Laser group received He-Ne Laser (lambda=632.8nm, P=24mW, ED=3.5J/cm(2)) while placebo received sham treatment just before radiation for 6.5weeks. OM (RTOG/EORTC Scale), its associated pain, and total parenteral nutrition (TPN), were assessed on every week by a blinded assessor. Also opioid analgesic use, weight loss and any CRT break were recorded. Data was analyzed using descriptive statistics, t-test and Man Whitney U test. Level of significance was set at $p<0.05$. RESULTS: Incidence of severe OM (29% vs. 89%, $p<0.001$) and its associated pain (18% vs. 71%, $p<0.001$), opioid analgesic use (7% vs. 21%, $p<0.001$)and TPN (30% vs. 39% $p=0.039$) was significantly less in laser than placebo group patients. Also duration of severe OM and pain experienced was less in laser than placebo group. CRT break required only for placebo group (9%) patients. CONCLUSION: Low Level He-Ne Laser decreased the incidence of CRT induced severe OM and its associated pain, opioid analgesics use and TPN.

Oral Oncol 2012 Apr 11

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Evaluation of low-level laser therapy in the prevention and treatment of radiation-induced mucositis: A double-blind randomized study in head and neck cancer patients.

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The purpose of this prospective study was to determine the effect of the low-level laser in the prevention and treatment of mucositis in head and neck cancer patients. A total of 70 patients with malignant neoplasms in the oral cavity or oropharynx were evaluated. The patients were randomized into two low-level laser therapy groups: Group 1 (660nm/15mW/3.8J/cm(2)/spot size 4mm(2)) or Group 2 (660nm/5mW/1.3J/cm(2)/spot size 4mm(2)) starting on the first day of radiotherapy. Oral mucositis was assessed daily and weekly using the NCI and WHO scales. Oral pain was scored daily with a visual analogue scale before laser application. The patients in Group 1 had a mean time of 13.5days (range 6 -26days) to present mucositis grade II, while the patients in Group 2 had a mean time of 9.8days (range 4 -14days) (both WHO and NCI p=0.005). In addition, Group 2 also presented a higher mucositis grade than Group 1 with significant differences found in weeks 2 (p=0.019), 3 (p=0.005) and 4 (p=0.003) for WHO scale and weeks 2 (p=0.009) and 4 (p=0.013) for NCI scale. The patients in Group 1 reported lower pain levels (p=0.004). Low-level laser therapy during radiotherapy was found to be effective in controlling the intensity of mucositis and pain.

Oral Oncol 2011 Sep 10

http://www.ncbi.nlm.nih.gov/pubmed/?term=21911312

Effect of intraoral low-level laser therapy on quality of life of patients with head and neck cancer undergoing radiotherapy.

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BrazilBACKGROUND: Low-level laser therapy has been used to reduce complications of head and neck cancer treatment. The aim was to assess the impact of laser in the quality of life (QOL) of patients receiving radiotherapy. METHODS: Sixty outpatients were randomly assigned into 2 groups. The laser group received applications and the placebo group received sham laser. QOL was assessed using the University of Washington QOL questionnaire. A repeated-measures analysis of variance (ANOVA) was used for comparisons of overall QOL scores and Mann-Whitney test compared changes in domain scores. RESULTS: A decrease in QOL scores was observed in both groups and the reduction in the laser group was significantly lower ($p < .01$). Changes in QOL scores regarding pain, chewing, and saliva domains were evident in the placebo group. Both health-related QOL and overall QOL were rated higher by patients who received laser therapy. CONCLUSION: Laser therapy reduces the impact of radiotherapy on the QOL of patients with head and neck cancer. (c) 2011 Wiley Periodicals, Inc. Head Neck, 2011.

Head Neck 2011 Apr 5

http://www.ncbi.nlm.nih.gov/pubmed/?term=21472883

Efficacy of low-level laser therapy and aluminum hydroxide in patients with chemotherapy and radiotherapy-induced oral mucositis.

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This study evaluated the efficacy of low-level laser therapy (LLLT) and aluminum hydroxide (AH) in the prevention of oral mucositis (OM). A prospective, comparative and non-randomized study was conducted with 25 patients with head and neck cancer subjected to radiotherapy (RT) or radiochemotherapy (RCT). Twelve patients received LLLT (830 nm, 15 mW, 12 J/cm(2)) daily from the 1st day until the end of RT before each sessions during 5 consecutive days, and the other 13 patients received AH 310 mg/5 mL, 4 times/day, also throughout the duration of RT, including weekends. OM was measured using an oral toxicity scale (OTS) and pain was measured using the visual analogue scale (VAS). EORTC questionnaires were administered to the evaluate impact of OM on quality of life. The LLLT group showed lower mean OTS and VAS scores during the course of RT. A significant difference was observed in pain evaluation in the 13th RT session (p=0.036). In both groups, no interruption of RT was needed. The prophylactic use of both treatments proposed in this study seems to reduce the incidence of severe OM lesions. However, the LLLT was more effective in delaying the appearance of severe OM.

