

## **Research Digest**

### **Low Level laser Therapy (LLLT) and photobiomodulation**

#### **Xerostomia, Hyposalivation or saliva**

James D Carroll

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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.

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.

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# Effect of low-level laser therapy on radiotherapy-induced hyposalivation and xerostomia: a pilot study.

Saleh J, Figueiredo MA, Cherubini K, Braga-Filho A, Salum FG

1 Oral Medicine Division, Sao Lucas Hospital, Pontifical Catholic University of Rio Grande do Sul-PUCRS, Porto Alegre - RS, Brazil .

**OBJECTIVE:** The present pilot study aimed to assess the effect of low-level laser therapy (LLLT) on hyposalivation and xerostomia as a consequence of head and neck radiotherapy. **BACKGROUND DATA:** The benefits of LLLT in salivary flow have been shown; however, there are no studies investigating its effects on patients who have already undergone radiotherapy and present hyposalivation and xerostomia as a sequela. **METHODS:** Twenty-three patients with a history of head and neck malignancy, who were treated by fractionated teletherapy (dosimetry ranging from 45 to 70 Gy) in the cervicofacial region were selected. They all presented with xerostomia and severe hyposalivation. Patients were randomly distributed into a laser group (n=12) and a control group (n=11). A GaAlAs laser (830 nm, 100 mW, illuminated area 0.028 cm<sup>2</sup>, 3.57 W/cm<sup>2</sup>, 20 sec, 2.0 J, 71 J/cm<sup>2</sup>) was used punctually in the major salivary glands, twice a week for 6 weeks, with a 12 session total. Stimulated and unstimulated salivary flow rate (SFR) were assessed, as well as the xerostomia and quality of life related to oral health (QLROH). **RESULTS:** The analysis did not show any significant difference between the groups with regards to the SFR and xerostomia, and the QLROH. However, at the end of the treatment, the xerostomia and the QLROH showed significant improvement in both groups compared with assessments performed at baseline, highlighting the importance of advice given to the irradiated patients, and their follow-up. **CONCLUSIONS:** With the parameters used, LLLT was not able to increase SFR or decrease xerostomia. The results may be associated with the late effects of radiotherapy on glandular structure, such as fibrosis and acinar atrophy.

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=25302460](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=25302460)

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

Silva GB, Sacono NT, Othon-Leite AF, Mendonca EF, Arantes AM, Bariani C, Duarte LG, Abreu MH, Queiroz-Junior CM, Silva TA, Batista AC

Hematopoietic Stem Cell Transplant Unit, Araujo Jorge Hospital, Associacao de Combate ao Cancer de Goias, Goiania, Goias, Brazil.

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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# Effect of laser acupuncture on salivary flow rate in patients with Sjogren's syndrome.

Cafaro A, Arduino PG, Gambino A, Romagnoli E, Broccoletti R

Department of Surgical Sciences, CIR-Dental School, University of Turin, Via Nizza 230, 10126, Turin, Italy.

Sjogren's syndrome (SS) is a multisystem autoimmune disease characterized by hypofunction of the salivary and lacrimal glands, frequently relieved with symptomatic treatments, such as saliva substitutes, eye lubricants, and cholinergic stimulators. The aim of this pilot randomized placebo-controlled study was to estimate the effects of laser acupuncture on salivary flow rates in patients with severe hyposalivation due to SS. A prospective cohort of 26 female patients affected by SS has been evaluated. The laser therapy equipment used was the Pointer Pulse, emitting light in the red visible spectrum (650 nm), with a power of 5 mW and an irradiation time of 120 s per acupoint, in an area of 3.14 mm<sup>2</sup> (fluence = 19.2 J/cm<sup>2</sup>, power density = 0.16 W/cm<sup>2</sup>, total dose = 0.6 J). The following acupuncture points were stimulated bilaterally: LI 2 Erjian, ST 5 Daying, ST 6 Jiache, ST 7 Xiaguan, SI 19 Tinggong, and BL 13 Feishu. True laser acupuncture led to a significantly higher amount of saliva production, measured after the end of the protocol (5 weeks), and during the 6-month follow-up period. The results are stable from the end of the protocol until the 3rd month of follow-up; during the last control, a slight but significant decrease in production has also been shown. This preliminary study proposes laser acupuncture as a possible treatment for improving salivary flow rates in patients with SS, but further validation on a larger sample is still necessary.

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=24820476](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=24820476)

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

Oton-Leite AF, Elias LS, Morais MO, Pinezi JC, Leles CR, Silva MA, Mendonca EF

Department of Oral Medicine (Oral Pathology), Dental School, Federal University of Goias.

