Therapeutic laser for pain relief after tonsillectomy

Analgesia com laser terapêutico após tonsilectomia

Felipe Costa Neiva[1], Fernando Mirage J. Vieira[2], Claudia Regina Figueiredo[3], Aldo Eden C. Stamm[4], Luc Louis M. Weckx[5], Shirley Shizue N. Pignatari[6]

ABSTRACT

Objective: The postoperative period of a tonsillectomy is usually very painful, requiring the use of pain-relieving drugs. The aim of this study was to evaluate the efficacy of low-level laser therapy in post-tonsillectomy pain control.

Methods: 18 children aged 5 to 15 years undergoing adenotonsillectomy between June 2005 and October 2006 were randomized to receive either local application of therapeutic laser immediately after surgery and 24 hours postoperatively (n=9) or routine analgesic drug therapy, if necessary. Pain was assessed by visual analog scale scores, need for analgesics, and acceptance of diet during the postoperative period.

Results: Patients undergoing laser applications had lower median pain scores and required less analgesic medication postoperatively than the control group. Acceptance of diet was similar in both groups.

Conclusions: Preliminary results showed that low-level laser therapy is effective in the reduction of post-tonsillectomy pain, minimizing the need of analgesic medication in children and adolescents.

Key-words: laser therapy; tonsillectomy; pain; child.

RESUMO

Objetivo: O pós-operatório da tonsilectomia é, em geral, bastante doloroso e os pacientes necessitam de analgésicos. Este estudo visou avaliar a eficácia da aplicação do *laser* terapêutico no controle da dor no pós-operatório de tonsilectomia.

Métodos: 18 crianças de cinco a 15 anos de idade foram submetidas à adenotonsilectomia, no período de junho de 2005 a outubro de 2006, sendo randomizadas para receber aplicações de *laser* terapêutico na área cirúrgica imediatamente após o procedimento e 24 horas após a cirurgia (n=9) ou seguir a rotina, com analgesia farmacológica, se necessário. A avaliação da dor foi realizada por escala analógica de dor, pela necessidade de analgésicos e pela aceitação da dieta no pós-operatório.

Resultados: Os pacientes submetidos à aplicação do *laser* apresentaram medianas das notas da escala de avaliação da dor menores e utilizaram menos analgésicos no pós-operatório em comparação aos pacientes controles. A aceitação da dieta nos dois grupos não foi diferente.

Conclusões: Os resultados preliminares mostraram que o *laser* terapêutico foi eficaz na diminuição da dor e na redução de uso de analgésicos no pós-operatório de tonsilectomias em crianças e adolescentes.

Palavras-chave: terapia a *laser*; tonsilectomia; dor; criança.

Instituição: Universidade Federal de São Paulo (Unifesp), São Paulo, SP, Brasil

[1]Mestrando do Departamento de Otorrinolaringologia e Cirurgia de Cabeça e Pescoço da Escola Paulista de Medicina da Universidade Federal de São Paulo (Unifesp-EPM), São Paulo, SP, Brasil

[2]Mestre pelo Departamento de Otorrinolaringologia e Cirurgia de Cabeça e Pescoço da Unifesp-EPM; São Paulo, SP, Brasil

[3]Doutora em Medicina pela Unifesp-EPM

[4]Doutor em Medicina pela Unifesp-EPM; Professor Afiliado do Departamento de Otorrinolaringologia e Cirurgia de Cabeça e Pescoço da Unifesp-EPM, São Paulo, SP, Brasil

[5]Professor Titular do Departamento de Otorrinolaringologia e Cirurgia de Cabeça e Pescoço da Unifesp-EPM, São Paulo, SP, Brasil

[6]Doutora; Professora Adjunta e Chefe da Disciplina de Otorrinolaringologia Pediátrica do Departamento de Otorrinolaringologia e Cirurgia de Cabeça e Pescoço da Unifesp-EPM, São Paulo, SP, Brasil

Endereço para correspondência:
Shirley Shizue N. Pignatari
Rua dos Otonis, 674 – Vila Clementino
CEP 04025-002 – São Paulo/SP
E-mail: pigna@terra.com.br