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http://www.ncbi.nlm.nih.gov/pubmed/?term=21203698

A randomized controlled trial of visible-light therapy for the prevention of oral mucositis.

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The objective of this study was to assess the efficacy of a novel visible-light therapy (VLT) device for the prevention of oral mucositis in hematopoietic stem cell transplantation (HSCT) patients. A VLT-device suitable for intra-oral use was applied to 20 patients undergoing HSCT. The study design was placebo-controlled, randomized and double-blind. Oral mucositis was assessed using the OMAS and WHO scales. Oral pain and acceptance levels were scored by the patient using a 10-step scale. Patients were evaluated once a week until day 21 post-HSCT. Mucositis rate, severity and pain score were compared. At the third visit, 1week post-HSCT, mucositis rates were significantly lower in the treatment group (for both WHO and OMAS p=0.02). Mucositis was also less severe in the treatment group (for WHO p=0.01; for OMAS p=0.01). Furthermore, the patients in the treatment group reported lower pain levels (p=0.04). The treatment was well tolerated and highly accepted, with no reports of adverse events related to the device. These findings suggest that the VLT-device is safe and effective for the prevention of oral mucositis in patients undergoing HSCT.

Oral Oncol 2010 Dec 15

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Oral Mucositis Prevention by Low-Level Laser Therapy in Head-and-Neck Cancer Patients Undergoing Concurrent Chemoradiotherapy: A Phase III Randomized Study.

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BrazilPURPOSE: Oral mucositis is a major complication of concurrent chemoradiotherapy (CRT) in head-and-neck cancer patients. Low-level laser (LLL) therapy is a promising preventive therapy. We aimed to evaluate the efficacy of LLL therapy to decrease severe oral mucositis and its effect on RT interruptions. METHODS AND MATERIALS: In the present randomized, double-blind, Phase III study, patients received either gallium-aluminum-arsenide LLL therapy 2.5 J/cm(2) or placebo laser, before each radiation fraction. Eligible patients had to have been diagnosed with squamous cell carcinoma or undifferentiated carcinoma of the oral cavity, pharynx, larynx, or metastases to the neck with an unknown primary site. They were treated with adjuvant or definitive CRT, consisting of conventional RT 60-70 Gy (range, 1.8 -2.0 Gy/d, 5 times/wk) and concurrent cisplatin. The primary endpoints were the oral mucositis severity in Weeks 2, 4, and 6 and the number of RT interruptions because of mucositis. The secondary endpoints included patient-reported pain scores. To detect a decrease in the incidence of Grade 3 or 4 oral mucositis from 80% to 50%, we planned to enroll 74 patients. RESULTS: A total of 75 patients were included, and 37 patients received preventive LLL therapy. The mean delivered radiation dose was greater in the patients treated with LLL (69.4 vs. 67.9 Gy, p = .03). During CRT, the number of patients diagnosed with Grade 3 or 4 oral mucositis treated with LLL vs. placebo was 4 vs. 5 (Week 2, p = 1.0), 4 vs. 12 (Week 4, p = .08), and 8 vs. 9 (Week 6, p = 1.0), respectively. More of the patients treated with placebo had RT interruptions because of mucositis (6 vs. 0, p = .02). No difference was detected between the treatment arms in the incidence of severe pain. CONCLUSIONS: LLL therapy was not effective in reducing severe oral mucositis, although a marginal benefit could not be excluded. It reduced RT interruptions in these head-and-neck cancer patients, which might translate into improved CRT efficacy.

Int J Radiat Oncol Biol Phys 2010 Dec 14

http://www.ncbi.nlm.nih.gov/pubmed/?term=21163585

The Prevention of Induced Oral Mucositis with Low-Level Laser Therapy in Bone Marrow Transplantation Patients: A Randomized Clinical Trial.

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BrazilAbstract Background Data and Objective: Patients who have received high doses of chemotherapy, either alone or in combination with total body irradiation often cite oral mucositis (OM) as the most debilitating 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). Methods: We randomized 42 patients who underwent autologous or allogeneic HSCT. A low-level InGaAlP diode laser was used, emitting light at 660 nm, 40 mW, and 4 J/cm(2). An evaluation of OM was carried out using the World Health Organization scale. Results and Conclusion: In the LLLT group, 57.1% of patients had an OM grade 0, 9.6% had grade 1, and 33.3% had grade 2, whereas in the control group, only 4.8% of patients were free of OM (grade 0). Our results indicate that the preventive use of LLLT in patients who have undergone HSCT is a powerful instrument in reducing OM incidence.

Photomed Laser Surg 2010 Oct 22

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Effects of low-level laser therapy on collagen expression and neutrophil infiltrate in 5-fluorouracil-induced oral mucositis in hamsters.