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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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=24164228](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=24164228)



# LED and laser photobiomodulation in the prevention and treatment of oral mucositis: experimental study in hamsters.

Freire MD, Freitas R, Colombo F, Valenca A, Marques AM, Sarmiento VA

Federal University of Bahia, Rua Araujo Pinho, 62 Canela, Salvador, Bahia, 40110-150, Brazil, rosariofreire@ufba.br.

**PURPOSE:** This paper aims to evaluate the effects of laser (660 nm) and light-emitting diode (LED) (670 nm) irradiation in the cheek pouch mucosa of hamsters with oral mucositis (OM) induced by chemotherapy (Che) with 5-fluorouracil (5-FU). **MATERIALS AND METHODS:** In the preventive groups, the photobiomodulation was started 1 day before the drug administration and was performed every 48 h (Ia, IIa, Ib, and IIb). In the therapeutic groups (IIIa, IIIb, IVa, and IVb), the irradiations were started on the third day after the Che d(0) and was performed every 48 h. In both groups, animals were sacrificed 7 or 14 days after Che. In the positive control groups, the hamsters were subjected to Che but did not receive irradiation, and they were sacrificed in 7 days (Va) or 14 days (Vb). In the negative control groups, no procedures were done and the animals were sacrificed 7 days (Vc) or 14 days (Vd) after the experiment started. **RESULTS:** The results indicated loss of body mass, xerostomia, and alopecia in the animals subjected to Che and the healing of OM to different degrees after the photobiomodulation treatment. Histologically, the positive control and experimental groups showed inflammation, predominately with lymphocytes and plasma cells, which tended to diminish with time. Epithelial atrophy, hyperemia, fibroblast proliferation, and vascular congestion were also observed at those intervals. **CONCLUSIONS:** The best results were obtained from the preventive laser and LED photobiomodulation groups; both treatments were effective in diminishing the OM lesions. **CLINICAL RELEVANCE:** A noninvasive and effective method with sparse side effects of OM would be desirable for use in cancer centers around the world.

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=23949015](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=23949015)

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

Arbabi-Kalati F, Arbabi-Kalati F, Moridi T

Brain and Spinal Injury Research Center, Tehran University of Medical Sciences, Tehran, Iran.  
farbabi@razi.tums.ac.ir.

Iran Radiotherapy 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.

Acta Med Iran 2013 51(3) 157-62

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=23605599](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=23605599)

# Proinflammatory cytokine levels in saliva in patients with burning mouth syndrome before and after treatment with low-level laser therapy.

Pezelj-Ribaric S, Kqiku L, Brumini G, Urek MM, Antonic R, Kuis D, Glazar I, Stadler P

Department of Oral Medicine and Periodontology, School of Dentistry, Faculty of Medicine, University of Rijeka, Brace Branchetta 20, Rijeka, Croatia, sonja.pezelj-ribaric@medri.hr.

The aim of this study was to determine the levels of proinflammatory tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) cytokines in whole unstimulated saliva in subjects with burning mouth syndrome (BMS) before and after treatment with low-level laser therapy (LLLT). BMS is characterized by a continuous, painful burning sensation in a clinically normal-appearing oral mucosa. A sample consisting of 40 consecutive subjects was selected on a voluntary basis from the pool of patients who presented for diagnosis and treatment of BMS at the Oral Medicine Unit of the Faculty of Medicine of the University of Rijeka. For determination of salivary levels of TNF-alpha and IL-6, ELISA (Sigma Immunochemicals, St. Louis, MO, USA) was performed to determine the salivary levels of TNF-alpha and IL-6. After 4 weeks of LLLT, the salivary levels of TNF-alpha and IL-6 in the experimental group decreased significantly ( $p < 0.001$ ). There was no significant difference in the experimental group regarding visual analogue scale.

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=22773117](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22773117)

# [The effects of low-level laser therapy on xerostomia (mouth dryness)].

Pavlic V

Katedra za parodontologiju i oralnu medicinu, Medicinski fakultet, Univerzitet u Banjaluci. dr.  
vericapavlic@gmail.com

**INTRODUCTION:** Xerostomia is a subjective complaint of mouth/oral dryness, caused by a reduction in normal salivary secretion due to different causes. Even though there are many available treatment modalities to enhance salivary flow, the therapy often remains unsatisfactory. The low-level laser therapy (low-level laser irradiation, photo-biomodulation) has been extensively used as a new, non-invasive approach and advantageous tool for reduction of xerostomia. Therefore, the aim of this study is to give a systematic overview on the effects of low-level laser therapy on xerostomia. **MATERIAL AND METHODS:** A systematic review of published articles in PubMed database was carried out using keywords: "low-level laser therapy", "xerostomia", "mouth dryness". **RESULTS:** In all published articles, which were considered adequate for this overview, positive effects of low-level laser therapy were reported. Low-level laser therapy could significantly enhance salivary secretion and improve antimicrobial characteristics of secreted saliva (increased level of secretory immunoglobulin A; sIgA). Furthermore, low-level laser therapy could improve salivary flow and regeneration of salivary duct epithelial cells. **CONCLUSION:** The current literature suggests that low-level laser therapy can be safely and effectively used as an advanced treatment modality for reduction of xerostomia. Further in vivo, in vitro and clinical studies using different irradiation parameters are suggested to determine the best laser parameters to be used.