Conflito de interesse: nada a declarar

Recebido em: 15/5/2009
Aprovado em: 7/12/2009

Introduction

Tonsillectomy is one of the most common surgical procedures performed by otolaryngologists, as a treatment for recurrent tonsillitis, peritonsillar abscesses, and upper airway obstruction due to tonsil hypertrophy. It is estimated that 750,000 patients undergo this procedure each year in the United States[1]. In Brazil, the most common surgical techniques for tonsillectomy are the ones performed with a scalpel or electrocautery, followed by blunt dissection using graspers/suction dissector. The Sluder technique (guillotine tonsillectomy) is also carried out in some medical centers. Trans and postoperative hemorrhage is the most common complication of this procedure, affecting 0.8% of patients in University hospitals[2]. An inevitable consequence that is present in all cases is odynophagia, which, similar to hemorrhage, is more severe in adults. In some cases, painful events may inhibit the intake of food and even oral pain relievers; most children refuse to swallow anything during the first days after surgery, thus the need to search for therapeutic alternatives in order to relieve suffering of tonsillectomy patients.

In 1964, Nogueira *et al* showed that the infiltration of the anterior tonsillar pillar with methylprednisolone just before the surgical resection of the tonsils reduces postoperative pain[3]. Several studies in the literature refer to intraoperative local anesthetic infiltration in the tonsillar fossae to reduce odynophagia after tonsillectomy[4-8]. Since the 1970s, Laser (Light Amplification by Stimulated Emission of Radiation) has been widely used in medical practice serving several purposes. Among their many applications in the medical practice, lasers have been used in several surgical procedures, including tonsillectomy. Furthermore, nonsurgical or therapeutic lasers, which do not cause tissue injury, have been widely used to stimulate tissue repair, as well as for analgesic purposes.

The types of lasers currently used for tonsillectomy or for ablation of palatine tonsils are known as high-power lasers or "hard" lasers; and among them, there are reports on the use of CO_2, YAG and KTP lasers. In general, the average power of these lasers ranges between 10- to 20W. Lasers used for analgesic, anti-inflammatory and healing purposes are known as low-level lasers or therapeutic lasers, with much lower power (around 30mW)[1,9-13]. Pain relief promoted by therapeutic laser application results from inhibition of peripheral nerve action potential, affecting the conduction of the nerve stimuli, reducing or interrupting the transmission of impulses evoked from the nociceptors to the spinal cord[14]. Vladimirov *et al*,[15] in a review of the medical literature on the photobiological principles of therapeutic applications of laser radiation, verified the following effects of low-intensity lasers on tissues: 1) Growth of the activity of certain cells, such as leukocytes and phagocytes, and increased content of calcium ions in the cytoplasm of these cells. 2) Enhancement of cell division and cell growth. 3) Activation of the synthesis of proteins and cytokines. 4) Improvement of blood circulation due to the relaxation of the vessel walls.

The efficacy of low-level laser application in reducing postoperative pain after endodontic surgery in adults was tested in the Department of Oral Surgery and Dentistry at University Mainz, in Germany, in 2004. The results revealed that the pain level was lower in the laser group than in the placebo group on the first seven postoperative days. The differences, however, were only significant for the first postoperative day[16]. The use of low-level laser appears to be a simple atraumatic technique for the prevention of mucositis of various origins. In a study carried out in 1999 by the Department of Radiotherapy of the Jean Godinot Institute, in Reims, France, patients with carcinoma of the pharynx and oral cavity treated by radiotherapy alone received periodic applications of therapeutic laser on the soft palate, anterior tonsillar pillars, and posterior third of the internal surfaces of the cheeks. When compared to the control group, the occurrence of mucositis decreased from 35.2 to 7.6% and the frequency of severe pain fell from 23.8 to 1.9%[17]. Hopkins *et al* indicated positive results in the reduction of healing time of skin lesions induced in healthy individuals in a triple-blind experimental study. Those authors observed a reduction in the time of wound healing in the group treated with therapeutic laser[18].

