Published Clinical Trials of Red Low-Level Laser Therapy (LLLT) Applied to Reducing Post-Surgical Pain

Seven randomized controlled clinical trials published in scientific peer-reviewed journal publications were identified wherein low-level laser therapy (LLLT) was evaluated for its therapeutic ability to reduce post- operative pain following surgical procedures. These studies are summarized and presented in tabular summary format below (Table 1)

Table 1: Summary of Published Clinical Trials of LLLT Applied to Reducing Post-Surgical Pain

Study	Study Goal	Device / Parameters	Study Design	Study Arms	Sample size	Sample characteristics	Primary outcome assessment and findings	Secondary outcome assessments & findings	Safety outcomes
1. Low-intensity Laser (660 NM) has Analgesic Effects on Sternotomy of Patients Who Underwent Coronary Artery Bypass Grafts Fernandes et al., 2017 Ann Card Anaesth.	To evaluate the effect of LLLT on pain after coronary artery bypass grafts.	- 660nm - 6 J/cm²	RCT: - randomized, - double-blind, - placebo controlled	- Active: laser application immediately after surgery and on post-operative days 2, 4 ,6 & 8 at 8 points around the surgical incisions, each point approx. 2cm apart. - Placebo: Same as active but laser not turned on. - Control: no laser	Total: n=90 - Active: n=30 - Placebo: n=30 - Control: n=30	- Approx. two-thirds male - average age around 60 years.	- VAS - McGill Pain Questionnaire - each assessed during hospitalization & one-month post-operative. - Active group had statistically significantly lower VAS pain ratings, & sensory & effective scores on McGill on days 6 and 8 post-operative compared with control & placebo groups ($p<0.05$).	N/A	No adverse events or other safety events reported.
2. The Effect of Low-Level Laser on Post-Operative Pain After Tibial Fracture Surgery: A Double-Blind Controlled Randomized Clinical Trial Nesioonpour et al. 2014	To investigate the effects of LLLT on acute pain after tibial fracture surgery.	1. 650nm 100mW Continuous mode 3 J/cm² Area: 1 cm² 30 s/point 2. 808nm 300mW Continuous mode 6 J/cm² Area: 1 cm²	Prospective, double-blind, randomized, sham controlled (control group received inactive treatments). Subjects matched between groups with	- Active: Laser administered to medial, lateral, anterior, posterior, and popliteal aspects of tibial fracture site plus 6-8 trigger points on muscles & surgical wounds post-operatively.	Total: n=54 - Active: n=27 -Control: n=27	- Average age: 25 years. - Average BMI: approx. 71 kg/m² No statistically significant differences in demographics nor surgical variables	1. VAS pain rating across the first 24 post-operative hours. - VAS pain ratings were statistically significant lower for active compared with sham subjects at each of 2, 4-, 8-, 12-, & 24-hours	1. Analgesic use across the first 24 post-operative hours: - Opioid use across first 24 hours following surgery was statistically significantly less for active compared with sham ($p<0.01$).	No adverse events reported. It was concluded that LLLT is a safe, painless, & non-invasive means to reduce post-operative pain and analgesic use that has none of the side

Anest Pain Med		20 s/point	respect to age, weight, and height.	- Sham: same as active, but device not turned on.		between treatment groups.	post-surgery ($p<0.5$).		-effects of other means and is easily accepted by patients.
Study	**Study Goal**	**Device / Parameters**	**Study Design**	**Study Arms**	**Sample size**	**Sample characteristics**	**Primary outcome assessment and findings**	**Secondary outcome assessments & findings**	**Safety outcomes**
3. The Effect of Low-Level Laser on Post-Operative Pain After Elective Cesarean Section Poursalehan et al. 2018 Anest Pain Med	To investigate the effects of LLL on acute pain after elective cesarean section.	1. 650nm 100mW 1 J/cm² Area: 1 cm² 10 secs 2. 804nm 200mW 2 J/cm² 10 secs	- Prospective, - double-blind, - randomized, - sham controlled (inactive treatments).	Active: - Irradiation along incision site approx. 7-10 cm², total combined dose of 3 J/cm²; total energy 21-30J. - Surrounding tissue also treated, 2 cm, 3 points above and below suture, each 1cm², 15 secs each. Total dose per point of 4.5 J/cm²; Total energy 27J. Control: same but device not turned on.	Total: n=80 - Active: n=40 -Control: n=40	No statistically significant differences in demographics nor surgical variables between treatment groups.	VAS pain rating across the first 24 post-operative hours. - VAS pain ratings statistically significantly lower for active compared with sham subjects at each of 1-, 4-, 8-, 12-, 16- & 24-hours post-surgery ($p<0.5$).	1. Analgesic doses taken across the first 24 post-operative hours. 2. Time to first request for analgesic. - Average number analgesic doses taken across the first 24 hours following surgery was statistically significantly less for active compared with sham group ($p<0.01$). - Time to first request for analgesic was statistically significant longer for active than sham group ($p<0.01$).	No adverse events reported. It was concluded that LLLT is a good method to reduce post-operative pain due to the fact that it is a safe and non-invasive method which is also accepted by patients.

Study	Study Goal	Device / Parameters	Study Design	Study Arms	Sample size	Sample characteristics	Primary outcome assessment and findings	Secondary outcome assessment and findings	Safety outcomes
4. Low Level Laser and Light-Emitting Diode Therapy for Pain Control in Hyperglycemic and Normoglycemic Patients Who Underwent Coronary Bypass Surgery With Internal Mammary Artery Grafts: A Randomized, Double-Blind Study With Follow-Up Lima et al. 2016 Photomed. & Laser Surgery	To evaluate the efficacy of LLLT and LED for reducing pain in hyperglycemic and normoglycemic patients who underwent coronary bypass surgery with internal mammary artery grafts.	LLLT: 660nm - 2.4 J - 6 J/cm² - 0.04 W - Spot size: 0.4cm² - 60 s/point - # spots: 8 - SAEF: 0.24 LED: 640±20nm - 10.1 J - 6 J/cm² - 0.07 W - Spot size:1.77cm² - 152 s/point - # spots: 8 - SAEF: 1.06	- prospective, - double-blind, - randomized, - sham and control design.	4 arms: 1. LLLT 2. LED 3. Placebo (sham) 4. Control Each arm further divided into 2 subgroups of hyperglycemic and normoglycemic according to their pre-surgery fasting blood glucose level.	Total: n=120 1. LLLT: n=40 2. LED: n=40 3. Placebo: n=40 4. Control: n=40	- Males and females aged 18-75 years - BMI ≤ 29.9 kg/m²: - hyperglycemic or normoglycemic.	Pain during coughing according to VAS and McGill Pain Questionnaire. LLLT & LED groups both demonstrated statistically significantly lower pain ratings on both VAS and McGill on post-operative days 6 & 8 compared with placebo and control ($p<0.05$). No differences found between LLLT and LED groups or between hyperglycemic and normoglycemic subgroups.	Pain during coughing at one-month post-operative follow-up. No pain reported by any subject in any group at one-month post-operative.	No adverse events of side effects reported related to the application of LLLT or LED. It was concluded that LLLT and LED had similar analgesic effects post-operatively for hyperglycemic and normoglycemic patients and both were better than for the placebo and control groups.

Study	Study Goal	Device / Parameters	Study Design	Study Arms	Sample size	Sample characteristics	Primary outcome assessment and findings	Secondary outcome assessment and findings	Safety outcomes
5. Low Level Laser Therapy improves pain in post-cesarean section: a randomized clinical trial. Araujo et al. 2020. Lasers In Medical Science	To evaluate the effect of LLLT on immediate postpartum pain relief during cesarean section.	660 nm, 30mW 1. Experimental treatment 1: - 4 J/cm² 2. Experimental treatment 2: - 2 J/cm² 2 treatment sessions: 12- & 24-hours post-partum. Laser administered perpendicular to skin, non-contact at 1 cm intervals along the length of the incision.	- prospective, - randomized, - double-blinded - sham & control.	4 arms: 1. Experimental group 1 2. Experimental group 2 3. Placebo (inactive laser) 4. Control (no treatment)	Total: n=88 Arm 1: n=22 Arm 2: n=22 Arm 3: n=22 Arm 4: n=22	Females aged 18 to 39 years with score on the Numeric Rating Scale (NRS) ≥ 3 in the immediate postpartum stage of c-section.	1. Numeric Rating Scale (NRS) 2. Algometry Recorded at 12-, 20-24-, & 44-48-hours post-partum. Significant interaction between time vs. Group for NRS and algometry ($p<0.001$) No significant differences between laser doses	Global Change Perception Scale (GCPS). Significant difference between groups at 20-24 & 44-48 hours postpartum ($p<0.05$).	No side effects reported. It was concluded that LLLT was effective in relieving surgical wound pain after c-section and seems to be a good non-pharmacological resource for pain improvement after c-section.

Study	Study Goal	Device / Parameters	Study Design	Study Arms	Sample size	Sample characteristics	Primary outcome assessment and findings	Secondary outcome assessment and findings	Safety outcomes
6. Effect of preoperative ibuprofen in controlling post-endodontic pain with and without LLLT in single visit endodontics: A randomized clinical study. Nabi et al. 2018 Indian J Dent Res	To evaluate the effect of LLL irradiation and ibuprofen in reducing the onset and severity of post-operative pain following single visit endodontics.	Combination Laser: 1. 905 nm: - 12-16mW 2. 875nm: - 60mW 3. 640 nm: - 7mW	- prospective, - randomized, - double-blinded - control group.	4 arms: 1. Active 1: 400mg Ibuprofen 1 hour pre-procedure 2. Active 2: LLLT after procedure for 3 mins. at periapical region on buccal and lingual aspect. 3. Active 3: pre-procedure Ibuprofen + post-procedure LLLT. 4. Control: no treatment.	Total: n=120 - Active 1: n=30 - Active 2: n=30 - Active 3: n=30 - Control: n=30	57% males aged 18 to 65 years.	Assessment of pain was made using the Heft Parker Pain Survey at treatment end and at 4-, 8-, 12-, 24-, & 48-hours post-operative. Pain scores on the Heft Parker Pain Survey were statistically significantly lower for each of the 3 active treatment groups compared with control, with the greatest difference occurring for subjects receiving both Ibuprofen and LLLT.	N/A	LLLT can be an effective alternative for conventional use of NSAIDs in controlling postendodontic pain, thereby eliminating the adverse effects of such drugs on patients.