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=22730712](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=22730712)

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

Oton-Leite AF, Correa de Castro AC, Morais MO, Pinezi JC, Leles CR, Mendonca EF

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

**BACKGROUND:** 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/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=21472883](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21472883)

# The Effect of Low-Level Laser Therapy on Salivary Glands in Patients With Xerostomia.

Loncar B, Mravak Stipetic M, Baricevic M, Risovic D

1 Department of Oral Medicine, School of Dental Medicine, University of Zagreb , Croatia .

**Abstract Objective:** The aim of this study was to investigate the effect of low-level laser irradiation on the secretory function of salivary glands in 34 patients with xerostomia (dry mouth). **Background Data:** Xerostomia, a common complaint of oral dryness within the elderly population, is caused by a reduction in normal salivary secretion due to different causes. Treatment is aimed at increasing salivary flow, although in most cases it remains palliative. **Materials and Methods:** In this study, laser light from a pulsed Ga-As laser operating at 904 nm was applied bilaterally on each salivary gland area: extraorally on the parotid and submandibular gland areas and intraorally on the sublingual gland area. The operational probe distance from the irradiated area was 0.5 cm resulting in an irradiance of 246 mW/cm<sup>2</sup>. The exposure time was 120 sec per daily treatment during 10 consecutive days. The average energy density per exposure was 29.5 J/cm<sup>2</sup>. The control group consisted of 16 patients who were treated with 15 mL of a 2% citric acid solution applied as a mouth rinse for 30 sec. **Results:** The average difference in the amount of salivation (dQ-sal, mL/min) before and after laser therapy increased linearly from dQ-sal = 0.05 mL/min on the first day, up to dQ-sal = 0.13 mL/min on the last (10th) day of therapy. In the control group, the average dQ-sal initially demonstrated a gradual increase, with a reversal of the trend toward the end of the therapy period and eventually yielding no correlation between the duration of therapy and dQ-sal. **Conclusion:** The results of our study indicate that the effects of low-level laser therapy on salivary glands are not only stimulating, but also regenerative to a degree since the glandular response to the same amount of applied laser energy increased linearly over time.

Photomed Laser Surg 2010 Nov 6

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=21054200](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=21054200)

## Effects of low-level laser treatment on mouth dryness.

Juras DV, Lukac J, Cekic-Arambasin A, Vidovic A, Canjuga I, Sikora M, Carek A, Ledinsky M

Dental Clinic, Zagreb University Hospital Center, Zagreb, Croatia. djuras@sfzg.hr

Mouth dryness (MD) is usually followed by inadequate mechanical cleaning of the mouth and decrease in the levels of salivary antimicrobial proteins (including secretory immunoglobulin A (sIgA)). It is accompanied by difficulties during speaking and food swallowing, with an unpleasant taste, burning sensations in the mouth and higher susceptibility to oral diseases. Low-level laser treatment (LLLT) can intensify cell metabolism and its application on salivary glands could improve salivation. The purpose of this study was to evaluate the effects of LLLT on salivation of patients suffering from MD. The study included 17 patients with MD. Their major salivary glands were treated with low intensity laser BTL2000 on 10 occasions. The whole unstimulated and stimulated saliva quantities were measured just before the 1st, after the 10th and thirty days following the last (10th) treatment. In the samples of unstimulated saliva concentrations of sIgA were estimated by using ELISA method and its quantity in the time unit was calculated. The visual analogue scale (VAS) score was used to assess burning and/or pain intensity at these three time points. Statistical tests revealed significant salivation improvement quantitatively and qualitatively, i.e. increase in the quantity of saliva and sIgA. VAS score was also significantly improved and no side effects were observed. Conclusions: According to the results of this study, application of LLLT to xerostomic patients' major salivary glands stimulates them to produce more saliva with better antimicrobial characteristics and improves the difficulties that are associated with MD. This simple non-invasive method could be used in everyday clinical practice for the treatment of MD.