Other specialists, such as physiatrists, orthopedists and rheumatologists, have investigated the use of low-level laser to reduce musculoskeletal pain. Although low-level laser therapy has not been effective in the treatment of ankle sprains, good results have been found in patients with carpal tunnel syndrome, acute low back pain and pain originated from exercise-induced muscle fatigue[23]. Despite these good results, the analgesic properties of low-level lasers remain controversial in the current literature. Some reports have not identified improvements in healing or postoperative pain in patients undergoing the extraction of the third molar teeth under general anesthesia after intraoperative application of therapeutic laser[9].

Although studies with application of low-level laser have been conducted for over 30 years in the medical practice, mainly for analgesic and anti-inflammatory purposes, no studies were found in the literature involving postoperative pain control in patients undergoing tonsillectomy. Therefore, the objective of the present study was to evaluate the analgesic effect of low-level laser therapy during the first seven postoperative days on children undergoing tonsillectomy. This study aimed to improve the quality of life on the first days following the surgical removal of palatine tonsils, a procedure routinely performed in children, usually causing much pain during the healing process.

Methods

The study protocol was approved by the Research Ethics Committee of the Institution. Children and adolescents were selected at the Pediatric Otolaryngology Outpatient Clinic of the Federal University of São Paulo, according to the following criteria: ages between 5 and 15 years and indication of tonsillectomy due to obstructive palatine tonsil hypertrophy, with clinical symptoms of mouth breathing, with or without respiratory sleep disorders. Patients younger than 5 or older than 15 years, those allergic to dipyrone or other analgesics or hypnotics routinely used for general anesthesia, those who were under antibiotictherapy within the first seven postoperative days, and those whose parents or guardians refused to sign the written consent form were excluded from the study.

All children underwent the same anesthetic regimen by the same anesthesiologist to avoid interference with the assessment of pain in the immediate postoperative period. All children were pre-medicated with oral midazolam at a dose of 0.3mg/kg before separation from their parents or guardians. Monitoring included noninvasive measurement of blood pressure, pulse oximetry, continuous ECG tracing, and capnography.

Anesthesia was induced with sevoflurane supplemented with IV 3mcg/kg fentanyl, 5mg/kg propofol and 0.6mg/kg rocuronium, and maintained with 0.5 to 2.0% isoflurane, 50% nitrous oxide, and 50% oxygen. All children were intubated with tracheal tubes with cuff. At the end of the surgery, the neuromuscular block was reversed with 0.015mg/kg atropine followed by 0.03mg/kg neostigmine, and extubation was performed when airway protective reflexes were present.

The same surgical technique was applied to all children and consisted in blunt dissection using graspers/suction dissector . Hemostasis was achieved with simple interrupted 2-0 catgut suture. Only two otolaryngologists performed all surgeries.

The 18 children selected at the Pediatric Otolaryngology Outpatient Clinic were randomly divided into two groups: *Control group:* composed of nine children undergoing tonsillectomy without intraoperative laser application. A simulation of laser application was performed 24 hours after the procedure, avoiding the knowledge from parents and children of which group they belonged until the seventh postoperative day. *Laser group:* composed of nine children who received application of therapeutic laser intraoperatively, immediately after the surgery, and on the first postoperative day, 24 hours after the surgical procedure.

A Dentoflex® laser was used, with power of 50mW, wavelength of 685nm, and beam area of 2mm^2. Each surgical wound was irradiated for 3 minutes and 20 seconds, at an energy density of 4 J/cm^2[12,13]. To ensure the safety of patients and the staff involved in the research, we used the safety protocol for laser-assisted tonsillectomy, described by Cannon *et al*,[24] modified due to the low-power laser used in this case. Intraoperatively, wet bandages were used on the oropharynx and wet compresses were used on the patient's face to prevent burns secondary to the reflection of the laser beam. Both the surgeon and the anesthesiologist wore safety goggles during laser applications. A notice of laser-assisted surgery was posted on the door of the operating room to prevent inadvertent entry of persons without the standard safety gear during the procedure.

Postoperative analgesic therapy included oral dipyrone (1 drop/kg) every 6 hours, only if necessary. The parents or guardians were instructed to record the patient's postoperative course using a diary with a subjective scale for assessing pain and mood, patient acceptance of diet, and number of dipyrone doses used by the child. The family was informed about the group to which the child belonged during the medical assessment on the seventh postoperative day.