Study	Study Goal	Device / Parameters	Study Design	Study Arms	Sample size	Sample characteristics	Primary outcome assessment and findings	Secondary outcome assessment and findings	Safety outcomes
7. Therapeutic Laser for pain relief after tonsillectomy Neiva et al 2018 Rev, paul pediatr	To evaluate the effect of LLLT on pain after tonsillectomy in children and adolescents.	Dentoflex® Laser 685nm 50mW 4J/cm²	RCT: - randomized, - double-blind, - control group	- Active: intra-operative laser + 24-hour post-operative laser - Control: standard of care pain medication / no intra-operative laser	Total: n=18: - Active: n=9 - Control: n=9	Males and females aged 5-15 years.	- VAS pain assessment daily for 7 days post-operative. - Median VAS scores were statistically significantly lower in active compared with control on 1st 2nd 4th & 5th ($p<0.05$) post-operative days.	- Use of rescue analgesics. - 45% of active subjects required at least one dose of analgesics on 1st post-operative day compared with 100% of placebo subjects ($p<0.01$). - Across first 7 post-operative days, active subjects consumed a statistically significant lower quantity of analgesics compared with control ($p<0.001$)	No adverse events or other safety events reported.

The list of references of the above articles is listed below.

1. de Holanda Araujo AMP, de Sena KRR, da Silva Filho EM, Pegado R, Micussi MTABC. Low-level laser therapy improves pain in postcesarean section: a randomized clinical trial. Lasers Med Sci. 2020 Jul;35(5):1095-1102. doi: 10.1007/s10103-019-02893-3. Epub 2019 Oct 28. PMID: 31659541.

2. Fernandes GA, Araújo Júnior RB, Lima AC, Gonzaga IC, de Oliveira RA, Nicolau RA. Low-intensity laser (660 NM) has analgesic effects on sternotomy of patients who underwent coronary artery bypass grafts. Ann Card Anaesth. 2017 Jan-Mar;20(1):52-56. doi: 10.4103/0971-9784.197836. PMID: 28074796; PMCID: PMC5290696.

3. Andréa Conceição Gomes Lima, Gilderlene Alves Fernandes, Isabel Clarisse Gonzaga, Raimundo de Barros Araújo, Rauirys Alencar de Oliveira, and Renata Amadei Nicolau. Low-Level Laser and Light-Emitting Diode Therapy for Pain Control in Hyperglycemic and Normoglycemic Patients Who Underwent Coronary Bypass Surgery with Internal Mammary Artery Grafts: A Randomized, Double-Blind Study with Follow-Up**.** Photomedicine and Laser Surgery. Jun 2016;34(6):244-251.http://doi.org/10.1089/pho.2015.4049.

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6. Nabi S, Amin K, Masoodi A, Farooq R, Purra AR, Ahangar FA. Effect of preoperative ibuprofen in controlling postendodontic pain with and without low-level laser therapy in single visit endodontics: A randomized clinical study. Indian J Dent Res. 2018 Jan-Feb;29(1):46-50. doi: 10.4103/ijdr.IJDR_327_15. PMID: 29442086.

7. Felipe Costa Neiva, Fernando Mirage J., VieiraClaudia Regina Figueiredo, Aldo Eden C., StammLuc Louis M., WeckxShirley Shizue N., Pignatari**.** Therapeutic laser for pain relief after tonsillectomy. Rev. paul. pediatr. Sept 2010:28 (3): https://doi.org/10.1590/S0103-05822010000300011

In summary, seven randomized controlled clinical trials published in scientific peer-reviewed journal publications were identified wherein low-level laser therapy (LLLT) was evaluated for its therapeutic ability to reduce post-operative pain following surgical procedures known to cause worse post-operative pain in terms of intensity and duration than in the two existing Erchonia post-operative trials of breast augmentation and liposuction surgery. These studies evaluated post-surgical pain related to:

- Coronary artery bypass graft surgery
- Coronary bypass surgery with internal mammary artery grafts
- Tibial fracture surgery
- Cesarean section (2 studies)
- Endodontic surgery
- tonsillectomy

APPENDIX A: SUPPORTIVE LITERATURE SEARCH COMPLETE ARTICLES

Original Article

Low-intensity Laser (660 NM) has Analgesic Effects on Sternotomy of Patients Who Underwent Coronary Artery Bypass Grafts

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Abstract

Background: The aim of this study was to evaluate the efficacy of low-level laser therapy for reducing the acute pain of sternotomy in patients who underwent a coronary artery bypass graft (CABG). **Methods:** This study was conducted with ninety volunteers who electively submitted to CABG. The volunteers were randomly allocated into three groups of equal size ($n = 30$): control, placebo, and laser (λ of 660 nm and spatial average energy fluency of 1.06 J/cm^2). Pain when coughing was assessed by a visual analog scale (VAS) and McGill Pain Questionnaire, according to sensory, affective, evaluative, and miscellaneous domains. The patients were followed for 1 month after the surgery. **Results:** The laser group had a greater decrease in pain with analogous results, as indicated by both the VAS and the McGill questionnaire ($P \leq 0.05$) on sensory and affective scores, on days 6 and 8 postsurgery compared to the placebo and control groups. **Conclusion:** Laser seems to be effective promoting pain reduction after coronary-arterial bypass grafting.

Keywords: *Low-level laser therapy, myocardial revascularization, pain, sternotomy*

Introduction

While the rate of mortality from cardiovascular disease (CVD) has been decreasing over the last four decades in European and other developed countries, CVD still causes the majority of deaths in certain age groups.[1] In developing countries, such as Brazil, the mortality rate of CVD is comparable to that in developed countries. CVD is one of the major causes of nontraumatic death and is responsible for approximately 20% of all deaths of individuals older than 30 years in Brazil.[2] The last epidemiological study on the subject revealed that 962,931 individuals older than 30 years had died in 2009, with CVD responsible for 95,449 deaths and stroke for 97,860 deaths.[3] Recently, clinical and public health efforts to reduce the impact of CVD have highlighted the importance of calculating the short-term death risk by examining trends in the predicted 10-year risk for CVD with algorithms derived from the Framingham Heart Study.[4] Furthermore, in many cases, the disease severity may lead patients to coronary artery bypass grafting (CABG).

The surgical procedure is complex, and most interventions need a sternal longitudinal incision, which can cause moderate to severe pain postsurgery, as well as nonnegligible incidence of chronic pain, which can persist for more than 1 year. Pain intensity around the incision has been described as higher on the 7th day postsurgery compared to 1 month after hospital discharge, and it has significant repercussions on functionality. Adequate analgesia after a sternotomy reduces postoperative adverse events and improves patient satisfaction and clinical outcomes.[5]

The analgesic effects of low-level laser therapy (LLLT) have been validated both *in vitro* and *in vivo*. Possible mechanisms of action include endorphin secretion stimulation, reduction of interstitial fluid at the site of inflammation with a marked increase in vasodilatation, and improvement in local circulation.[6] LLLT also can stimulate immediate analgesia to control neuropathic pain by releasing local neurotransmitters such as serotonin, promoting the release of endorphins, or increasing mitochondrial ATP production, or through anti-inflammatory effects.[7] Although many studies have been performed to help understand the analgesic and tissue repair mechanisms of LLLT,[8,9]

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additional clinical studies are necessary to better understand those effects.

The aim of this study was to evaluate the efficacy of LLLT for reducing acute pain from sternotomy in patients who underwent CABG.

Methods

All of the individuals provided written, informed consent, and their rights were protected. The protocol for this study was approved by the Local Research Ethics Committee, CAAE 0127.0.043.000-11, and registered with the Brazilian Clinical Trial Registry and the International Clinical Trials Registry Platform of the World Health Organization under RBR-38wgx6 and Universal Trial Number U1111-1128-9666, respectively.

This was a randomized, double-blind clinical trial containing both a placebo and a control group. It was carried out at Santa Maria Hospital that performs cardiac surgery for the Brazilian public health system, in Teresina, Piaui, Brazil. All patients admitted to the hospital during the study period were invited to participate if they had indicated interest in having CABG and met the inclusion criteria. The study was conducted with ninety volunteers who were randomly allocated into three groups of equal size (n = 30): control, placebo, and laser groups.

Patients who underwent elective coronary artery bypass surgery with a longitudinal sternotomy incision and extracorporeal circulation and patients between ages 18 and 75 years and of both sexes who were hemodynamically stable and had a body mass index (BMI) of less than 29.9 kg/m^2 were included in the study. Exclusion criteria consisted of previous thoracic surgery, emergency or urgent coronary artery bypass surgery, respiratory or renal insufficiency after surgery, low cardiac output syndrome, clinical complications that demanded changes in analgesic protocols, and any other postsurgery complications. Patients who could not be monitored during the 1st month after the operation were also excluded from the study.

The randomization and blinding procedures consisted of simply drawing cards marked 1, 2, 3, or 4, where 1 meant the control group, 2 meant the placebo group, and 4 meant the laser group, whereas 3 meant that the individual should be part of another group irradiated with light-emitting diode (LED), as part of secondary studies carried on by research group.[10] The drawing was performed during the patient's hospital admission, which always occurred at least 24 h before the surgery. The researchers were separated into therapists and evaluators. The therapists were assistants responsible for conducting the therapy and registering the procedures, and the evaluators were responsible for assessing the patients and their outcomes. Each patient was identified by a code registered by one of the therapist researchers, who ensured that the evaluating researchers were blinded to the code until the final statistical analysis was performed. The patients were blinded to the study by the use of opaque goggles during the laser irradiation.

A preoperative assessment consisted of an explanation of the procedures; inclusion and exclusion criteria certification; a clinical assessment, including laboratory tests; and group drawing. The laser group was subjected to irradiation immediately after surgery and on subsequent days 2, 4, 6, and 8. The irradiation was performed at spots alongside the incision 2 cm apart, perpendicularly and in contact with the skin, for a total of eight points. A translucent film protected the probe. The equipment's characteristics and irradiation parameters are described in Table 1. The placebo group was subjected to the laser application process but with the equipment turned off. The control group was only subjected to the assessment protocols and the follow-up. The outcome assessed was pain during the hospitalization period and after the 1st month postsurgery.

The evaluating researchers participated in a training program for intra- and inter-examiner agreement to calibrate their level of concordance. Pain was assessed using an 11-point visual analog scale (VAS) and the McGill Pain Questionnaire from day 2 to the 1st month postsurgery. Patients were stimulated to cough, and their level of pain was recorded at that moment. Coughing is important for these patients because they must be stimulated to keep their airways free from obstructions, which helps prevent respiratory complications in the postoperative period. The employed analgesic protocol was the one routinely set by the hospital, which consisted of tramadol hydrochloride and dipyrone administered intravenously on a fixed 6-h schedule. Morphine sulfate was administered on an as-needed basis. Those patients who needed morphine were excluded from the study. The patients were followed for 1 month after surgery, and their pain was also evaluated during this period.