Coll Antropol 2010 Sep 34(3) 1039-43

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=20977100](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=20977100)

## [Buccal manifestations in patients submitted to chemotherapy]

Hespanhol FL, Tinoco EM, Teixeira HG, Falabella ME, Assis NM

Faculdade de Odontologia, Suprema - Faculdade de Ciências Médicas e da Saúde de Juiz de Fora, Salvaterra, Juiz de Fora MG, Brazil. hespanhol@croe.com.br

Several changes in the oral cavity due to chemotherapy can be observed and can lead to important systemic complications, increasing the time of the patient in hospital and the costs of the treatment as well as affect the quality of life of the patients. The aim of this study was to assess the oral manifestation in patients treated with chemotherapy according to sex, age and tumor type. Data was collected in an oncology hospital in Juiz de Fora, Minas Gerais State, from patients' records that were submitted to oncologic treatment. It was possible to verify that mucositis, associated or not to other type of lesions, was the most common lesion in both sex of all ages (15.5%). Xerostomia and other lesions, such as Candida infection and aphthous lesions, were also present. It is possible to improve the quality of life of the patient during and after anti-neoplastic therapies through a protocol of odontological assistance that includes changes of the oral environment previous to chemotherapy such as profilaxis, caries removal, treatment of periodontal and periapical lesions, oral hygiene instructions, diet orientation and laser therapy. It is very important the insertion of the dentist in the oncologic medical team for the early diagnosis of the oral manifestation and follow-up during treatment time.

Cien Saude Colet 2010 Jun 15 Suppl 1 1085-94

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=20640266](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=20640266)



# Laser as a therapy for dry mouth symptoms in a patient with Sjogren's syndrome: a case report.

Simoes A, Platero MD, Campos L, Aranha AC, Eduardo Cde P, Nicolau J

Oral Biology Research Center, Department of Biomaterials and Oral Biochemistry, School of Dentistry, University of Sao Paulo, Sao Paulo, Brazil. lysimoes@usp.br

This clinical case study reports on dry mouth symptoms in a patient with Sjogren's syndrome (SS) who was treated with laser phototherapy (LPT). A 60-year-old woman diagnosed with SS was referred to the laboratory for lasers in dentistry to treat her severe xerostomia. A diode laser (780 nm, 3.8 J/cm<sup>2</sup>, 15 mW) was used to irradiate the parotid, submandibular, and sublingual glands, three times per week, for a period of 8 months. The salivary flow rate and xerostomia symptoms were measured before, during, and after LPT. Dry mouth symptoms improved during LPT. After LPT, the parotid salivary gland pain and swelling were no longer present. Treatment with LPT was an effective method to improve the quality of life of this patient with SS.

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=19938253](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=19938253)

# Laser Phototherapy as Topical Prophylaxis Against Radiation-Induced Xerostomia.

Simoes A, de Campos L, de Souza DN, de Matos JA, Freitas PM, Nicolau J

1 Department of Dental Materials, Division of Oral Biology, Faculdade de Odontologia, Universidade de Sao Paulo , Sao Paulo, SP, Brazil .

**Abstract** The common consequences of radiotherapy (RT) to the head and neck are oral mucositis, xerostomia, and severe pain. The aim of this study was to verify how laser phototherapy (LPT) used for oral mucositis could influence xerostomia symptoms and hyposalivation of patients undergoing RT. Patients were divided into two groups: 12 individuals receiving three laser irradiations per week (G1) and 10 patients receiving one laser irradiation per week (G2). A diode laser (660 nm, 6 J/cm<sup>2</sup>, 0.24 J, 40 mW) was used until completely healing of the lesions or the end of the RT. At the first and last laser sessions, whole resting and stimulated saliva were collected, and questionnaires were administered. According to Wilcoxon and Student statistical test, xerostomia for G1 was lower than for G2 ( $p < 0.05$ ), and salivary flow rate was no different before and after RT, except for stimulated collection of G2, which was lower ( $p < 0.05$ ). Our results suggest that LPT can be beneficial as an auxiliary therapy for hypofunction of salivary glands.

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[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=19814701](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=19814701)