Clinical assessment of pain was performed daily, for seven postoperative days, being described by the children with the assistance of parents or guardians. The parents or guardians received a questionnaire with the purpose of assessing the presence and intensity of pain by means of a visual analog scale,[25] need and number of dipyrone doses used during the follow-up, and patient acceptance of diet. The children and adolescents were evaluated by the same physicians who performed the surgical procedure on the first and seventh postoperative days.

Statistical analysis was performed using the Fisher's test to assess the need (or not) for dipyrone use and patient acceptance of diet and the Mann-Whitney test to compare median pain scores, with a significance level of 5% ($p<0.05$). Mean dipyrone doses used in both groups throughout the seven-day follow-up period were analyzed using two-way ANOVA for repeated measures and *a posteriori* Tukey's test when necessary ($p<0.05$).

Results

The patients' age ranged from 5 to 15 years (mean = 8.5 years): 5 to 15 years (mean = 8.6 years) in the control group and 6 to 13 years (mean = 8.3 years) in the laser group. Twelve children (66%) were male (6 in each group) and six (33%) were female (3 in each group).

All patients underwent surgical removal of palatine tonsils and adenoids, and no complications were observed during or after the procedure. The results of pain assessment, number of dipyrone doses and patient acceptance of diet on the seven days after tonsillectomy are described in Table 1. Median visual analog scale pain scores were lower in the group receiving laser applications, with a statistically significant difference on the first ($p=0.01$), second ($p=0.01$), fourth ($p=0.05$), and fifth ($p=0.03$) postoperative days (Figure 1).

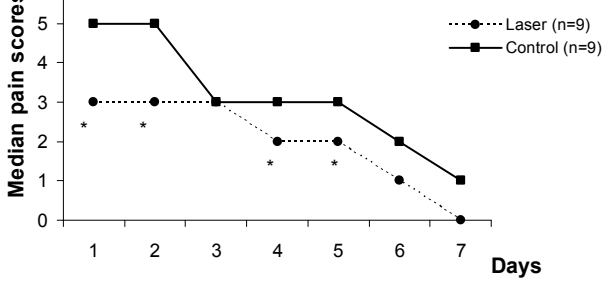
Regarding dipyrone use, the Fisher's test revealed that 55% of children in the laser group did not require analgesics on the first postoperative day, whereas all children in the control group used at least one dose of dipyrone ($p=0.01$). On the other days, the analysis of the need (or not) for analgesic use per day did not show any statistical difference.

Two-way ANOVA revealed that, regarding mean dipyrone doses used in both groups throughout the seven-day follow-up period, the laser group needed a lower quantity of analgesics than the control group ($F(6.96) = 4.74$; $p<0.001$). *A posteriori* Tukey's test demonstrated that on the first ($p<0.01$) and second ($p<0.03$) postoperative days the patients in the laser group used fewer doses of dipyrone than the control group (Figure 2).

Patient acceptance of diet was similar in both groups throughout the seven-day follow-up period.

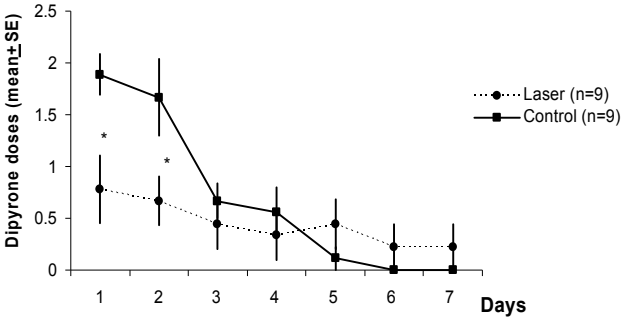
Discussion

Pain is the most uncomfortable symptom following tonsillectomy, being responsible for decreased food intake or food refusal and reduction in the patient's daily activities. Concern has always existed about relieving the patient's pain during this period, improving recovery and promoting an early return to normal activity. Comparisons between different techniques employed for the surgical removal of tonsils, anesthetic or corticosteroid injections in the peritonsillar space, and use of antibiotics postoperatively are resources which have been used aiming to relieve pain and improve the patient's quality of life[3-8]. Adenotonsillectomy is an easy procedure to perform from a technical point of view that brings almost immediate benefits, in relation to breathing improvement in children, in cases of palatine tonsil and



*$p<0.05$ when compared to control group, after Mann-Whitney test.