The results were evaluated using the software STATISTICA 7.0 StatSoft® (Dell Statistica (Headquarters), Tulsa,

Table 1: Parameters of the instruments used for phototherapy

Parameters	Values
Equipment	Laser Hand MM Optics®
Energy density (J/cm^2)	6
Energy (J)	2.4
Power (W)	0.04
Spot diameter (cm)	0.5
Spot size (cm^2)	0.4
Time of irradiation (s)	60
Power density (W/cm^2)	0.1
Treatment time per point (s)	60
Number of spots	8
SAEF	0.24
Wavelength (nm)	660

SAEF = Power output × time treatment per point × point numbers/total treated area. SAEF: Spatial average energy fluency

United States). Intergroup comparisons were performed by the Kruskal–Wallis test with multiple comparison by Dunn's test. All significance levels were set at $P \leq 0.05$.

Results

Ninety patients were subjected to the study, and their anthropometric characteristics are described in Table 2. No significant differences in age, weight, height, or BMI were found among the groups. According to preoperative clinical registers, all participants were using antihypertensive drugs of different classes, such as thiazide diuretics, calcium channel blockers, angiotensin II receptor antagonists, and beta-blockers. Control and placebo groups have also been a part of the study carried on by the same research group, comparing the healing and analgesic effects of LED at λ 640 ± 20 nm, previously published by de Oliveira *et al.*[11]

Pain according to the visual analog scale

Figure 1 shows a significant decrease in the pain level for all groups from the 1st to the 8th day and a complete absence of pain perception after the 1st month. Nevertheless, the laser group experienced less pain on days 6 and 8 postsurgery compared to the control and placebo groups, according to an intergroup Kruskal–Wallis test with multiple comparison by Dunn's test ($P \leq 0.05$).

Pain according to the McGill Pain Questionnaire

Figure 2 shows pain perception based on the McGill Pain Score. It is possible to note a significant decrease in the pain level for all groups from the 1st to the 8th day, but the laser group experienced lower pain scores on days 6 and 8 postsurgery compared to the control and placebo groups ($P \leq 0.05$).

Discussion

Ninety individuals were included in the present study based on the inclusion and exclusion criteria. Table 2 shows the anthropological data of the participants. Variables such as weight, height, and BMI presented no significant differences among the groups. Regarding gender, males had 2 times greater prevalence, which corresponds to epidemiological statistics for CVD.[11]

Cardiac surgery with sternotomy causes acute pain immediately after surgery. A number of studies have suggested

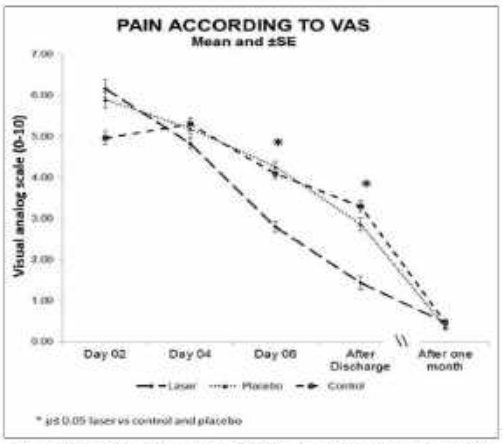

Figure 1: Pain according to visual analog scale (mean ± standard error)

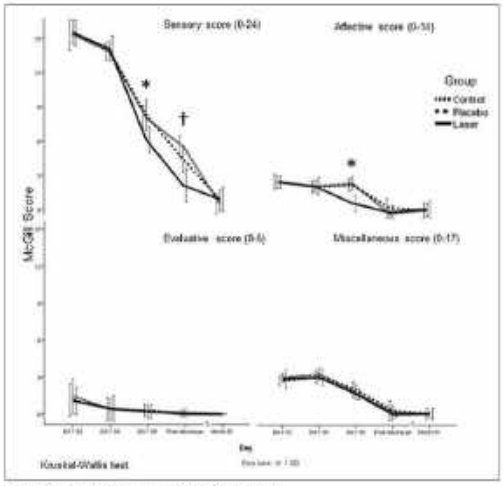

Figure 2: Pain according to McGill score

Table 2: Anthropometric characteristics of participants (means±standard deviation)

	Group					
	Control		Placebo		Laser	
	n (%)	Mean±SD	*n* (%)	Mean±SD	*n* (%)	Mean±SD
Gender						
Female	11 (36.7)		10 (33.3)		11 (36.7)	
Male	19 (63.3)		20 (66.7)		19 (63.3)	
Age		60.2±10		59.0±8.8		60±8
Weight		64.66±10		63.3±8.9		65.33±10.00
Height		1.6±0.1		1.6±0.1		1.60±0.07
BMI		25.42±2.5		25.2±3		25.55±3.94

BMI: Body mass index

that cardiac surgery patients have significant pain after surgery in both the Intensive Care Unit and after their transfer to the floor. This pain is believed to be caused by peripheral mechanoreceptors that are stimulated during surgical procedures with sternal retraction. Most of the pain after a sternotomy is caused by damage to the skin and subcutaneous tissues, bone, and sternal cartilage.[12] The principal thoracic nerves providing sternum sensitivity are T2–T6. Intercostal nerves arising from the thoracic nerve roots innervate the sternum, ribs, and surrounding subcutaneous tissue. The pericardium is innervated with pain fibers that ascend from the phrenic nerve, vagus nerve, and sympathetic trunks.[9]

After CABG, patients experience considerable pain during the critical postoperative period. Cardiac postsurgery pain can cause complications such as atelectasis, pneumonia, and deep vein thrombosis because pain can limit a patient's ability to cough and mobilize efficiently. Moreover, persistent postoperative pain can have a negative psychological effect and delay postoperative recovery.[13,14] In this study, pain was assessed by the VAS and the McGill questionnaire for the first time on the 2nd day after surgery. At this time, patients were conscious, extubated, breathing spontaneously, and, consequently, able to cooperate. The patients were stimulated to cough, and their pain level was recorded. The assessment was repeated every 2 days until the 1st day after hospital discharge, on the 8th day postsurgery, and again at the 1-month postsurgery follow-up. Yorke *et al.*[13] studied 104 patients' perceptions of pain after cardiac surgery and reported that 46.1% of patients experienced pain with coughing, 26.5% with physical therapy, 32.4% with self-moving, and 27.4% with movement assisted by nurses. Lahtinen *et al.*[15] also testified that cough was the main trigger for sternotomy pain after CABG. In their study with 113 patients, 78% mentioned pain when coughing as severe.

The VAS has been proven to be one of the most reliable scales for the evaluation of pain intensity.[17] Although the VAS is a subjective method of pain assessment, it is one of the best available options for pain studies.[18] In Figure 1, we can see that all groups experienced a pain decrease from the 2nd day to the end of the 1st month postsurgery, when patients recorded a pain level of zero. On the 2nd to 4th days, all groups had similar pain perception. Nevertheless, on the 6th day to 1st day after hospital discharge (the 8th day postsurgery), we noticed that the pain reduction was statistically greater in the laser group than in the placebo or control groups ($P \leq 0.05$) when coughing.

Figure 2 shows a graph with pain perception according to the McGill Pain Questionnaire. This questionnaire was developed by Melzack to assess the sensory, affective, and evaluative dimensions of pain,[19] and it has been translated into Brazilian Portuguese and used to complement the VAS.[20,21] This instrument has also been used to evaluate pain after cardiac surgery.[10,22] According to the sensory dimension, the laser group experienced a lower pain level on days 6 and 8 postsurgery as compared to the control and placebo groups. When assessed by the affective dimension, the analgesic effect was observed on the 6th day. Evaluative and miscellaneous dimensions did not present any significant difference among the groups in pain perception. Sensory scores are comparable with those on the VAS assessment [Figure 1], revealing an analgesic effect on the 6th and 8th days. However, the other dimensions were not capable of detecting this effect, which could be explained by the fact that sensory words are easier for patients who just underwent surgery to express. Yorke *et al.*[15] mentioned that sensory expressions had been used to describe surgical pain, including words such as sharp, stabbing, aching, and dull, and are expressed more easily by patients. Pimenta and Teixeira[21] also mentioned that the sensory dimension had a higher impact on the McGill questionnaire on pain assessment. This idea was reinforced by Gauthier *et al.*[20] when validating the McGill Pain Questionnaire to assess pain in younger and older people with cancer.

Similarly, postoperative cardiac surgical patients related strong emotional components of pain, which could explain why that dimension could be considered more effective for revaluating postsurgical pain. This fact has important clinical implications. Patients are expected to ambulate and participate in a physiotherapy regimen beginning the day after surgery. When pain is not properly managed, patients may experience difficulties in reaching the planned goals of care. Khoueiry *et al.*[23] reported that at baseline and 1 month postoperative, 98% of patients had some level of anxiety. Those findings were also reported by Lima *et al.*[24] and Karlekar *et al.*[25] and could support the higher influence of affective aspects on the McGill scores when applied to postoperative cardiac patients.

A number of studies revealed that LLLT could affect pain in multiple ways. de Jesus *et al.*[26] showed that in rats with partially injured Achilles tendons, LLLT probably modulated the pro-inflammatory agents by reducing the interleukin-1β (IL-1β) and cyclooxygenase-2 (COX-2) messenger RNA (mRNA) expressions and, consequently, reducing the PGE2 levels, and also by reducing cell migration and the quantity of neutrophils, mast cells, and macrophages in the injured tissue. Furthermore, comparable results were found by Prianti *et al.*,[27] who studied the COX-2 mRNA expression in both subplantar and total brain tissues in a model of peripheral inflammation induced by the administration of carrageenan. Souza *et al.*[28] reported that LLLT could reduce oxidative stress because it is associated with a mechanism involving the upregulation of histone deacetylase activity and the inhibition of lipopolysaccharide/H_2O_2-induced tumor necrosis factor and IL-8 secretion, which also results in pain control.

Limitations

As "adequate pain relief" was not defined, most of the patients remained with pain scores more than 5, up to day 6. This is a gross limitation, which we did not overcome.

In this study, we investigated the efficiency of a therapy protocol using LLLT (with 6 J/cm^2) for analgesic purposes in patients who underwent CABG. With the present therapy parameters, it may be assumed from our data that LLLT was effective in controlling pain mainly after the 6th day postsurgery. Further study is needed to clarify the influence of different protocols and doses and their effects on mediators and cell types in inflammatory models and clinical trials.

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Conflicts of interest

There are no conflicts of interest.