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BACKGROUND AND OBJECTIVES: Several studies have suggested that low-level laser therapy (LLLT) can ameliorate oral mucositis; however, the mechanisms involved are not well understood. The aim of this study was to investigate the mechanisms of action of LLLT on chemotherapy-induced oral mucositis, as related to effects on collagen expression and inflammation. MATERIALS AND METHODS: A hamster cheek pouch model of oral mucositis was used with all animals receiving intraperitoneal 5-fluorouracil, followed by surface irritation. Animals were randomly allocated into three groups, and treated with an InGaAlP diode laser at a wavelength of 660 nm and output power of 35 or 100 mW laser, or no laser. Clinical severity of mucositis was assessed at four time-points by a blinded examiner. Buccal pouch tissue was harvested from a subgroup of animals in each group at four time-points. Collagen was qualitatively and quantitatively evaluated after picrosirius staining. The density of the neutrophil infiltrate was also scored. RESULTS: Peak clinical severity of mucositis was reduced in the 35 mW laser group as compared to the 100 mW and control groups. The reduced peak clinical severity of mucositis in the 35 mW laser group was accompanied by a decrease in the number of neutrophils and an increase in the proportion of mature collagen as compared to the other two groups. The total quantity of collagen was significantly higher in the control (no laser) group at the day 11 time-point, as compared to the 35 mW laser group, consistent with a more prolonged inflammatory response in the control group. CONCLUSION: This study supports two mechanisms of action for LLLT in reducing mucositis severity. The increase in collagen organization in response to the 35 mW laser indicates that LLLT promotes wound healing. In addition, LLLT also appears to have an anti-inflammatory effect, as evidenced by the reduction in neutrophil infiltrate.

Lasers Surg Med 2010 Aug 42(6) 546-52

http://www.ncbi.nlm.nih.gov/pubmed/?term=20662031

Cyclooxygenase-2 and vascular endothelial growth factor expression in 5-fluorouracil-induced oral mucositis in hamsters: evaluation of two low-intensity laser protocols.

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GOAL OF WORK: The aim of this study was to investigate the mechanisms whereby low-intensity laser therapy may affect the severity of oral mucositis. MATERIALS AND METHODS: A hamster cheek pouch model of oral mucositis was used with all animals receiving intraperitoneal 5-fluorouracil followed by surface irritation. Animals were randomly allocated into three groups and treated with a 35 mW laser, 100 mW laser, or no laser. Clinical severity of mucositis was assessed at four time-points by a blinded examiner. Buccal pouch tissue was harvested from a subgroup of animals in each group at four time-points. This tissue was used for immunohistochemistry for cyclooxygenase-2 (COX-2), vascular endothelial growth factor (VEGF), and factor VIII (marker of microvessel density) and the resulting staining was quantified. MAIN RESULTS: Peak severity of mucositis was reduced in the 35 mW laser group as compared to the 100 mW laser and control groups. This reduced peak clinical severity of mucositis in the 35 mW laser group was accompanied by a significantly lower level of COX-2 staining. The 100 mW laser did not have an effect on the severity of clinical mucositis, but was associated with a decrease in VEGF levels at the later time-points, as compared to the other groups. There was no clear relationship of VEGF levels or microvessel density to clinical mucositis severity. CONCLUSION: The tissue response to laser therapy appears to vary by dose. Low-intensity laser therapy appears to reduce the severity of mucositis, at least in part, by reducing COX-2 levels and associated inhibition of the inflammatory response.

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Low-level infrared laser therapy in chemotherapy-induced oral mucositis: a randomized placebo-controlled trial in children.

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BACKGROUND: Oral mucositis (OM) is one of the most frequent complications of chemotherapy for which there is no standard therapy; treatment is mostly conservative. This study was conducted to determine whether low-intensity laser therapy (LLLT) can reduce the duration of chemotherapy-induced OM. PROCEDURE: A placebo-controlled randomized trial was carried out using LLLT or placebo (sham treatment). Children and adolescents with cancer receiving chemotherapy or hematopoietic stem-cell transplantation between October 2005 and May 2006 were eligible as soon as they developed OM. Patients received intervention for 5 days. The LLLT group was treated with laser GaAlAs, wavelength (lambda): 830 nm (infrared), power: 100 mW, dose: 4 J/cm, and placebo group underwent sham treatment. The grade of OM was clinically assessed by the National Cancer Institute, Common Toxicity Criteria scale. RESULTS: Twenty-one patients developed OM and were evaluable for analysis; 18 (86%) patients had a diagnosis of leukemia or lymphoma and 3(14%) had solid tumors. The mean age was 8.2 (+/-3.1) years. Nine patients were randomized in the laser group and 12 in the placebo-control group. Once OM was diagnosed, the patients had daily OM grading assessments before laser or sham application and thereafter until complete healing of the lesions. On day 7 after OM diagnosis, 1/9 of patients remained with lesions in laser group and 9/12 of patients in the placebo-control group (P=0.029). In the laser group, the mean of OM duration was 5.8+/-2 days and in the placebo group was 8.9+/-2.4 days (P=0.004). CONCLUSIONS: Our study has shown evidence that laser therapy in addition to oral care can decrease the duration of chemotherapy-induced OM. Our results confirm the promising results observed in adult cancer patients and should encourage pediatric oncologists to use laser therapy as first-line option in children with chemotherapy-induced OM.