# Salivary Levels of TNF-alpha and IL-6 in Patients with Denture Stomatitis Before and After Laser Phototherapy.

Simunovic-Soskic M, Pezelj-Ribaric S, Brumini G, Glazar I, Grzic R, Miletic I

1 Department of Prosthodontics, School of Dentistry, Medical Faculty, University of Rijeka , Croatia .

**Abstract Objective:** The aim of this study was to monitor therapeutic response by determining the level of proinflammatory cytokines TNF-alpha and IL-6 in whole unstimulated saliva in patients with denture stomatitis (DS), before and after laser phototherapy (LPT). **Background:** DS is an inflammatory condition that occurs in subjects who wear dentures, and it is a common oral mucosal lesion. A potential noninvasive treatment for DS patients is LPT. **Materials and Methods:** A sample consisting of 40 consecutive subjects was selected on a voluntary basis from patients who presented for the diagnosis and treatment of DS at the Oral Medicine Unit of the Medical Faculty at the University of Rijeka. A clinical examination was performed according to the standard clinical criteria. Lesions described as palatal inflammation were diagnosed as Newton type II denture stomatitis. The patients were randomly assigned to either an experimental group (20 patients receiving real LPT) or a control group (20 patients receiving inactive/placebo laser treatment). In order to determine the salivary levels of TNF-alpha and IL-6, ELISA (Sigma Immunochemicals, St Louis, MO) was performed. **Results:** Following treatment with LPT for 4 wk, the levels of TNF-alpha and IL-6 decreased significantly ( $p < 0.001$ ) and were significantly different from controls ( $p < 0.001$ ). **Conclusion:** The results of this study suggest that LPT may be an efficacious choice of therapy.

Photomed Laser Surg 2009 Oct 1

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# Improvement in quality of life of an oncological patient by laser phototherapy.

Campos L, Simoes A, Sa PH, Eduardo Cde P

Oral Biology Research Center, Department of Biomaterials and Oral Biochemistry, School of Dentistry, University of Sao Paulo, Sao Paulo, Brazil.

**OBJECTIVE AND BACKGROUND DATA:** Common side effects of radiotherapy (RT) to the head and neck include oral mucositis, xerostomia, and severe pain. The aim of this study is to report improvement in the quality of life of an oncological patient by laser phototherapy (LPT). **CLINICAL CASE AND LASER PHOTOTHERAPY PROTOCOL:** The patient, a 15-year-old girl diagnosed with mucoepidermoid carcinoma, underwent surgical excision of a tumor of the left palatomaxilla. After that, she was subjected to 35 sessions of RT (2 Gy/d). Clinical examination revealed the spread of severe ulcerations to the jugal mucosa, gums, lips, hard palate, and tongue (WHO mucositis score 3). She had difficulty in moving her tongue and she was unable to eat any solid food. Oral hygiene orientation and LPT were performed throughout all RT sessions. A continuous diode laser, 660 nm, 40 mW, 6 J/cm<sup>2</sup>, 0.24 J per point in contact mode, with spot size of 0.04 cm<sup>2</sup> was used in the entire oral cavity. A high-power diode laser at 1 W, 10 sec per cm of mucositis, approximately 10 J/cm<sup>2</sup>, was used in defocused mode only on ulcerative lesions. After the first laser irradiation session, decreases in pain and xerostomia were reported; however, a more significant improvement was seen after five sessions. At that point although the mucositis score was still 2, the patient reported that she was free of pain, and consequently a palatine plate could be made to rehabilitate the entire surgical area. Seventeen laser irradiation sessions were necessary to eliminate all oral mucositis lesions. **CONCLUSION:** Normal oral function and consequent improvements in the quality of life of this oncologic patient were observed with LPT.

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# Laser phototherapy effect on protein metabolism parameters of rat salivary glands.

Simoes A, Siqueira WL, Lamers ML, Santos MF, Eduardo Cde P, Nicolau J

Oral Biology Research Center, Faculty of Dentistry, University of Sao Paulo, Av. Prof. Lineu Prestes, 2227, Cidade Universitaria, Sao Paulo, SP, 05508-000, Brazil. lysimoes@usp.br

The aim of this study was to evaluate the effects of infrared diode laser phototherapy (LP) on tissues of the submandibular gland (SMG) and parotid gland (PG). Wistar rats were randomly divided into experimental (A and B) and control (C) groups. A diode laser, 808 nm wavelength, in continuous wave mode, was applied to the PG, SMG and sublingual gland in the experimental groups on two consecutive days. The doses were 4 J/cm<sup>2</sup> and 8 J/cm<sup>2</sup>, and total energy was 7 J and 14 J, respectively. The power output (500 mW) and power density (277 mW/cm<sup>2</sup>) were the same for both experimental groups. In order to visualize the area irradiated by the infrared laser, we used a red pilot beam (650 nm) with 3 mW maximum power for the experimental groups. For the control group, the red pilot beam was the only device used. The SMG and PG were removed after 1 week of the first irradiation. Total protein concentration, amylase, peroxidase, catalase and lactate dehydrogenase assays were performed, as well as histological analysis. Statistical tests revealed significant increase in the total protein concentration for groups A and B in the parotid glands ( $P < 0.05$ ). Based on the results of this study, LP altered the total protein concentration in rats' parotid glands.

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# Effect of defocused infrared diode laser on salivary flow rate and some salivary parameters of rats.