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Published online 2014 June 21. **Research Article**

The Effect of Low-Level Laser on Postoperative Pain After Tibial Fracture Surgery: A Double-Blind Controlled Randomized Clinical Trial

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Background: Postoperative pain is a common complication that can lead to serious morbidities and delayed recovery.
Objectives: The aim of this study was to investigate the effect of low-level laser therapy on acute pain after tibial fracture surgery.
Patients and Methods: In this randomized clinical trial, 54 patients who were candidate for tibial fracture surgery were allocated randomly to two groups, namely, control and laser therapy. Both groups had the same type of surgery and technique of spinal anesthesia. Patients in laser group were treated with the combination of two lasers (GaALAs, 808 nm; and GaALInP, 650 nm) at the end of the surgery while control group received laser in turn-off mode with the same duration as laser group. Patients were evaluated for pain intensity according to the visual analogue scale (VAS) and the amount of analgesic use during 24 hours after surgery.
Results: Laser group experienced less pain intensity in comparison with control group at second, fourth, eighth, 12th, and 24th hours after surgery (P Value < 0.05). In addition, the amount of consumed opioid in laser group was significantly less than the control group (51.62 ± 29.52 and 89.28 ± 35.54 mg, respectively; P Value, 0.008).
Conclusions: Low Level Laser Therapy is a proper method to reduce postoperative pain because it is painless, safe and noninvasive and is easily accepted by patients.

Keywords: Low Level Laser Therapy; Postoperative Pain; Tibial Fracture Surgery

1. Background

One of the undesirable complications of surgery is postoperative pain that may result in serious morbidities such as agitation, hypertension, mood changing, tachycardia (1, 2) and delay in wound healing, which can be more dangerous in patients with the underlying diabetes mellitus, hypertension, or coronary heart diseases as it may lead to fatal complications such as myocardial infarction (3). There is a high variability among patients in tolerance to pain and analgesic requirement (4, 5). The studies show that about 80% of patients experience a mild to severe pain after surgery (6). There is inadequate postoperative analgesia in the half of all surgeries, can lead to chronic postoperative pain (7). Several methods are available to control and reduce postoperative pain such as administering opioids or nonsteroidal anti-inflammatory drugs (NSAIDs) and patient-controlled analgesia (PCA). It is established that the use of systemic opioids alone is not sufficient to relieve postoperative pain. In most cases, inadequate dosage is prescribed to reduce the side effects of these drugs like respiratory depression and therefore, the medication cannot control pain completely (8, 9). Analgesic nephropathy, skin reactions, and peptic ulcers are common side effects of nonsteroidal anti-inflammatory drugs (10). Recent advances present new techniques for prevention and reduction of postoperative pain. One of the most important technologies of this century is the use of low-level laser (LLL) at the site of surgery (11).

Low-level laser therapy (LLLT) was pioneered at Russia and Hungry and then at Europe in early 1960s. It is a branch of laser treatments that has been indicated for pain killing and wound healing. LLLT uses irradiation with laser light of low intensity and its effects are not due to producing heat. These nonthermal effects are thought to be mediated by a photochemical reaction that alters cell membrane permeability, leading to increased mRNA synthesis and cell proliferation. FDA has started differ-

Implication for health policy makers/practice/research/medical education:
Postoperative pain is a common complication that can lead to serious morbidities and delayed recovery. The aim of this study was to investigate the effect of low-level laser therapy on acute pain after tibial fracture surgery

ent investigations on LLLT for 15 years and has approved the use of LLLT for pain relief in carpal tunnel syndrome since 2002 (11, 12). It is also used to treat damages in sport injuries and musculoskeletal disorders. In addition, it is applicable to reduce neck pain and the size of keloid scarring after surgery (13-17). Many studies found that LLL stimulates respiratory cycle in mitochondria and increases adenosine triphosphate molecules (14) that reduce swelling and pain (16). In another study, applying LLL directly over painful points was useful in treatment of stress fracture of tibia (18). The LLL is effective in relieving pain of knee osteoarthritis, breast augmentation surgery, and cryosurgical treatment of oral leukoplakia (15, 17).

2. Objectives

Pain following orthopedic surgeries are considered severe pain (19, 20); hence, the aim of this study was to investigate the effect of LLLT on acute pain after tibial fracture surgery.

3. Patients and Methods

This double-blind, controlled, randomized clinical trial was conducted in 2012-2013 in Imam Khomeini Hospital, Ahvaz, Iran. The study was approved by the Ethical Committee of Jundishapur University of Medical Sciences (ETH-654) and all subjects signed an informed consent.

Sample size was calculated at 27 in each arm of the study by setting the power at 80% and the values for $Z_{\alpha/2}$, $Z_{1-\beta}$, P_1, and P_2 at 1.96, 0.84, 0.68, and 0.32, respectively, based on a previous observational study (21). A total of 54 patients aged between 18 and 60 years who were candidate for tibial fracture surgery in American Society of Anesthesiologists (ASA) classes I and II were allocated randomly to two equal groups of control and laser. All subjects were matched based on their age, weight, and height. Patients who were pregnant, those with malignant tumors, benign tumors with malignant potential, hypersensitivity to light, e.g. systemic lupus erythematosus, coagulopathies, high intracranial pressure, history of chronic pain, those on long-term opioids or other painkillers during the preceding month, or those who did not agree to undergo spinal anesthesia were excluded from the study.

Monitoring equipment including electrocardiograph, pulse oximeter and sphygmomanometer were employed for all patients; they received 10-mL/kg intravenous lactated Ringers' solution and then spinal anesthesia was induced by the anesthesiologist.

Spinal anesthesia was induced by intrathecal administration of 10-mg 0.5% bupivacaine (Astrazeneca Co., Germany) with 25-gauge needle in the sitting position and with the midline technique.

If the systolic blood pressure dropped by 20% or more, 10-mg ephedrine would be injected intravenously. Upon achieving successful anesthesia, pull-tight elasticated tourniquet was clamped and operation was started. The surgical procedures were similar in both groups and included open reamed interlocking intramedullary nailing, which is the preferred approach for treatment of tibial shaft fractures (22).

After the surgery and before the final bandage in surgery room, patients in laser group were treated with a combination of two lasers (Canadian Optic and Laser Center, Canada): (1) GaALAs hand held probe (PLP-IR) with wavelength of 808 nm and 300-mW output power in continuous mode (dose, 6 J/cm^2; area, 1 cm^2; and time, 20 s/point); and (2) GaALInP hand held probe (PLP-R) with wavelength of 650 nm and 100-mW output power in continuous mode, (dose, 3 J/cm^2; area, 1 cm^2; and time, 30 s/point).

Each tibial fracture was radiated from four sides in contact technique with the combination of IR and R laser in dose of 9 J/cm^2 (medial, lateral, anterior, and posterior sides of fracture region and popliteal fossa). For radiation on popliteal fossa, the legs were elevated by 60° angels.

In addition, trigger points on muscles and surgical wounds (6-8 points) were radiated with 4 J/cm^2 by the same combination of IR and R lasers (ten seconds of each laser; 3 J/point IR plus 1 J/point R laser).

For placebo laser treatment in control group, all those sites were treated with the lasers in turn-off mode with the same duration.

One of authors who was blind to the group allocation and did not participate in the laser therapy procedures, filled out the questionnaires. The amount of total analgesic and pain intensity at second, fourth, eighth, 12th, and 24th hours after the surgery were investigated in both groups. Pain intensity was quantified by visual analogue scale (VAS) in which zero and ten represented analgesia and worst possible perception of pain, respectively. If VAS was three or more, 0.3 mg/kg of pethidine was injected intravenously.

3.1. Statistical Analysis

The data are presented as mean ± standard deviation (SD). We performed Shapiro-Wilk test and Levene's test for normality of the data distribution and equality of variances. Independent samples t test, repeated measure test, and Bonferroni post hoc test were used to analyze the data. P Value of less than 0.05 was considered as statistically significant. All the statistical analyses were done by SPSS software version 16 (SPSS Inc, Chicago, IL, USA).

4. Results

Demographic characteristics of participants are presented in Table 1. Two groups were similar in terms of age, weight, height, and body mass index. There was no significant difference between groups regarding the duration of surgery (57.34 ± 3.2 and 56.29 ± 3.4 minutes in control and laser groups, respectively; P = 0.71) and anesthesia duration (84.14 ± 5.21 and 85.02 ± 4.98 minutes in control and laser groups, respectively; P = 0.69).

Table 1. Demographic Characteristics of the Participants [a,b]

Groups	Age, y	Weight, kg	Height, cm	BMI, kg/m^2
Control Group	24.61 ± 2.76	71.22 ± 11.34	169 ± 6	72.16 ± 12.71
LLLT Group	25.05 ± 2.68	72.27 ± 10.80	171 ± 5	70.09 ± 13.23
P value	0.628	0.777	0.791	0.706

[a] Abbreviations: LLLT, low level laser therapy; and BMI, body mass index.
[b] Data are presented as mean ± SD.

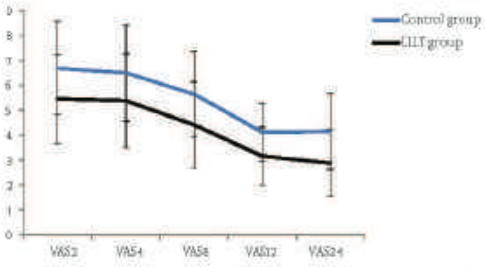

Figure 1. Pain Intensity at Different Hours in lllt and Control Groups

Table 2. Postoperative Pain Intensity [a,b]

Groups	VAS at Different Time Points After Surgery				
	2nd h	4th h	8th h	12th h	24th h
Control Group	6.69 ± 1.87	6.50 ± 1.94	5.65 ± 1.71	4.12 ± 1.15	4.15 ± 1.53
LLLT Group	5.46 ± 1.79	5.38 ± 1.89	4.42 ± 1.72	3.16 ± 1.16	2.88 ± 1.36
P value	0.019	0.041	0.013	0.006	0.012

[a] Abbreviations: LLLT, low-level laser therapy; and VAS, visual analogue scale.
[b] Data are presented as mean ± SD.

Based on VAS, mean scores of pain intensity after operation in different periods are presented in Table 2. Pain reduced considerably at second, fourth, eighth, 12th, and 24th hours after surgery in laser group in comparison with the control group. Although there were no significant differences in pain intensity between the second and fourth, the fourth and eighth, the eighth and 12th, as well as the 12th and 24th hours in each group ($P > 0.999$, $P = 0.110$, $P = 0.681$, and $P > 0.999$ in control group; $P > 0.999$, $P = 0.099$, $P = 0.097$, and $P > 0.999$ in laser group, respectively), there were significant differences between the second and eighth, the second and 12th, the second and 24th, the fourth and 12th, the fourth and 24th, as well as the eighth and 24th in each group ($P < 0.001$, $P = 0.010$, $P < 0.001$, $P = 0.009$, $P < 0.001$, and $P = 0.002$ in control group; $P < 0.001$, $P = 0.002$, $P < 0.001$, $P = 0.002$, $P < 0.001$, and $P < 0.001$ in lase group, respectively; Figure 1).

The mean of total amount of analgesic (pethidine) used in laser group was significantly less than control group. The mean of total amount of analgesic was 51.62 ± 29.52 and 89.28 ± 35.54 mg in laser and control groups, respectively ($P = 0.008$).