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http://www.ncbi.nlm.nih.gov/pubmed/?term=19125084

LED phototherapy to prevent mucositis: a case report.

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OBJECTIVE: The purpose of this case report was to evaluate the efficacy of phototherapy using light-emitting diodes (LEDs) to prevent oral mucositis in a Hodgkin's disease patient treated with the ABVD (doxorubicin [Adriamycin], bleomycin, vinblastine, and dacarbazine) chemotherapy regimen. BACKGROUND DATA: Mucositis is a common dose-limiting complication of cancer treatment, and if severe it can lead to alterations in treatment planning or suspension of cancer therapy, with serious consequences for tumor response and survival. Therefore, low-power lasers and more recently LEDs, have been used for oral mucositis prevention and management, with good results. MATERIALS AND METHODS: In this study, a 34-year-old man received intraoral irradiation with an infrared LED array (880 nm, 3.6 J/cm2, 74 mW) for five consecutive days, starting on chemotherapy day 1. In each chemotherapy cycle, he received the ABVD protocol on days 1 and 15, and received LED treatment for 5 d during each cycle. To analyze the results, the World Health Organization (WHO) scale was used to grade his mucositis, and a visual analogue scale (VAS) was used for pain evaluation, on days 1, 3, 7, 10, and 13 post-chemotherapy. RESULTS: The results showed that the patient did not develop oral mucositis during the five chemotherapy cycles, and he had no pain symptoms. CONCLUSION: LED therapy was a safe and effective method for preventing oral mucositis in this case report. However, further randomized studies with more patients are needed to prove the efficacy of this method.

Photomed Laser Surg 2008 Dec 26(6) 609-13

http://www.ncbi.nlm.nih.gov/pubmed/?term=19025412

Light-emitting diode therapy in chemotherapy-induced mucositis.

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BACKGROUND AND OBJECTIVE: Mucositis is the most common oral complication of cancer chemotherapy, which causes pain on mastication and swallowing, impairs patients' ability to eat and take oral drugs and may determine interruption of the treatment. The aim of this study was to evaluate the effect of light-emitting diode (LED) therapy on chemotherapy-induced mucositis in hamsters. STUDY DESIGN/MATERIALS AND METHODS: Animals of both experimental (Group I; n = 32) and positive control (Group II; n = 32) groups received intraperitoneal injections of 5-fluorouracil on days 0 and 2. All animals had their right and left cheek pouch irritated by superficial scratching on days 3 and 4. In Group I, LED irradiation (630 nm+/-10 nm, 160 mW, 12 J/cm2) was applied during 37.5 seconds at days 3, 4, 6, 8, 10, 12, and 14. In Group II, mucositis was induced, but LED therapy was not performed. The oral mucosa was photographed from day 4 to 14 at 2-day intervals. Photographs were randomly scored according to the severity of induced mucositis (0 to 5). In the negative control group (Group III; n = 6), no mucositis was induced. Biopsies of the cheek pouches of 8 animals (Group I and Group II) were surgically obtained on days 5, 9, 13 and 15 and processed for histological examination. RESULTS: The statistical analysis showed significant differences between irradiated and non-irradiated groups ($P<0.05$). However, muscular degeneration was observed in 18% of the samples of Group I. CONCLUSION: It may be concluded that the LED therapy protocol established for this in vivo study was effective in reducing the severity of oral mucositis, although the oral lesions were not completely prevented.

Lasers Surg Med 2008 Nov 40(9) 625-33

http://www.ncbi.nlm.nih.gov/pubmed/?term=18951429

Low-level laser therapy in the prevention and treatment of chemotherapy-induced oral mucositis in young patients.

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OBJECTIVE: A pilot clinical study was conducted to evaluate the efficacy and feasibility of low-level laser therapy (LLLT) in the prevention and treatment of chemotherapy (CT)-induced oral mucositis (OM) in young patients. BACKGROUND DATA: Besides compromising the patient's nutrition and well-being, oral mucositis represents a portal of entry into the body for microorganisms present in the mouth, which may lead to sepsis if there is hematological involvement. Oncologic treatment tolerance decreases and systemic complications may arise that interfere with the success of cancer treatment. LLLT appears to be an interesting alternative to other approaches to treating OM, due to its trophic, anti-inflammatory, and analgesic properties. MATERIALS AND METHODS: Patients undergoing chemotherapy (22 cycles) without mucositis were randomized into a group receiving prophylactic laser-irradiation (group 1), and a group receiving placebo light treatment (group 2). Patients who had already presented with mucositis were placed in a group receiving irradiation for therapeutic purposes (group 3, with 10 cycles of CT). Serum granulocyte levels were taken and compared to the progression of mucositis. RESULTS: In group 1, most patients (73%) presented with mucositis of grade 0 ($p = 0.03$ when compared with the placebo group), and 18% presented with grade 1. In group 2, 27% had no OM and did not require therapy. In group 3, the patients had marked pain relief (as assessed by a visual analogue scale), and a decrease in the severity of OM, even when they had severe granulocytopenia. CONCLUSION: The ease of use of LLLT, high patient acceptance, and the positive results achieved, make this therapy feasible for the prevention and treatment of OM in young patients.