Simoes A, Nicolau J, de Souza DN, Ferreira LS, de Paula Eduardo C, Apel C, Gutknecht N

Oral Biology Research Center, Department of Dental Materials, Faculty of Dentistry, University of Sao Paulo, 05508-000, Sao Paulo, Brazil, lysimoes@gmail.com

This study aims to investigate whether infrared diode low-level laser therapy (LLLT) increased salivary flow rate and altered pH value, protein concentration, and peroxidase and amylase activities in saliva of rats. Wistar rats were used and divided into three groups. Experimental groups (A and B) had their parotid, submandibular and sublingual glands submitted to diode laser, 808-nm wavelength, on two consecutive days. The dose results were 4 and 8 J/cm<sup>2</sup>, respectively. A red guide light was used to visualize the irradiated area. Group C was irradiated only with red pilot beam and served as control. The saliva samples were collected after each irradiation step (first and second collection days) and 1 week after the first irradiation (seventh day). Statistical analysis was performed, and differences were observed according to different days of salivary collection. The results showed that salivary flow rate for groups A and B was higher on the seventh day if it is compared to data obtained for the first day ( $p < 0.05$ ). LLLT applications on salivary glands are a therapy procedure that requires further studies.

Clin Oral Investig 2008 Mar 12(1) 25-30

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=17624559](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17624559)

## [The CO2 laser in stomatology. Part 2]

Bornstein MM, Suter VG, Stauffer E, Buser D

Klinik für Oralchirurgie und Stomatologie, Zahnmedizinische Kliniken, Universität Bern, Freiburgstrasse 7, 3010 Bern. michael.bornstein@zmk.unibe.ch

The second part of this review presents and discusses evidence in the recent literature for the application of the CO<sub>2</sub> laser for the therapy of stomatologic lesions. Clinical outcomes and complications for the use of the CO<sub>2</sub> laser are presented for the following stomatological conditions: leukoplakia, lichen planus, benign soft-tissue and salivary gland tumors, reactive soft tissue changes (i.e., fibroepithelial polyps), recurrent aphthous stomatitis, drug-induced gingival hyperplasia, mucous extravasation and mucous retention cysts, herpes simplex virus-induced lesions, maxillary midline frenum, and ankyloglossia (tongue-tie). This review outlines indications in which the CO<sub>2</sub> laser is the treatment method of choice and in which situations the laser has still to be applied with caution.

Schweiz Monatsschr Zahnmed 2003 113(7) 766-85

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12956039](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12956039)

# NASA light-emitting diodes for the prevention of oral mucositis in pediatric bone marrow transplant patients.

Whelan HT, Connelly JF, Hodgson BD, Barbeau L, Post AC, Bullard G, Buchmann EV, Kane M, Whelan NT, Warwick A, Margolis D

Department of Neurology, Medical College of Wisconsin, Milwaukee, Wisconsin 53226, USA.  
hwhelan@mcw.edu

**OBJECTIVE:** The purpose of this study was to determine the effects of prophylactic near-infrared light therapy from light-emitting diodes (LEDs) in pediatric bone marrow transplant (BMT) recipients. **BACKGROUND DATA:** Oral mucositis (OM) is a frequent side effect of chemotherapy that leads to increased morbidity. Near-infrared light has been shown to produce biostimulatory effects in tissues, and previous results using near-infrared lasers have shown improvement in OM indices. However, LEDs may hold greater potential for clinical applications. **MATERIALS AND METHODS:** We recruited 32 consecutive pediatric patients undergoing myeloablative therapy in preparation for BMT. Patients were examined by two of three pediatric dentists trained in assessing the Schubert oral mucositis index (OMI) for left and right buccal and lateral tongue mucosal surfaces, while the patients were asked to rate their current left and right mouth pain, left and right xerostomia, and throat pain. LED therapy consisted of daily treatment at a fluence of 4 J/cm<sup>2</sup> using a 670-nm LED array held to the left extraoral epithelium starting on the day of transplant, with a concurrent sham treatment on the right. Patients were assessed before BMT and every 2-3 days through posttransplant day 14. Outcomes included the percentage of patients with ulcerative oral mucositis (UOM) compared to historical epidemiological controls, the comparison of left and right buccal pain to throat pain, and the comparison between sides of the buccal and lateral tongue OMI and buccal pain. **RESULTS:** The incidence of UOM was 53%, compared to an expected rate of 70-90%. There was also a 48% and 39% reduction of treated left and right buccal pain, respectively, compared to untreated throat pain at about posttransplant day 7 ( $p < 0.05$ ). There were no significant differences between sides in OMI or pain. **CONCLUSION:** Although more studies are needed, LED therapy appears useful in the prevention of OM in pediatric BMT patients.