5. Discussion

Pain as a stressor, stimulates the physiological and psychological responses. Its outcomes have a direct effect on the postoperative complications, recovery time, and patient's satisfaction with the health system. The aim of this study was to investigate the effect of LLL with the wavelengths 650 and 808 nm on pain after tibial fracture surgery. The results of this study showed that pain reduction was significant at the second, fourth, eighth, 12th, and 24th hours after surgery (P Value ≤ 0.05). Similarly, Moore et al. showed that low level gallium-aluminum-arsenide laser for four to six minutes at the end of the cholecystectomy had no significant effect on pain reduction at the first and the fourth hours after surgery; however, the effect was significant at the eighth, 12th, 24th, and 48th hours after surgery (21). Hegedus et al. reported that the use of LLL (wavelength, 830 nm; continuous wave; and power, 50 mW) in patients with knee osteoarthritis resulted in pain reduction and improvement in joint movement (15). Jackson et al. found that laser irradiation with wavelength of 630 to 640 nm at the beginning and at the end of breast augmentation surgery reduced the postoperative pain (23). Moreover, Ribeiro et al. reported that AsGaAl laser (660 nm) could decrease the pain as well as postoperative recurrence rate in patients with oral leukoplakia (17).

The results of our study showed the mean total amount of analgesic use in laser group was significantly lower than the control group ($P < 0.05$). This finding is consistent with the findings of other researchers who reported that LLLT could decrease pain during and after the surgery and had a positive effect on wound healing and edema (12). LLLT is used in muscular fatigue (24), wound healing, and pain reduction in dental procedures in patients with and without diabetes (25-27). The researches showed that LLL could cause analgesia by reducing prostaglandin E2 (28, 29), raising endorphin level, and increasing urinary excretion of serotonin, the pain receptors stimuli. LLLT also has a negative effect on pain neurotransmitters and prevents accumulation of acetylcholine, a pain stimulus in the receptors (30).

The results of this study showed that the combination of laser therapy and analgesic medications had better effect during the 24 hours of recovery after the surgery. Laser radiation at wavelengths of 650 and 808 nm (R and IR laser) can decrease postoperative pain and analgesic use in postoperative period. LLLT does not have side effects like respiratory depression, skin reaction, and analgesic nephropathy that are seen with other methods. It is recommended to perform more studies concerning the applications of LLLT in anesthesia field as it is a noninvasive, safe, and acceptable analgesic method in patients in recovery or surgery room.

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Authors' Contributions

Study concept and design: Sholeh Nesioonpour and Soheila Mokmeli. Analysis and interpretation of data: Sarah Hojjati and Salman Vojdani. Manuscript preparation: Salman Vojdani, Ahmadreza Mohtadi, Reza Akhondzadeh, Kaveh Behaeen, and Shahnam Moosavi. Collection of data: Salman Vojdani and Sarah Hojjati. Critical revision: Sholeh Nesioonpour.

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The Effect of Low-Level Laser on Postoperative Pain After Elective Cesarean Section

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Abstract

Background: Postoperative pain is one of the major concerns about a cesarean in pregnant women that can lead to serious complications and delayed recovery for patients.
Objectives: The objective is to investigate the effect of low power laser on acute pain after elective cesarean.
Methods: In this randomized, double-blind clinical trial, 80 candidates for an elective cesarean were divided randomly into two groups, control and laser. The type of surgery was the same for both groups, which contained the spinal anesthesia technique. At the end of surgery, the surgical incision in patients who were treated with laser, (GaAlAs: 804 nm and GaAlInp: 650 nm) was irradiated by laser. The control group also received laser off by the same method. Patients were monitored for 24 hours to assess the severity of postoperative pain by VAS, the first request for analgesic and the total consumption of analgesic.
Results: The results demonstrated significant reduction of pain in the laser group 1, 4, 8, 12, 16, 24 hours after surgery, compared with the control group (P value < 0.05). Additionally, the average of total received analgesic in the group laser was less than the controls (P value = 0.006). The first request for analgesic in the laser received group was significantly longer than the controls (P value = 0.005).
Conclusions: Low power laser therapy is a good method to reduce postoperative pain due to the fact that it is a safe and non-invasive method which is also accepted by patients.

Keywords: Low Level Laser, Postoperative Pain, Cesarean

1. Background

Postoperative pain is one of the major concerns regarding a cesarean for pregnant women (1). In addition to developing the fear in patients to consent the surgery, pain also impacts their spirits adversely (2).

The pain after cesarean delivery affects the mother's ability to feed and care for the baby, which limits her abilities. Since the risk of thromboembolism increases during the pregnancy, lack of mobility, due to pain, increases the possibility of thromboembolism for them. Chronic pain is known as a common complication after the cesarean section; however, studies have shown that 12.3% of patients experience pain six months after a cesarean. Experience of severe acute pain, especially during the first 24 hours after a cesarean, can be the cause of persistent pain and postpartum depression at eight weeks after that (3).

Therefore, optimal perioperative pain management is of utmost importance and contributes to greater patient satisfaction, fewer adverse events, shorter hospital stays, and reduction in health care costs (4).

Currently, there are several methods to relieve pain after cesarean. The most common method of analgesics administration after surgery is applying a multi-modal approach using opioids and non-steroidal anti-inflammatory drugs, however, the use of opiates has side effects such as respiratory depression, nausea and vomiting, urinary retention and constipation. In addition, intrathecal or epidural injection of opioids, acupuncture, and patient controlled analgesia have been used to relieve pain after the surgery (5, 6).

In the present century, laser irradiation on the surgical field is one of the methods, which is used to prevent and reduce post-operative pain (7).

Low level laser therapy (LLLT) was approved by the Food and Drug Administration (FDA) for the treatment of pain in 2002 (8). Low level laser therapy is a treatment method, which uses the low intensity light in the range of 540 - 830

nm.

Light emitted by the laser does not cause heat generation and is used to treat pain and wound healing. Therapeutic effects of this method are achieved by the photochemical reactions, which lead to change in the permeability of cell membrane, increase the mRNA synthesis, and also raise the cell proliferation (9). LLLT shows the greatest potential to prevent tissue death and stimulates tissue regeneration in a wide range of diseases in neurology (10), ophthalmology (11), cardiology (12), and otorhinolaryngology (13). Many studies have found that low level laser can stimulate the respiratory cycle in the mitochondria and induces the production of adenosine triphosphate (ATP), which further reduces pain and edema (14, 15). LLLT has been effective to reduce the pain, inflammation, and edema for orthopedic injuries and degenerative diseases, for the treatment of sport injuries and musculoskeletal diseases (16, 17), for reducing postoperative pain after tibial fracture operation (18), for reducing the pain after surgery of Breast augmentation (8), for reduction of the size of keloid scar (15), and also for prevention of oral mucositis after cancer treatment (19).

The purpose of this study was to evaluate the effect of low level laser on postoperative pain after elective caesarean section.

2. Methods

This study was a prospective, double-blind clinical trial that was conducted during the period of 2014 - 2013. Groups of patients were selected among the admitted patients for elective cesarean from Imam Khomeini hospital in Ahvaz, Iran. Setting the power at 80% and the values for α, β, $Z\alpha$, and $Z\beta$ at 0.05, 0.2, 1.96, and 0.84, respectively, the sample size was calculated to include 40 subjects in each of the case and control groups. After approval of the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences (ajums.rec.1392.40) and written consent was taken from 80 pregnant women between 40 - 18 years, women with their first or second pregnancy and the American Society of Anesthesiologists (ASA) classes I and II were candidates for elective cesarean and were selected as the inclusion criteria of study. The subjects were randomly divided into two groups of 40 individuals for laser and controlled groups through a computer - generated list of random numbers. The exclusion criteria of the study included individuals determined as the patients with previous classical incision, malignancy, benign tumors with the possibility to become malignant, sensitivity to light such as lupus, history of epilepsy or seizure, the patient's refusal of spinal anesthesia, elevated ICP, coagulopathy, infection of the skin or soft tissue around the insertion of the needle, and peripheral neuropathy of lower limb. After arriving to the operating room, patients received 10 mL/kg Ringer's lactate solution. Monitoring equipment employed were electrocardiogram, pulse oximetry, and sphygmomanometer; spinal anesthesia was done with 12 mg bupivacaine 0.5% (Astrazeneca Co. Germany) in the sitting position at the L4 - L5 space with midline technique. After ensuring the neuroxial block with the lack of sense with the tip of a needle at dermatome T4, the patients were operated as by Pfannenstiel incision.

During operation, at 5 minute intervals, systolic and diastolic blood pressure, oxygen saturation, and heart rate were monitored.

The treatment were done in the surgery room after the end of surgery and before the bandage. Laser group was treated with the combination of IR and red lasers (PLP-IR 808 nm - 200 mW, PLP-R 650 nm - 100 mW). For the control group, lasers were set to "off" during the treatment as placebo. Lasers were designed and manufactured by Canadian optic and laser center (COL Center). The power density for red laser was 0.1 W/cm^2 and for IR laser was 0.2 W/cm^2 (Figures 1 and 2).

The incisions were treated by the red laser, 1 J/cm^2 for 10 seconds, and IR laser, 2 J/cm^2 for 10 seconds. The total combination dose was 3 J/cm^2 (1 J Red + 2 J IR) on the surgical suture. The size of the incisions was between 7 - 10 cm^2, therefore, the total energy was between 21 - 30 J, depending on the size of the incision line.

The surrounding tissue was treated with the same combination of lasers with the interval of 2 cm, three points above and three points below the suture and each point's area was equal 1 cm^2. Each point was treated for 15 seconds by Red and IR. The total dose for each point was 4.5 J/cm^2 (3

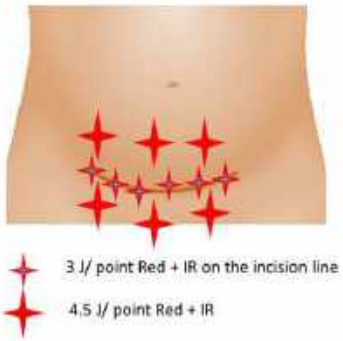

Figure 1. The points and locations irradiated in patients

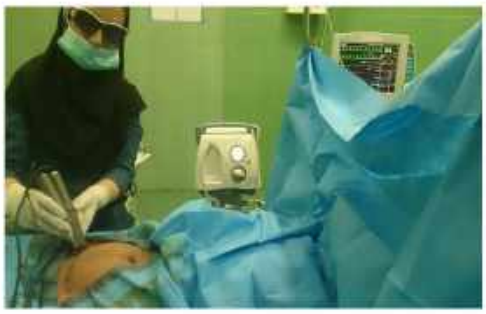

Figure 2. Laser radiation to surgical site

J IR + 1.5 J Red), and the total energy was 27 J.