Photomed Laser Surg 2008 Aug 26(4) 393-400

http://www.ncbi.nlm.nih.gov/pubmed/?term=18754720

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

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Abstract Background Data and Objective: Oral mucositis (OM) is one of the worst cytotoxic effects of chemotherapy and radiotherapy in patients undergoing hematopoietic cell transplantation (HCT), and it causes severe morbidity. Laser phototherapy has been considered as an alternative therapy for prevention and treatment of OM. The aim of this study was to describe the incidence and severity of OM in HCT patients subjected to laser phototherapy, and to discuss its effect on the oral mucosa. Patients and Methods: Information concerning patient age and gender, type of basic disease, conditioning regimen, type of transplant, absence or presence of pain related to the oral cavity, OM grade, and adverse reactions or unusual events were collected from 30 patients undergoing HCT (allogeneic or autologous). These patients were given oral laser phototherapy with a InGaAIP laser (660 nm and 40 mW) daily. The data were tabulated and their frequency expressed as percentages. Results: In the analysis of those with OM, it was observed that 33.4% exhibited grade I, 40% grade II, 23.3% grade III, and 3.3% grade IV disease. On the most critical post-HCT days (D+5 and D+8), it was observed that 63.3% of patients had grade I and 33.3% had grade II disease; no patients had grade III or IV disease in this period. This severity of OM was similar to that seen in other studies of laser phototherapy and OM. Conclusion: The low grades of OM observed in this survey show the beneficial effects of laser phototherapy, but randomized clinical trials are necessary to confirm these findings.

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The use of low-energy laser (LEL) for the prevention of chemotherapy- and/or radiotherapy-induced oral mucositis in cancer patients: results from two prospective studies.

Genot-Klastersky MT, Klastersky J, Awada F, Awada A, Crombez P, Martinez MD, Jaivenois MF, Delmelle M, Vogt G, Meuleman N, Paesmans M

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BACKGROUND: Low-energy laser (LEL) treatment has been suggested as an effective and safe method to prevent and/or treat oral mucositis induced by chemotherapy and/or radiotherapy; however, it has not gained wide acceptance so far. MATERIALS AND METHODS: We conducted two clinical trials testing the LEL technique: firstly, as a secondary prevention in patients with various solid tumors treated with chemotherapy who all developed severe mucositis after a previous identical chemotherapy and, secondly, as therapeutic intervention (compared to sham illumination in a randomized way) in patients with hematological tumors receiving intensive chemotherapy and having developed low-grade oral mucositis. RESULTS: We entered 26 eligible patients in the first study and 36 were randomized in the second study. The success rate was 81% (95%CI = 61-93%) when LEL was given as a preventive treatment. In the second study, in patients with existing lesions, the therapeutic success rate was 83% (95%CI = 59-96%), which was significantly different from the success rate reached in the sham-treated patients (11%; 95%CI = 1-35%); the time to development of grade 3 mucositis was also significantly shorter in the sham-treated patients ($p < 0.001$). CONCLUSION: Our results strongly support the already available literature, suggesting that LEL is an effective and safe approach to prevent or treat oral mucositis resulting from cancer chemotherapy.

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http://www.ncbi.nlm.nih.gov/pubmed/?term=18458964

Literature news.

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AIM: To evaluate the clinical effects of laser therapy on the prevention and reduction of oral mucositis in patients who underwent hematopoietic stem cell transplantation (HSCT).Patients and methods: From January 2003 to September 2004, 24 patients received prophylactic laser therapy (L+ group). The applications started from the beginning of the conditioning regimen up to day +2. The oral assessment was performed daily until day +30. This group was compared with historical controls, namely 25 patients, who did not receive laser therapy (L? group). RESULTS: All patients developed some grade of mucositis. However, the L? group presented initial mucositis by 4.36 days, whereas the L+ group presented it in 6.12 days (P = 0.01). The maximum mucositis occurred between day +2 and day +6 with healing by day +25 in the L? group and between day +2 and day +7 with healing by day +14 for the L+ group (P = 0.84). Laser therapy also reduced the time of oral pain from 5.64 to 2.45 days (P = 0.04), and decreased the consumption of morphine (P = 0.07). CONCLUSION: This study suggests that laser therapy can be useful in oral mucositis to HSCT patients and improve the patient's quality of life. However, controlled randomized trials should be performed to confirm the real efficacy of laser therapy.

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Low-energy laser therapy for prevention of oral mucositis in hematopoietic stem cell transplantation.