J Clin Laser Med Surg 2002 Dec 20(6) 319-24

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=12513918](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12513918)



## Low-level laser therapy after molar extraction.

Kucerova H, Dostalova T, Himmlova L, Bartova J, Mazanek J

Institute of Dental Research, General Faculty Hospital, Prague, Czech Republic.

**OBJECTIVE:** The aim of the study was to evaluate effect of the different frequencies of low-level laser radiation (diode 670 nm and Helium-Neon 632.8 nm) on the healing process after human molar extractions. Frequencies of 5 Hz, 292 Hz, and 9,000 Hz were used in experiments. Monitoring of secretory IgA and albumin level in saliva and changes in bone density were used as objective markers of biostimulatory effect. **SUMMARY BACKGROUND DATA:** From the literature, it is known that if the alveolus is irradiated after extraction along with the lingual and buccal bony wall, faster coagulation, less postoperative discomfort, and quicker healing can be expected. **Methods:** Subjective evaluation of therapy was observed using a scale (from -, negative therapeutic effect, to +++++, excellent treatment effect). Changes of secretory immunoglobulin A (sIgA), albumin levels, and bone density were compared in a group of 150 patients (nonlaser therapy, 30 patients). **RESULTS:** Differences in levels of the saliva markers (sIgA and albumin) were found to be significant when comparing irradiated and nonirradiated groups, and in comparison with those groups irradiated by various modulatory frequencies. Significant differences were observed between the increase of sIgA res. albumin and subjective feelings during treatment. Bone density after extraction and 6 months after surgical treatment was examined using dental digital radiovisiography. No significant differences were detected between bone density in irradiated and nonirradiated groups, perhaps due to our therapy protocol. **CONCLUSIONS:** The low-level laser has no influence on the process of osseointegration. This effect was observed on fracture healing in rats using He-Ne laser radiation. We found no differences in the bone density when compared to the control group.

J Clin Laser Med Surg 2000 Dec 18(6) 309-15

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=11572225](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11572225)

# Oral mucositis in myelosuppressive cancer therapy.

Epstein JB, Schubert MM

Vancouver Hospital, Dentistry Department, BC, Canada.

Because the etiology of mucositis is multifactorial, approaches to prevention and management have also been multifactorial. Effective prevention and management of mucositis will reduce the pain and suffering experienced during cancer treatment. Oropharyngeal pain in cancer patients frequently requires systemic analgesics, adjunctive medications, physical therapy, and psychologic therapy in addition to oral care and topical treatments. Good oral hygiene reduces the severity of oral mucositis and does not increase the risk of bacteremia. Current approaches to management include frequent oral rinsing with saline or bicarbonate rinses, maintaining excellent oral hygiene, and using topical anesthetics and analgesics. Cryotherapy is a potential adjunctive approach in some cases. There are a number of approaches that appear to represent viable candidates for further study. Biologic response modifiers offer the potential for prevention and for acceleration of healing. Various cytokines will enter clinical trials in the near future; these offer the potential for reduction of epithelial cell sensitivity to the toxic effects of cancer therapy or for stimulation of repair of the damaged tissue. Other approaches include the use of medications to reduce exposure of the oral mucosa to chemotherapeutic drugs that are secreted in saliva. Antimicrobial approaches have met with conflicting results, little effect being seen with chlorhexidine and systemic antimicrobials in the prevention of mucositis in radiation patients. In patients with BMT and patients with leukemia, chlorhexidine may not be effective in preventing mucositis, although there may be reduction in oral colonization by *Candida*. Initial studies of topical antimicrobials that affect the gram-negative oral flora have shown reductions in ulcerative mucositis during radiation therapy but have not been assessed in leukemia/BMT. Among other approaches that require further study are low-energy lasers and anti-inflammatory medications. These approaches to management have undergone initial study, but additional investigation is needed to determine their effectiveness with respect to the prevention of mucositis and symptom management and to determine appropriate doses and frequencies of intervention. Current studies and our increasing understanding of the pathogenesis of oral mucositis will lead to new approaches to management and improved quality of life for these patients.

Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999 Sep 88(3) 273-6

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=10503852](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10503852)

## [The combined treatment of patients with digestive tract diseases by the action of the enterosorbent Enterosgel and of the intravascular laser irradiation of the blood]

Shevchenko IuN, Osypenko NI, Zlochevskaia LL, Kocherga TV, Komarnitskaia NI

Rehabilitative, medical treatment involved a combined use of enterosorption (the drug Enterosgel) and intravascular laser irradiation of blood (ILIB). The results obtained showed the adopted combined mode of treatment (Enterosgel + ILIB) to have a positive effect on the patients' body. The above alternative while eliminating the remainder from the body promotes an increase in the content of large granule-containing lymphocytes, which events result in restoration of those morphology of those leucocytes having undergone degeneration, with crystallization of saliva getting back to normal. Considering the present health-hazard conditions, negative environmental effects on human organism, the above treatment option is indicated not only to patients having disorders of the alimentary canal but also to those presenting with other pathologies, as well as for preventive and health-promoting purposes.