The patients and anesthesia resident who completed the questionnaires were blinded to the patient groups and did not know the study groups. Only the operator of the LLL was aware of the study group. Considering the end of anesthesia, as the onset of pain through Visual Analogue Scale (VAS), a measure, which is considered the least pain equal to zero and the worst imaginable pain of 10, were examined at 1, 4, 8, 12, 16, and 24 hours and they received intravenous Pethidine 0.3 mg/kg in the presence of pain with VAS equal to three or greater than that. The severity of postoperative pain, first request of tranquilizer, and total consumed Pethidine after 24 hours were recorded in the questionnaire by the assistant of anesthesia who didn't know about patient groups. Side effects including nausea, vomiting, dizziness, and hypotension were also studied at stated hours.

2.1. Statistical Methods

Data were reported as the mean ± standard deviation (SD). In order to compare the groups after analyzing the normal distribution and homogeneity of variances, the Independent sample *t*-test, repeated measure test, and Bonferroni post hoc test were applied. Significant level of data was considered as $P < 0.05$. Statistical analyses were performed using SPSS software (version 16).

3. Results

In this study, 80 patients were divided into two groups of laser and control. According to the results in Table 1, the two groups were similar in terms of demographic characteristics (age, weight, and height), and the duration of surgery (46.7 ± 3.4 and 47.7 ± 5.59 minutes; P = 0.71) did not differ significantly from each other.

Table 1. Demographic Characteristics of the Participants[a,b]

Group	Age, y	Weight, kg	Height, cm
Control group	25.05 ± 1.78	74.55 ± 6.14	158.6 ± 5.96
Laser group	24.62 ± 2.23	75.52 ± 6.12	159.8 ± 6.26
P value	0.662	0.479	0.819

[a] Values are expressed as mean ± SD.
[b] $P < 0.05$ shows significant difference between groups.

Postoperative pain severity was achieved by VAS scores based on criteria at different periods in Table 2. Due to the results, post-operative pain severity decreased significantly in the laser group based on the VAS criteria at 4, 6, 8, 12, 16, and 24 hours after the operation ($P < 0.05$).

According to the results of Table 3, the laser group needed the tranquilizer later than the control; there was a significant difference between two groups ($P < 0.005$).

Based on the results of Table 4, the average of total tranquilizer (analgesic) in the group receiving the laser was significantly less than the control group ($P = 0.006$).

The side effects of nausea, vomiting, hypotension, and dizziness weren't also observed in any of the two groups.

4. Discussion

In this study, the effect of GaAlAs laser, with wavelength of 804 nm and GaAlInp with wave length of 650 nm were examined on the post-operative pain of cesarean. The results showed a significant reduction of pain in the 1, 4, 8, 12, 16 and 24 hours after the operation.

In the research of Moor and colleagues GaAlAs laser with wavelength of 830 nm for 6 - 8 minutes after the operation of cholecystochetomy reduced the pain after 8, 12, 24, and 48 hours of the operation significantly; however, it wasn't significant after one and four hours (20). In the research of Kreisler and colleagues, in 2004 on 52 patients who were treated by endodontic surgery, it was found out that GaAlAs laser, with the wavelength of 809 nm, reduced the pain in the place of surgery the after first 7 days of operation, however, the pain reduction was significant only one day after the surgery (P value = 0.04) while pain reduced in next days, however, the difference wasn't significant (21).

Bjordal and colleagues reported in 2008 that low power laser irradiation GaAlAS, with the dose of 904 nm to the lateral elbow tendon directly, reduced the pain and improves the ability to move patients clearly (22). Hegadus and colleagues, in 2009, reported that laser irradiation (wavelength 830 nm; continuous wave; and power, 50 mW) in patients with osteoarthritis of the knee led to reduce pain and improve joint movement (16). Jackson and colleagues, in 2009, using the low power laser with 360 - 640

Table 2. Postoperative Pain Intensity[a,b]

Group	VAS at Different Time Points After Surgery					
	1 H	4 H	8 H	12 H	16 H	24 H
Control group	6.77 ± 2.08	6.42 ± 1.51	5.60 ± 1.08	4.42 ± 1.65	4.20 ± 1.71	4.03 ± 1.53
Laser group	4.22 ± 2.01	4.05 ± 1.33	3.37 ± 1.37	2.7 ± 1.59	2.22 ± 1.69	2.12 ± 1.36
P value	0.01	0.031	0.019	0.006	0.041	0.005

[a] Values are expressed as mean ± SD.
[b] Significant difference between groups (P< 0.05).

Table 3. First Analgesic Request Time[a,b]

Group	First Analgesic Request Time, min
Control group	88.5 ± 15.78
Laser group	226.5 ± 14.56
P value	0.005

[a] Values are expressed as mean ± SD.
[b] Significant difference between groups (P < 0.05).

Table 4. Total Used Dosage of Analgesic[a,b]

Group	Total Used Dosage of Analgesic, mg
Control group	107.78 ± 34.28
Laser group	57.83 ± 29.57
P value	0.006

[a] Values are expressed as mean ± SD.
[b] Significant difference between groups (P< 0.05).

nm wavelengths for four minutes at the initiation and the end of breast augmentation operation and its repetition 24 hours and one week after by the same protocol and follow up of patients after 7, 14, 21, and 24 hours, demonstrated that VAS level reduced at the mentioned times, however, the differences were significant only in the first 24 hours rather than control group (P value = 0.001). The analgesics used in the first 24 hours and one week later was significantly reduced in laser group (8).

Ribeiro et al. in 2011, reported that using a GaAlAS laser with a wavelength of 660 nm reduced the postoperative pain in patients with oral leukoplakia and the recurrence rate after surgery was lower in the group receiving laser compared to controls (23). In one study, in 2014, using GaAlAs laser with wavelength of 808 nm and GaAlInp laser with wavelength of 650 nm, demonstrated significant reduction of postoperative pain after Tibial fracture surgery at 2, 4, 8, 12, and 24 hours after surgery (18).

The results also showed that the first request time of analgesic, in the group who underwent laser was significantly longer than the control group (P < = 0.05).

Additionally, the average of total analgesic in the group receiving the laser was significantly lower than the control group ($P \leq 0.05$).

These finding are matched with the results of studies that suggest using the LLLT, which reduces the consumption of analgesics at the postoperative period, reduces the edema and inflammation after surgery, and speeds up the healing process (24). Researches show that LLLT can cause the painless by reducing the PGE2 (21, 22), preventing the production of stimulating compounds and adjusting the inflammation process, stimulating the release of exogenous endorphin, and altering excitation and nerve conduction in peripheral nerves (25).

The results of this study showed that GaAlAs laser, with the wave length of 804 and GaAlInp laser and with wavelength of 650 nm can reduce postoperative pain and analgesic consumption after the operation. The side effects of such respiratory depression, skin reactions, analgesic nephropathy, and ulcer peptic have been seen in other forms of analgesia consumption methods, are not seen in LLLT. Finally, it is recommended that further studies should be conducted about using the LLLT in anesthesiology, due to the fact that LLL is a safe, non-invasive, and accepted method by patients.

Footnotes

Authors' Contribution: Study concept and design: Sholeh Nesioonpour and Soheila Mokmeli. Analysis and interpretation of data: Sholeh Nesioonpour, Sarah Poursalehan. Manuscript preparation: Sara Poursalehan, Reza Akhondzadeh. Collection of data: Sara Poursalehan. Critical revision: Sholeh Nesioonpour.

Ethical Considerations: http://behsan.ajums.ac.ir/webdocument/load.action?webdocument_code=1000&masterCode=33004722.

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Low-Level Laser and Light-Emitting Diode Therapy for Pain Control in Hyperglycemic and Normoglycemic Patients Who Underwent Coronary Bypass Surgery with Internal Mammary Artery Grafts: A Randomized, Double-Blind Study with Follow-Up

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Abstract

Objective: This study aimed to evaluate the efficacy of low-level laser therapy (LLLT) and light-emitting diodes (LEDs) for reducing pain in hyperglycemic and normoglycemic patients who underwent coronary artery bypass surgery with internal mammary artery grafts. ***Methods:*** This study was conducted on 120 volunteers who underwent elective coronary artery bypass graft (CABG) surgery. The volunteers were randomly allocated to four different groups of equal size ($n=30$): control, placebo, LLLT [$\lambda=640$ nm and spatial average energy fluence (SAEF) $=1.06$ J/cm^2], and LED ($\lambda=660\pm20$ nm and SAEF $=0.24$ J/cm^2). Participants were also divided into hyperglycemic and normoglycemic subgroups, according to their fasting blood glucose test result before surgery. The outcome assessed was pain during coughing by a visual analog scale (VAS) and the McGill Pain Questionnaire. ***Results:*** The patients were followed for 1 month after the surgery. The LLLT and LED groups showed a greater decrease in pain, with similar results, as indicated by both the VAS and the McGill questionnaire ($p\leq0.05$), on the 6th and 8th postoperative day compared with the placebo and control groups. The outcomes were also similar between hyperglycemic and normoglycemic patients. One month after the surgery, almost no individual reported pain during coughing. ***Conclusions:*** LLLT and LED had similar analgesic effects in hyperglycemic and normoglycemic patients, better than placebo and control groups.

Introduction

Cardiovascular diseases (CVD) are the major cause of nontraumatic deaths in Brazil, being responsible for ~20% of all deaths in individuals >30 years of age.[1] In many cases, the disease severity may lead the patient to coronary artery bypass grafting (CABG). The surgery procedure is complex, and most interventions need a sternal longitudinal incision, the sternotomy, which can cause moderate to severe pain postsurgery. Additionally, anastomosing the left internal mammary artery (LIMA) to the left anterior descending artery is still considered to increase the risk of deep sternal wound infection.[2]

The pain intensity around the incision has been described as higher on the 7th postoperative day than at 1 month after hospital discharge, and has a significant effect on functionality. Borges et al.[3] showed that after CABG, patients' functional capacity was reduced. The functionality level was also lower on the 7th postoperative day than after hospital discharge, with significant changes in day-to-day activities. This impairment can affect the quality of life, and must be considered an important prognostic factor after discharge from hospital.

Apart from being at high risk of CVD and also postsurgical complications, such as incision dehiscence, mediastinitis, and delay in wound healing, hyperglycemic patients can also develop peripheral polyneuropathy resulting in sensorial abnormalities specifically related to pain perception.[4] During the postoperative period, pain can be an important factor limiting the patients' functional activities and restricting chest expansion during respiration.