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Aim: To evaluate the clinical effects of laser therapy on the prevention and reduction of oral mucositis in patients who underwent hematopoietic stem cell transplantation (HSCT). Patients and methods: From January 2003 to September 2004, 24 patients received prophylactic laser therapy (L+ group). The applications started from the beginning of the conditioning regimen up to day +2. The oral assessment was performed daily until day +30. This group was compared with historical controls, namely 25 patients, who did not receive laser therapy (L- group). Results: All patients developed some grade of mucositis. However, the L- group presented initial mucositis by 4.36 days, whereas the L+ group presented it in 6.12 days (P = 0.01). The maximum mucositis occurred between day +2 and day +6 with healing by day +25 in the L- group and between day +2 and day +7 with healing by day +14 for the L+ group (P = 0.84). Laser therapy also reduced the time of oral pain from 5.64 to 2.45 days (P = 0.04), and decreased the consumption of morphine (P = 0.07). Conclusion: This study suggests that laser therapy can be useful in oral mucositis to HSCT patients and improve the patient's quality of life. However, controlled randomized trials should be performed to confirm the real efficacy of laser therapy.

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Cancer treatment-induced oral mucositis.

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Oral mucositis is one of the main complications in non-surgical cancer treatments. It represents the major dose-limiting toxicity for some chemotherapeutic agents, for radiotherapy of the head and neck region and for some radiochemotherapy combined treatments. Many reviews and clinical studies have been published in order to define the best clinical protocol for prophylaxis or treatment of mucositis, but a consensus has not yet been obtained. This paper represents an updated review of prophylaxis and treatment of antineoplastic-therapy-related mucositis using a MEDLINE search up to May 2006, in which more than 260 clinical studies have been found. They have been divided according to antineoplastic therapy (chemotherapy, radiotherapy, chemo-radiotherapy, high-dose chemotherapy). The prophylactic or therapeutic use of the analysed agents, the number of enrolled patients and the study design (randomized or not) were also specified for most studies. Accurate pre-treatment assessment of oral cavity hygiene, frequent review of symptoms during treatment, use of traditional mouthwashes to obtain mechanical cleaning of the oral cavity and administration of some agents like benzydamine, imidazole antibiotics, tryazolic antimycotics, povidone iodine, keratinocyte growth factor and vitamin E seem to reduce the intensity of mucositis. Physical approaches like cryotherapy, low energy Helium-Neon laser or the use of modern radiotherapy techniques with the exclusion of the oral cavity from radiation fields have been shown to be efficacious in preventing mucositis onset. Nevertheless a consensus protocol of prophylaxis and treatment of oral mucositis has not yet been obtained.

Anticancer Res 2007 Mar-Apr 27(2) 1105-25

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A phase III randomized double-blind placebo-controlled clinical trial to determine the efficacy of low level laser therapy for the prevention of oral mucositis in patients undergoing hematopoietic cell transplantation.

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INTRODUCTION: Oral mucositis (OM) is a significant early complication of hematopoietic cell transplantation (HCT). This phase III randomized double-blind placebo-controlled study was designed to compare the ability of 2 different low level GaAlAs diode lasers (650 nm and 780 nm) to prevent oral mucositis in HCT patients conditioned with chemotherapy or chemoradiotherapy. MATERIALS AND METHODS: Seventy patients were enrolled and randomized into 1 of 3 treatment groups: 650 nm laser, 780 nm laser or placebo. All active laser treatment patients received daily direct laser treatment to the lower labial mucosa, right and left buccal mucosa, lateral and ventral surfaces of the tongue, and floor of mouth with energy densities of 2 J/cm2. Study treatment began on the first day of conditioning and continued through day +2 post HCT. Mucositis and oral pain was measured on days 0, 4, 7, 11, 14, 18, and 21 post HCT. RESULTS: The 650 nm wavelength reduced the severity of oral mucositis and pain scores. Low level laser therapy was well-tolerated and no adverse events were noted. DISCUSSION: While these results are encouraging, further study is needed to truly establish the efficacy of this mucositis prevention strategy. Future research needs to determine the effects of modification of laser parameters (e.g., wavelength, fluence, repetition rate of energy delivery, etc.) on the effectiveness of LLE laser to prevent OM.

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Macroscopic and microscopic effects of GaAIAs diode laser and dexamethasone therapies on oral mucositis induced by fluorouracil in rats.