Lik Sprava 1998 Aug -6 149-52

[http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?  
cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=9844904](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9844904)

# 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.

**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/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list\\_uids=9240635](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9240635)

# (Double blind study on the biostimulatory effects of laser irradiation on the parotid gland in patients affected by Sjogrens syndrome)

Fructuoso F. J. G., Moset J. M.

Estudio randomizado doble ciego sobre los efectos bioestimulantes del laser en la irradiacion de glandula parotida en pacientes afectos de sindrome de Sjogren

Randomized double blind study on the biostimulatory effects of laser irradiation of the parotid gland in patients suffering of Sjogren syndrom

Fernando Jose Garcia Fructuoso y Juan Morros Moset\*

La dificultad que implica el tratamiento sintomático de la xerostomía en el síndrome de Sjogren ha motivado la búsqueda de terapias alternativas. En este trabajo se ensaya el laser en la irradiación de la glandula parotida de pacientes afectos del síndrome. Las diferencias frente al grupo control han resultado ser estadísticamente significativas.

Palabras clave: Síndrome de Sjogren. Glandula parotida. Laser y síndrome de Sjogren. Bioestimulación de glandula parotida.

The difficulties that the xerostomy of Sjogren syndrome present regarding its treatment, has motivated the search for alternative therapies. In this work Laser radiation has been tried on the parotid gland of patients affected by Sjogren syndrome and it has been observed that in comparison to those patients of the control group, the results of the laser - treated patients are better (statistically significant).

Key words: Sjogren syndrome. Parotid gland. Laser and Sjogren syndrome. Biostimulation of the parotid gland.

## RESULTADOS

Si bien al proponer este estudio lo hicimos con la firme creencia de que la terapia laser podía aportar mucho en la terapéutica sintomática del SS, hemos de confesar que los resultados nos han sorprendido en gran medida.

El estudio, que continua actualmente con el seguimiento de los pacientes, debe abarcar un mínimo de cinco años hasta que podamos cuantificar si existen diferencias significativas en cuanto a degeneración maligna de nuestra serie.

Valgan pues las siguientes conclusiones a modo de preinforme.

La utilización de la radiación laser diódica se ha mostrado eficaz en el tratamiento sintomático del SAR, con diferencias estadísticamente significativas respecto al grupo placebo ( $p < 0,02$ ).

Debemos diferenciar los parámetros de cuantificación, ya sean objetivos o bien subjetivos. Dentro de los objetivos, debemos hacer constar que el Test de Shirmer no se ha visto afectado en absoluto, así como tampoco lo ha sido la VSG, hemograma ni medidas de mayor sofisticación como la Beta-2-

# PREVENÇÃO DA XEROSTOMIA E DA MUCOSITE ORAL INDUZIDAS POR RADIOTERAPIA COM USO DO LASER DE BAIXA POTÊNCIA\*

Carlos de Oliveira Lopes<sup>1</sup>, Josepa Rigau I Mas<sup>2</sup>, Renato Amaro Zângaro<sup>3</sup>

Brazil Low level laser therapy in the prevention of radiotherapy-induced xerostomia and oral mucositis.

**OBJECTIVE:** To verify if the use of InGaAlP laser with 685 nm wave length can reduce the xerostomy incidence, the oral mucositis severity and the pain related to mucositis in patients with head and neck cancer submitted to radiotherapy. **MATERIALS AND METHODS:** Sixty patients presenting head and neck carcinoma were submitted to radiotherapy with daily doses of 1.8 to 2.0 Gy and a final dose of 45 to 72 Gy. The salivary volume was evaluated in the first and fifteenth days, at the end of the treatment and after 15 and 30 days. The oral mucositis was evaluated on a weekly basis. Twenty-nine patients were submitted to radiotherapy without laser and 31 were submitted to radiotherapy and laser with daily doses of 2 joules/ cm<sup>2</sup> in predetermined areas of the oral mucosa and the parotid and submandibular glands. **RESULTS:** In the group submitted to radiotherapy and laser the incidence of mucositis ( $p < 0.001$ ) and pain ( $p < 0.016$ ) was significantly lower and the salivary volume ( $p < 0.001$ ) was kept higher during and after the treatment. **CONCLUSION:** The group of patients submitted to radiotherapy and laser had lower incidence of xerostomy, oral mucositis and pain when compared to the group treated with radiotherapy without laser, producing statistically significant results.

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<http://www.scielo.br/pdf/rb/v39n2/29196.pdf>