Figure 1 – Median of visual analog scale pain scores in laser and control groups throughout the seven-day follow-up period after tonsillectomy. The number of patients in each group is indicated in parentheses.



*$p<0.05$ when compared to control group, after two-way ANOVA.

Figure 2 – Mean and standard error (SE) for the number of dipyrone doses used in laser and control groups throughout the seven-day follow-up period after tonsillectomy. The number of patients in each group is indicated in parentheses.

Table 1 – Assessment of pain, number of dipyrone doses, and patient acceptance of diet in laser and control groups during the first seven days after tonsillectomy

Postoperative day	Group	Pain score	Doses of dipyrone	Acceptance of diet
1st day	Laser	Median: 3	None: 5 (55%) 1 dose: 1 (11%) 2 doses: 3 (33%) 3 doses: 0	Good: 3 (33%) Average: 5 (55%) Poor: 1 (11%)
	Control	Median: 5	None: 0 1 dose: 2 (22%) 2 doses: 6 (66%) 3 doses: 1 (11%)	Good: 4 (44%) Average: 2 (22%) Poor: 3 (33%)
2nd day	Laser	Median: 3	None: 4 (44%) 1 dose: 4 (44%) 2 doses: 1 (11%) 3 doses:	Good: 4 (44%) Average: 4 (44%) Poor: 1 (11%)
	Control	Median: 5	None: 2 (22%) 1 dose: 1 (11%) 2 doses: 2 (22%) 3 doses: 2 (22%)	Good: 3 (33%) Average: 5 (55%) Poor: 1 (11%)
3rd day	Laser	Median: 3	None: 6 (66%) 1 dose: 2 (22%) 2 doses: 1 (11%) 3 doses: 0	Good: 4 (44%) Average: 4 (44%) Poor: 1 (11%)
	Control	Median: 3	None: 3 (33%) 1 dose: 6 (66%) 2 doses: 0 3 doses: 0	Good: 6 (66%) Average: 2 (22%) Poor: 1 (11%)
4th day	Laser	Median: 2	None: 7 (77%) 1 dose: 1 (11%) 2 doses: 1 (11%) 3 doses: 0	Good: 6 (66%) Average: 2 (22%) Poor: 1 (11%)
	Control	Median: 3	None: 5 (55%) 1 dose: 3 (33%) 2 doses: 1 (11%) 3 doses: 0	Good: 7 (77%) Average: 1 (11%) Poor: 1 (11%)
5th day	Laser	Median: 2	None: 6 (66%) 1 dose: 2 (22%) 2 doses: 1 (11%) 3 doses: 0	Good: 6 (66%) Average: 2 (22%) Poor: 1 (11%)
	Control	Median: 3	None: 8 (88%) 1 dose: 1 (11%) 2 doses: 0 3 doses: 0	Good: 7 (77%) Average: 2 (22%) Poor: 0
6th day	Laser	Median: 1	None: 8 (88%) 1 dose: 0 2 doses: 1 (11%) 3 doses: 0	Good: 9 (100%) Average: 0 Poor: 0
	Control	Median: 2	None: 9 (100%) 1 dose: 0 2 doses: 0 3 doses: 0	Good: 9 (100%) Average: 0 Poor: 0
7th day	Laser	Median: 0	None: 8 (88%) 1 dose: 0 2 doses: 1 (11%) 3 doses: 0	Good: 9 (100%) Average: 0 Poor: 0
	Control	Median: 1	None: 9 (100%) 1 dose: 0 2 doses: 0 3 doses: 0	Good: 9 (100%) Average: 0 Poor: 0

adenoid hypertrophy. However, this procedure should be indicated with caution due to the risk associated with general anesthesia, postoperative bleeding and suffering of children related to acute odynophagia. Thus, otolaryngologists and pediatricians need to find new alternatives to relive or even avoid pain suffered on the days following tonsillectomy.