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Although many studies have reported the use of low-level laser therapy (LLLT) as a coherent light source for analgesic purposes, the mechanism whereby it relieves pain is still not clear. It has been assumed that any biological effects are secondary to the direct effects of photonic radiation, and are not the result of thermal processes.[5] In the case of neuropathic pain, LLLT has been proposed to mediate analgesia by stimulating the local release of neurotransmitters such as serotonin, promoting the release of endorphins, increasing mitochondrial adenosine triphosphate (ATP) production, and through anti-inflammatory effects.[6] On the other hand, recent studies have suggested that light- emitting diode (LED) therapy, with noncoherent light, has effects comparable to those of LLLT, which suggests that coherence of light is not the key factor for pain control in phototherapy.

The aim of this study was to evaluate the efficacy of LLLT and LED therapy for reducing pain in hyperglycemic and normoglycemic patients who underwent CABG.

Materials and Methods

All subjects signed a written declaration of informed consent, and their rights were protected. The protocol for this study was approved by the local research ethics committee (CAAE 0180.0.415.000-11) and registered at the Brazilian Clinical Trial Registry and the International Clinical Trials Registry Platform of the World Health Organization under RBR-38wgx6 and Universal Trial Number U1111-1128-9666, respectively.

This was a randomized, double-blind, clinical trial consisting of both a placebo and a control group. It was conducted in a private hospital that performs cardiac surgery for the Brazilian public health system. All patients admitted to the hospital during the study period were invited to participate, subject to indication for CABG and fulfilling of the inclusion criteria. The study was conducted on 120 volunteers who were randomly allocated to four different groups of equal size ($n=30$ each group): control, placebo, LLLT, and LED groups. Each group was also subdivided into two subgroups—hyperglycemic and normoglycemic subjects—according to the blood glucose levels before CABG, following the American Diabetes Association (ADA) and World Health Organization (WHO) criteria.[7]

The individuals in the study were subjected to elective coronary artery bypass surgery with a longitudinal sternotomy incision and extracorporeal circulation, anastomosing the LIMA to the left anterior descending artery. If necessary, saphenous vein grafts (SVG) were used to anastomose other coronary arteries. Patients between 18 and 75 years of age, of both genders, hemodynamically stable, and with body mass index (BMI) <29.9 kg/m^2 were included. The exclusion criteria were (1) a diagnosis of type I diabetes mellitus; (2) a diagnosis of type II diabetes mellitus made within the past 2 years, or not under regular treatment with hypoglycemic drugs; (3) previous thoracic surgery, or emergency or urgent coronary artery bypass surgery; or (4) respiratory or renal insufficiency after surgery, low cardiac output syndrome, clinical complications that demanded changes in analgesic protocols, or any other postoperative complications. Individuals who could not be monitored during the 1st month after the operation were also excluded.

The randomization and blinding procedures consisted of the subjects simply drawing cards marked 1, 2, 3, or 4, where 1 meant the control group, 2 the placebo group, 3 the LLLT group, and 4 the LED group. The cards were drawn at the time of the patient's hospital admission, which always occurred at least 24 h before the surgery. The researchers were separated into therapists and evaluators. The therapists were assistants responsible for conducting the therapy and registering the procedures, and the evaluators were responsible for assessing the patients and their results. Each patient was identified by a code registered by one of the therapist researchers, who ensured that the evaluating researchers were blinded to the code until the final statistical analysis was performed. The patients were blinded to the study by the use of opaque goggles during the laser and LED irradiation.

On the day before the surgery, patients were subjected to a preoperative assessment that consisted of an explanation of the procedures, the inclusion and exclusion criteria

TABLE 1. PARAMETERS OF THE INSTRUMENTS USED FOR PHOTOTHERAPY

Parameters	*Gallium-aluminium-indium-phosphate (GaAlInP) Laser (λ660 nm)*	*Gallium-aluminium-arsenium (GaAlAs) LED (λ640 ± 20 nm)*
Equipment	Laserhand MM Optics® portable equipment[a]	LED Microdont® portable equipment[b]
Energy density (J/cm^2)	6	6
Energy (J)	2.4	10.1
Power (W)	0.04	0.07
Spot diameter (cm)	0.5	1.5
Spot size (cm^2)	0.4	1.77
Time of irradiation (sec)	60	152
Power density (W/cm^2)	0.1	0.03
Treatment time per point (sec)	60	152
Number of spots	8	8
Spatial average energy fluence (SAEF)[c]	0.24	1.06

[a]Manufacturer: MMOptics, São Carlos – SP, Brazil.
[b]Manufacturer: Microdont, São Paulo – SP, Brazil.
[c]SAEF = power output × time treatment per point × point numbers/total treated area.

TABLE 2. ANTHROPOMETRIC CHARACTERISTICS OF PARTICIPANTS (MEAN ± STANDARD DEVIATION)

	Group							
	Control		*Placebo*		*Laser*		*LED*	
	Diabetes Mellitus							
	Not	*Yes*	*Not*	*Yes*	*Not*	*Yes*	*Not*	*Yes*
n	18	12	19	11	19	11	19	11
Age (years)	57.8 ± 10.6	63.8 ± 7.5	58.5 ± 8.7	59.9 ± 9.9	58.2 ± 8.6	62.4 ± 7.9	61.2 ± 8.7	59.7 ± 8.9
Weight (kg)	62.7 ± 9.8	67.6 ± 10.3	60.5 ± 6.3	68.1 ± 10.8	65.3 ± 9.9	65.4 ± 10.7	61.4 ± 8.6	61.5 ± 8.4
Height (m)	1.56 ± 0.08	1.63 ± 0.10	1.57 ± 0.07	1.61 ± 0.09	1.59 ± 0.07	1.62 ± 0.06	1.59 ± 0.08	1.53 ± 0.09
BMI (kg/m^2)	25.6 ± 3.0	25.2 ± 1.3	24.6 ± 2.8	26.3 ± 3.2	25.9 ± 4.1	24.9 ± 3.7	24.3 ± 2.7	26.3 ± 3.29
Blood glucose (g/dL)	86.0 ± 6.97	141.3 ± 3.4	90.7 ± 7.6	138.2 ± 4.6	93.1 ± 7.1	137.8 ± 5.2	88.95 ± 6.9	138.8 ± 5.7

certification, clinical assessment including fasting capillary blood glucose test, and the group drawing. The experimental groups (LLLT and LED) were subjected to irradiation immediately after surgery and on subsequent days 2, 4, 6, and 8. The irradiation was performed at spots alongside the incision, 2 cm from each other, perpendicularly and in contact to the skin, for a total of eight points. The probes were protected by a translucent film. The equipment characteristics and irradiation parameters are described in Table 1. The placebo group was subjected to the LED application process but with the equipment turned off. The control group was only subjected to the assessment protocols and the follow-up. The outcome assessed was pain during the hospitalization period and at the 1st month after surgery.

The evaluating researchers underwent a training program for intra- and interexaminer agreement to calibrate their level of concordance. Pain was assessed using an 11 point visual analog scale (VAS) and the McGill pain questionnaire from postoperative day 2 to 1 month postsurgery. Patients were stimulated to cough, and their level of pain was registered at that moment. Coughing is important to these patients, because they must be stimulated to keep their airways free from obstructions, which helps prevent respiratory complications during the postoperative period. The employed analgesic protocol was the one routinely used by the hospital, consisting of tramadol hydrochloride and dipyrone administered intravenously on a fixed 6 h schedule. Morphine sulfate was administered on an as-needed basis. Those patients who

TABLE 3. PAIN ACCORDING TO VISUAL ANALOG SCALE. INTRAGROUP COMPARISON OF HYPERGLYCEMIC VERSUS NORMOGLYCEMIC PATIENTS. MANN–WHITNEY *U* TEST

		Rank sum			*Valid* n		
		Hyperglycemic		*Z*	*Hyperglycemic*		*2 sided*
Group	*Day*	*Yes*	*Not*	*adjusted*	*Yes*	*Not*	*exact* p
Control	Day 2	288.0	177.0	0.41	12	18	0.72
	Day 4	274.0	191.0	−0.23	12	18	0.86
	Day 6	233.0	232.0	−2.18	12	18	0.06
	Postdischarge	272.0	193.0	−0.32	12	18	0.79
	1 Month	303.0	162.0	1.18	12	18	0.33
Placebo	Day 2	303.0	162.0	0.38	11	19	0.73
	Day 4	295.0	170.0	0.02	11	19	1.00
	Day 6	306.0	159.0	0.54	11	19	0.64
	Postdischarge	293.0	172.0	−0.07	11	19	0.97
	1 Month	280.0	185.0	−0.75	11	19	0.55
Laser	Day 2	289.5	175.5	−0.22	11	19	0.83
	Day 4	272.0	193.0	−1.04	11	19	0.35
	Day 6	277.0	188.0	−0.82	11	19	0.47
	Postdischarge	277.0	188.0	−0.80	11	19	0.47
	1 Month	311.5	153.5	0.85	11	19	0.47
LED	Day 2	282.0	183.0	−0.56	11	19	0.61
	Day 4	282.0	183.0	−0.57	11	19	0.61
	Day 6	266.0	199.0	−1.37	11	19	0.23
	Postdischarge	279.5	185.5	−0.7	11	19	0.52
	1 Month	293.5	171.5	−0.06	11	19	0.97

Marked tests are significant at $p \leq 0.05$.

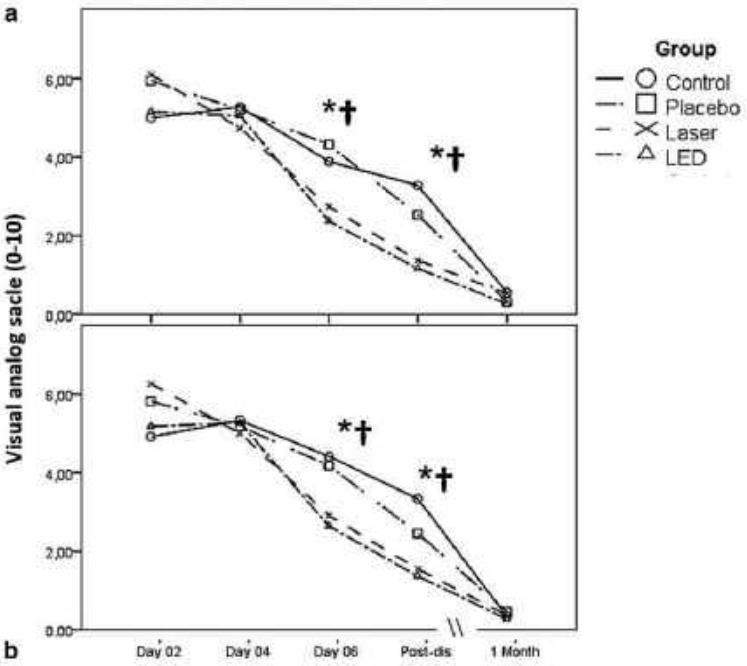

FIG. 1. Pain according to visual analog scale. Intergroup comparison. **(a)** Normoglycemic patients. **(b)** Hyperglycemic patients. Kruskal–Wallis with multiple comparison by Dunn's test. Marked tests are significant at $p \leq 0.05$. $*p \leq 0.05$ laser × placebo and control; $\dagger p \leq 0.05$ light-emitting diode (LED) × placebo and control.