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PURPOSE: To present an animal model for mucositis induced by fluorouracil in rats, and test two therapeutic options, the GaAIAs laser and topical dexamethasone, analysing them with regard to the quality and quantity of tissue alterations and comparing them with the phases of mucositis. MATERIALS AND METHODS: Forty-five Wistar rats (250 g) were treated with fluorouracil (60 mg/kg) and, in order to mimic the clinical effect of chronic irritation, the palatal mucosa was irritated by superficial scratching with an 18-gauge needle. When all of the rats presented oral ulcers of mucositis, they were randomly allocated to one of three groups: group I was treated with laser (GaAIAs), group II was treated with topical dexamethasone, and group III was not treated. Excisional biopsies of the palatal mucosa were then performed, and the rats were killed. Tissue sections were stained with haematoxylin and eosin for morphological analyses, and with toluidine blue for mast-cell counts. RESULTS: Group I specimens showed higher prevalence of ulcers, bacterial biofilm, necrosis and vascularisation, while group II specimens showed higher prevalance of granulation tissue formation. There were no significant statistical differences in the numbers of mast cells and epithelial thickness between groups. CONCLUSION: For the present model of mucositis, rats with palatal mucositis treated with laser (GaAIAs) showed characteristics compatible with the ulcerative phase of oral mucositis, and rats treated with topical dexamethasone showed characteristics compatible with the healing phase of mucositis. Topical dexamethasone was more efficient in the treatment of rats' oral mucositis than the laser.

Oral Health Prev Dent 2007 5(1) 63-71

http://www.ncbi.nlm.nih.gov/pubmed/?term=17366763

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

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BrazilWe 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.

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Influence of low-energy laser in the prevention of oral mucositis in children with cancer receiving chemotherapy.

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BrazilBACKGROUND: This study assessed the use of low-energy laser in the prevention or reduction of the severity of oral mucositis. PROCEDURE: A randomized clinical trial was carried out. Patients from 3 to 18 years of age treated with chemotherapy or hematopoietic stem-cell transplantation between May, 2003 and February, 2005 were eligible. The intervention group received laser application for 5 days following the start of chemotherapy. The grade of oral mucositis was assessed by the WHO per NCI-CTC common toxicity criteria and the assessments were made on days 1, 8 and 15 by a trained examiner blind to the intervention. RESULTS: Sixty patients were evaluable for analysis; thirty-nine (65%) were males, 35 (58%) patients had a diagnosis of leukemia or lymphoma, and 25 (42%) had solid tumors. The mean age was 8.7 +/- 4.3 years. Twenty-nine patients were randomized in the laser group and 31 in the control group. On day 1, no patients presented with mucositis. On day 8, of 20 patients (36%) who developed mucositis, 13 of them were from the laser group and 7 from the control group. On day 15, of 24 patients (41%) who developed mucositis, 13 of them were from the laser group and 11 from the control group. There was no significant difference between groups concerning the grades of mucositis on day 8 (P = 0.234) or on day 15 (P = 0.208). CONCLUSIONS: This study showed no evidence of benefit from the prophylactic use of low-energy laser in children and adolescents with cancer treated with chemotherapy when optimal dental and oral care was provided.

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http://www.ncbi.nlm.nih.gov/pubmed/?term=16862549

Low-energy He/Ne laser in the prevention of radiation-induced mucositis. A multicenter phase III randomized study in patients with head and neck cancer.

Bensadoun RJ, Franquin JC, Ciais G, Darcourt V, Schubert MM, Viot M, Dejou J, Tardieu C, Benezery K, Nguyen TD, Laudoyer Y, Dassonville O, Poissonnet G, Vallicioni J, Thyss A, Hamdi M, Chauvel P, Demard F

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Use of the low-energy helium-neon laser (LEL) appears to be a simple atraumatic technique for the prevention and treatment of mucositis of various origins. Preliminary findings, and significant results obtained for chemotherapy-induced mucositis in a previous phase III study, prompted a randomized multicenter double-blind trial to evaluate LEL in the prevention of acute radiation-induced stomatitis. Irradiation by LEL corresponds to local application of a high-photon-density monochromatic light source. Activation of epithelial healing for LEL-treated surfaces, the most commonly recognized effect, has been confirmed by numerous in vitro studies. The mechanism of action at a molecular and enzymatic level is presently being studied. From September 1994 to March 1998, 30 patients were randomized. Technical specification: 60 mW (25 mW at Reims, 1 patient), He-Ne, wavelength 632.8 nm. The trial was open to patients with carcinoma of the oropharynx, hypopharynx and oral cavity, treated by radiotherapy alone (65 Gy at a rate of 2 Gy/fraction, 5 fractions per week) without prior surgery or concomitant chemotherapy. The malignant tumor had to be located outside the tested laser application areas (9 points): posterior third of the internal surfaces of the cheeks, soft palate and anterior tonsillar pillars. Patients were randomized to LEL or placebo light treatment, starting on the first day of radiotherapy and before each session. The treatment time (t) for each application point was given by the equation : t(s)= energy (J/cm2) x surface (cm2)/Power (W). Objective assessment of the degree of mucositis was recorded weekly by a physician blinded to the type of treatment, using the WHO scale for grading of mucositis and a segmented visual analogue scale for pain evaluation. Protocol feasibility and compliance were excellent. Grade 3 mucositis occured with a frequency of 35.2% without LEL and of 7.6% with LEL ($P<0.01$). The frequency of "severe pain" (grade 3) was 23.8% without LEL, falling to 1.9% with LEL ($P<0.05$). Pain relief was significantly reduced throughout the treatment period (weeks 2-7). LEL therapy is capable of reducing the severity and duration of oral mucositis associated with radiation therapy. In addition, there is a tremendous potential for using LEL in combined treatment protocols utilizing concomitant chemotherapy and radiotherapy.