Therapeutic laser is a technological resource widely used in dentistry and oral medicine with favorable results[16-21]. Due to their anti-inflammatory properties, therapeutic lasers have been used in the prevention of radiation-induced stomatitis and in the postoperative period after endodontic procedures with good results[16,17]. Although there is no other study published to date using low-level laser after removal of palatine tonsils, low-level laser therapy was chosen in this study because our research team believed that it could reduce the child's pain after tonsillectomy, given its role in the acceleration of wound healing and postoperative pain reduction after dental surgery[9,26,27].

Despite our small sample size with only 18 children, laser therapy proved to be effective in reducing pain after removal of palatine tonsils in children when laser was applied during surgery and on the first postoperative day. The difference between median pain scores was statistically significant, being lower in the laser group on the first, second, fourth, and fifth postoperative days. The need for dipyrone use was lower in the laser group on the first four postoperative days, this difference being statistically significant only on the first postoperative day. Regarding mean dipyrone doses used in both groups, we observed that, in the laser group, the means were statistically lower on the first and second postoperative days.

The preliminary results observed in this study are consistent with other studies in the literature that show an analgesic effect of laser therapy on other types of diseases and procedures[16-21]. Laser therapy stimulates cell growth and division of cells such as leukocytes and phagocytes and improves blood circulation in the irradiated tissue, facilitating the healing process; it also has analgesic effects related to the inhibition of peripheral nerve action potential[14,15]. The use of laser therapy has several advantages compared to other procedures already used in postoperative pain control, since it is a noninvasive, inexpensive, fast and easy to perform technique.

Unfortunately, the present study did not observe better acceptance of diet in children undergoing application of therapeutic laser. This result shows that, although these children needed a lower quantity of dipyrone doses, the analgesic effect of only two laser applications alone cannot prevent odynophagia and, therefore, does not facilitate acceptance of diet in a very clear manner.

Although the results concerning the reduction of pain and need for analgesics are encouraging, further studies need to be conducted with a larger number of patients in order to verify the analgesic effect of laser therapy after tonsillectomy. This study showed, therefore, that low-level laser therapy with only two applications, during surgery and on the first postoperative day, was effective in the reduction of post-tonsillectomy pain and analgesic medication use in children. The series will be expanded so that, in the near future, the procedure can be recommended routinely after tonsillectomy, minimizing pain and consequently the suffering of children.

References

1. Krespi YP, Ling EH. Laser-assisted serial tonsillectomy. J Otolaryngol 1994;23:325-7.
2. Vieira FM, Diniz FL, Figueiredo CR, Weckx LL. Hemorrhage in adenoidectomy and/or tonsillectomy: 359 cases study. Rev Bras Otorrinolaringol 2003;69:338-41.
3. Nogueira JR, Miniti A, Paiva LJ. Contribuição para o controle da dor no pós-operatório da amigdalectomia no adulto. Rev Bras Otorrinolaringol 1964;32:63-6.
4. Jebeles JA, Reilly JS, Gutierrez JF, Bradley EL Jr, Kissin I. The effect of pre-incisional infiltration of tonsils with bupivacaine on the pain following tonsillectomy under general anaesthesia. Pain 1991;47:305-8.
5. Jebeles JA, Reilly JS, Gutierrez JF, Bradley EL, Kissin I. Tonsillectomy and adenoidectomy pain reduction by local bupivacaine infiltration in children. Int J Pediatr Otorhinolaryngol 1993;25:149-54.
6. Stuart JC, MacGregor FB, Cairns CS, Chandrachud HR. Peritonsillar infiltration with bupivacaine for pediatric tonsillectomy. Anaesth Intensive Care 1994;22:679-82.
7. Pasinato RC, Gavazzoni FB, Catani GS, Richter AF, Stahlke LG, Brotto ML. Eficácia da aplicação de anestésico local durante adenoamigdalectomia na dor pós-operatória. Rev Bras Otorrinolaringol 1999;65:36-42.
8. Albernaz PL, Ganança MM, Gasel JJ. Estudo comparativo entre a bupivacaina e a lidocaina na anestesia local e analgesia pós-operatória das amigdalectomias. Rev Bras Otorrinolaringol 1973;39:100-6.
9. Fernando S, Hill CM, Walker R. A randomised double blind comparative study of low level laser therapy following surgical extraction of lower third molar teeth. Br J Oral Maxillofacial Surg 1993;31:170-2.
10. Volk MS, Wang Z, Pankratov MM, Perrault DF Jr, Ingrams DR, Shapshay SM. Mucosal intact laser tonsillar ablation. Arch Otolaryngol Head Neck Surg 1996;122:1355-9.
11. Kothari P, Patel S, Brown P, Obara L, O'Malley S. A prospective double-blind randomized controlled trial comparing the suitability of KTP laser tonsillectomy with conventional dissection tonsillectomy for day case surgery. Clin Otolaryngol Allied Sci 2002;27:369-73.

12. Enwemeka CS, Parker JC, Dowdy DS, Harkness EE, Sanford LE, Woodruff LD. The efficacy of low-power lasers in tissue repair and pain control: a meta-analysis study. Photomed Laser Surg 2004;22:323-9.
13. Giuliani A, Fernandez M, Farinelli M, Baratto L, Capra R, Rovetta G *et al*. Very low level laser therapy attenuates edema and pain in experimental models. Int J Tissue React 2004;26:29-37.
14. Cruz FM, Ladalardo TC, Brugnera Jr A. Interação do laser com o tecido. In: Ladalardo TC, Bologna ED, dos Santos AE, Brugnera Jr A, editores. Atlas de laserterapia aplicada à clínica odontológica; 2003. p. 2-6.
15. Vladimirov YA, Osipov AN, Klebanov GI. Photobiological principles of therapeutic applications of laser radiation. Biochemistry (Mosc) 2004;69:81-90.
16. Kreisler MB, Haj HA, Noroozi N, Willershausen B. Efficacy of low level laser therapy in reducing postoperative pain after endodontic surgery – a randomized double blind clinical study. Int J Oral Maxillofac Surg 2004;33:38-41.
17. Bensadoun RJ, Franquin JC, Ciais G, Darcourt V, Schubert MM, Viot M *et al*. 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. Support Care Cancer 1999;7:244-52.
18. Hopkins JT, McLoda TA, Seegmiller JG, David Baxter G. Low-level laser therapy facilitates superficial wound healing in humans: a triple-blind, sham-controlled study. J Athl Train 2004;39:223-9.
19. Basford JR, Sheffield CG, Harmsen WS. Laser therapy: a randomized controlled trial of the effects of low-intensity Nd: YAG laser irradiation on musculoskeletal back pain. Arch Phys Med Rehabil 1999;80:647-52.
20. de Bie RA, de Vet HC, Lenssen TF, van den Wildenberg FA, Kootstra G, Knipschild PG. Low-level laser therapy in ankle sprains: a randomized clinical trial. Arch Phys Med Rehabil 1998;79:1415-20.
21. Irvine J, Chong SL, Amirjani N, Chan KM. Double-blind randomized controlled trial of low-level laser therapy in carpal tunnel syndrome. Muscle Nerve 2004;30:182-7.
22. Djavid GE, Mehrdad R, Ghasemi M, Hasan-Zadeh H, Sotoodeh-Manesh A, Pouryaghoub G. In chronic low back pain, low level laser therapy combined with exercise is more beneficial than exercise alone in the long term: a randomised trial. Aust J Physiother 2007;53:155-60.
23. Leal Junior ECP, Lopes-Martins RAB, Dalan F, Ferrari M, Sbabo FM, Generosi RA *et al*. Effect of 655-nm low-level laser therapy on exercise-induced skeletal muscle fatigue in humans. Photomed Laser Surg 2008:26:419-24.
24. Cannon RC. Safety protocol for laser-assisted tonsillectomy. Laryngoscope 1998;108:1249-51.
25. McGrath PA, Seifert CE, Speechley KN, Booth JC, Stitt L, Gibson MC. A new analogue scale for assessing children's pain: an initial validation study. Pain 1996;64:435-43.
26. Herascu N, Velciu B, Calin M, Savastru D, Talianu C. Low-level laser therapy efficacy in post-operative wounds. Photomed Laser Surg 2005;23:70-3.
27. Ozcelik O, Haytac MC, Kunin A, Seydaoglu G. Improved wound healing by low-level laser irradiation after gingivectomy operations: a controlled clinical pilot study. J Clin Periodontol 2008;35:250-4.