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

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FrancePURPOSE: 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.

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

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

[Laser therapy in the prevention and treatment of mucositis caused by anticancer chemotherapy]

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The appearance of mucositis is a frequent and painful secondary effect of anticancer chemotherapy. Patients who develop oral toxicity during the first course of treatment will almost assuredly show identical side effects during each subsequent course unless the drugs are changed or the doses are lowered. In the absence of an efficacious antidote or preventive prophylaxis for such lesions to date, this report presents the results of a preliminary retrospective non-randomized study of the effect of soft-laser treatments on mucositis in cancer patients receiving combination chemotherapy, including 5-fluorouracil. Iatrogenic mucositis was observed during 43% of 53 chemotherapy cycles in the case control population. Curative laser therapy reduced the time to repair lesions and the rate of therapeutic modifications. For patients who received soft-laser therapy as a preventive measure, the incidence of oral complications was reduced to 6% during 101 cycles of chemotherapy. All of these patients, even those who have encountered mucositis before receiving preventive laser therapy, terminated their cancer therapy as originally scheduled. Well designed and carefully controlled trials will be necessary to define the place of helium-neon laser therapy in the repair and prevention of oral complications due to cancer chemotherapy.

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Radiation-and chemotherapy-induced mucositis in oncology results of multicenter phase III studies

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FrancePurpose: Following several positive randomized trials in the field of chemotherapy-induced mucositis, a randomized multicenter trial was conducted to evaluate low-level He:Ne laser therapy (LLLT) for the prevention of acute radiation-induced oropharyngeal mucosal lesions. Materials and Methods: The trial was open to patients with carcinoma of the oropharynx, hypopharynx, and oral cavity being treated by external radiotherapy, with a total dose of 65 Gy at a rate of 1 fraction of 2 Gy/day, 5 days a week, from cobalt-60 or linear accelerator photons. Patients were assigned to either laser treatment (L+) or sham-treatment (L-) by computer blocked randomization. The protocol called for the inclusion of 30 patients, 15 in each arm. Analgesics could be prescribed, but not during the 2 days preceding each week evaluation. Patients received He:Ne laser applications daily for five consecutive days during the seven days of head and neck radiotherapy. The 9 treatment areas included: posterior third of buccal mucosa, soft palate, and anterior tonsillar pillars. The treatment time (t) for each application point was given by the equation: t (s) = energy (j/cmï¿½) x surface (cmï¿½) /Power (W). The average energy density delivered to the treatment areas was 2 J/cmï¿½. All laser illuminations were performed by the same individual in each center. Criteria for evaluation were the standard WHO scale for mucositis in the oropharynx and a segmented visual analogic scale for pain (patient self-evaluation). Results: Laser applications delayed time of onset, attenuated the peak severity, and shortened the duration of oral mucositis. The difference between L+ and L- patients was statistically significant from week 4 to week 7. During the 7 weeks of treatment, the mean grade of mucositis in L+ patients was significantly lower (p = 0.01) than the mean grade in L- patients. Results of decrease in pain intensity were also quite convincing. Laser applications reduced the incidence and duration of morphine administration. Ability to swallow was also improved. Conclusion: Low level He: Ne laser (LLL) seems to be a safe and efficient method for the prevention of radiation-induced stomatitis and chemo-induced mucositis, with a tremendous potential interest for combined modality treatment.

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http://jola.quintessenz.de/index.php?doc=abstract&abstractID=7801

Use of Laser photobiomodulation in the evolution of oral mucositis associated with CMF chemotherapy protocol in patients with breast cancer-Case Report.

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BrazilThe aim of this study was to evaluate the effectiveness of using a laser photobiomodulation on prevention and treatment of oral mucositis induced by chemotherapy protocol CMF (cyclophosphamide, methotrexate, 5-Fluouracil) in patients with breast cancer. Patients and Methods: We selected 12 patients who underwent 6 cycles of 21 days of treatment, with diagnosis of infiltrating ductal carcinoma (ICD C50.9). Were randomly divided into two groups: Group A with 6 patients (Protocol CMF + + Laser Protocol of stomatological CACON) Group B (Group C1 6 patients) were the control patients who received CMF hospital protocol established by CACON. The patients in Group A received the preventive use of FBML 24 hours before the start of chemotherapy cycle, then every 48 hours and was extended to one week after completion of chemotherapy. Results: In groups of oral mucositis grade 0 (64.29%), grade I (7.14%), grade II (14.29%), grade III (7.14%), grade IV (14.29 %) compared to group B, had mucositis grade 0 (35.71%), grade I (21.43%), grade II (28.57%), grade III (14.29%), grade IV (14.29%), patients who made use of FBML and as preventive therapy showed a reduction and pain relief in 42.86%. Conclusion: The low-power laser when used preventively or as therapeutic and showed immediate relief of pain and accelerate tissue repair.

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