TABLE 4. PAIN ACCORDING TO MCGILL PAIN QUESTIONNAIRE. INTRAGROUP COMPARISON OF HYPERGLYCEMIC VERSUS NORMOGLYCEMIC PATIENTS, MANN–WHITNEY *U* TEST

		Rank sum			*Valid* n		
		Hyperglycemic			*Hyperglycemic*		
Group	*Day*	*Yes*	*Not*	*Z adjusted*	*Yes*	*Not*	*2 sided exact p*
Control	Day 2	314.0	151.0	1.50	12	18	0.15
	Day 4	278.5	186.5	−0.02	12	18	0.98
	Day 6	270.0	195.0	−0.39	12	18	0.72
	Postdischarge	256.5	208.5	−0.97	12	18	0.35
	1 Month	305.0	160.0	1.21	12	18	0.29
Placebo	Day 2	288.0	177.0	−0.28	11	19	0.8
	Day 4	273.5	191.5	−0.93	11	19	0.37
	Day 6	253.5	211.5	−1.8	11	19	0.08
	Postdischarge	323.5	141.5	−0.42	11	19	0.22
	1 Month	286.0	179.0	−0.42	11	19	0.73
Laser	Day 2	181.0	284.0	0.46	11	19	0.67
	Day 4	195.0	270.0	1.08	11	19	0.31
	Day 6	282.0	183.0	−0.55	11	19	0.61
	Postdischarge	179.0	286.0	0.37	11	19	0.73
	1 Month	145.0	320.0	−1.20	11	19	0.29
LED	Day 2	302.0	163.0	−0.36	11	19	0.75
	Day 4	337.5	127.5	1.25	11	19	0.23
	Day 6	325.0	140.0	0.69	11	19	0.53
	Postdischarge	284.0	181.0	−1.20	11	19	0.27
	1 Month	296.5	168.5	−0.73	11	19	0.56

Marked tests are significant at $p \leq 0.05$.

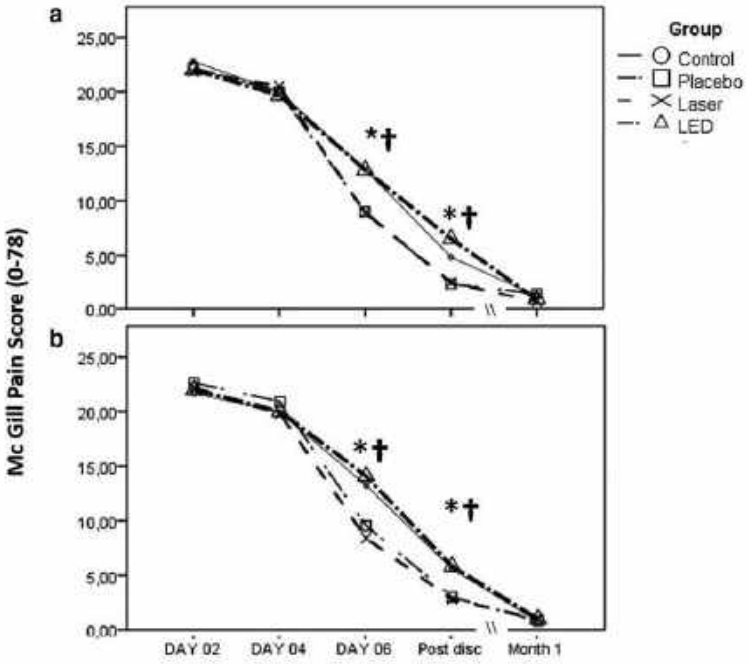

FIG. 2. Pain according to McGill Pain Questionnaire. Intergroup comparison. (**a**) Normoglycemic patients. (**b**) Hyperglycemic patients. Kruskal–Wallis with multiple comparison by Dunn's test. Marked tests are significant at $p \leq 0.05$. *$p \leq 0.05$ laser and placebo × control; †$p \leq 0.05$ light-emitting diode (LED) and placebo × control.

needed doses of morphine were excluded from the study. The patients were followed up for 1 month after surgery, and the pain was evaluated during this period.

The results were evaluated using the software STATISTICA 7.0 StatSoft©. Intragroup comparisons of pain scores were performed using the Mann–Whitney *U* test. Intergroup comparisons were performed using the Kruskal–Wallis test with multiple comparisons by Dunn's test. All significance levels were set at $p \leq 0.05$.

Results

A total of 120 patients were included in the study; their anthropometric characteristics are presented in Table 2. No significant differences in age, weight, height, or BMI were found among the groups. Individuals with blood glucose levels >126 g/dL were considered hyperglycemic according to the ADA and WHO criteria.[7] Twelve subjects were diagnosed as hyperglycemic in the control group, 11 in the placebo group, 11 in the LLLT group, and 11 in the LED group. According to preoperative clinical registers, all participants were using antihypertensive drugs of different classes, such as thiazide diuretics, calcium channel blockers, angiotensin II receptor antagonists (ARBs), and beta-blockers. All patients were underwent internal mammary artery grafting (Table 2).

Pain scores on the VAS

Table 3 shows the results of the Mann–Whitney *U* test for VAS pain scores between the normoglycemic and hyperglycemic subgroups within each group. The results suggest that there were no statistical differences between them ($p \geq 0.05$). These findings indicate that normoglycemic and hyperglycemic individuals experienced similar pain severity after sternotomy, whether or not they received phototherapy. Each result was compared one by one between the normoglycemic and hyperglycemic subgroups. The same analysis was performed in each group (control, placebo, LLLT, and LED) independently.

As shown in Fig. 1, all the groups showed a significant decrease in pain intensity from postoperative day 1 to 8, and a complete absence of pain at 1 month postsurgery. Nevertheless, the LLLT and LED groups experienced less pain on postoperative days 6 and 8 than did the control and placebo groups, according to the intergroup Kruskal–Wallis test with multiple comparison by Dunn's test ($p \leq 0.05$).

Pain severity according to the McGill Pain Questionnaire

The McGill questionnaire included two pain measures: the number of pain descriptive words chosen and the pain score. This questionnaire is organized into classes of word descriptors, including sensory, affective, evaluative, and miscellaneous words. Table 4 presents an intragroup McGill Pain Score comparison between hyperglycemic and normoglycemic patients. Similar to the results of the VAS scores in Table 3, the results for the McGill questionnaire also suggest that there was no difference in pain perception between hyperglycemic and normoglycemic patients ($p \geq 0.05$).

At 1 month after surgery, almost no individual mentioned pain during coughing.

Figure 2 shows an intergroup comparison (i.e., among the control, placebo, LLLT, and LED groups) of pain perception based on the McGill pain scores; hyperglycemic and normoglycemic individuals were evaluated separately. A significant decrease in pain level can be observed in all groups from postoperative day 1 to day 8; however, the LLLT and LED groups presented lower pain scores on postoperative days 6 and 8, compared with the control and placebo groups ($p \leq 0.05$).

Discussion

Among the 120 individuals included in this study, at least one third were diagnosed with hyperglycemia with lasting blood glucose levels >126 mg/dL, among other risk factors for CVD, as shown in Table 2. According to Bloomgarden , two thirds to three quarters of patients with diabetes will eventually die of CVD.[8] Diabetes is becoming one of the most important risk factors of CVD because of its increasing prevalence as a result of the high incidence in many countries and the increasing obesity in the population. Hyperglycemia can also be responsible for postsurgical complications after CABG, such as delay in wound healing and pain dysfunction, because of its neurological involvement. Further, anastomosing the LIMA to the left anterior descending artery is still considered to increase the risk of deep sternal wound infection,[2] which can delay the healing process and aggravate inflammation, and consequently pain.

One of the neurological problems found in hyperglycemic persons is symmetrical diffuse distal sensorimotor neuropathy (SDSN). Daousi at al.[9] reported a prevalence of 16.2% for chronic, painful, peripheral neuropathy in people with diabetes, which is significantly higher than the prevalence among people without diabetes. Evidence of diffuse damage to the peripheral nerves has been found to be a characteristic of the early stages of diabetes mellitus. As a result, these patients may develop hypoesthesia and other sensory abnormalities, affecting pain perception, mainly in the limbs.[10] Although the limb extremities are the most affected areas, Abad et al.,[4] in their studies on subclinical pain and thermal sensory dysfunction in individuals with Type 1 diabetes mellitus, showed that sensory dysfunctions were highly correlated throughout different sites in the body, indicating a generalized sensory dysfunction. It has been suggested that the small sensory fibers conveying thermal sensations—thinly myelinated Aδ and unmyelinated C—are more severely affected than the large, myelinated fibers during the initial phase of diabetes mellitus.[11]

Dyslipidemia, high blood pressure, and high BMI are involved in the risk of diabetic neuropathy. Most of the participants in the present study were overweight (Table 2) and had hypertension. According to Bădescu et al.,[12] diabetic peripheral neuropathy may develop regardless of intensive hyperglycemic control. To explain how hyperglycemia affects nerve conduction, there are two theories: metabolic and vascular. The metabolic theory indicates that complex processes such as oxidation stress and glycosylation of proteins are involved in reducing the nervous speed.[13] The vascular theory states that arteriolar narrowing, venous distension, arterial and venous shunts, and vascular neoformation resulting in hyperplasia and hypertrophy lead to denervation and reduced neuropeptide expression in epineurial vessels.[14] Nevertheless, SDSN can result in reduced pain perception, even after a surgery such as CABG.

Both hyperglycemic and normoglycemic patients who underwent CABG surgery experienced chest pain near the sternotomy incision during the 1st postoperative week, mainly when they had to move their chest, for example, while coughing or while drawing a deep breath. Good lung ventilation and a pervious airway are necessary to prevent respiratory complications. Therefore, it is important to stimulate coughing amid respiratory exercises during the hospitalization period, and a good analgesic protocol is essential. Phototherapy has been reported to have analgesic effects in many clinical and experimental studies. Despite the numerous studies, controlled studies comparing laser and LED are few in number, and clinical studies investigating pain control in hyperglycemic patients treated with coherent light versus noncoherent light, at equal doses and protocols, have not been reported so far.

Doses in the range of 0.3–19 J/cm^2 (median dose 7.5 J/cm^2) have been used in studies investigating inflammation and pain modulation with LED therapy and LLLT.[15] Oliveira,[16] using LED therapy at 6 J/cm^2, and Carvalho,[17] using LLLT at the same dose, observed inflammation modulation and tissue repair. Baptista et al.[18] studied LLLT to prevent sternotomy dehiscence, and concluded that the therapy is effective when provided during the initial inflammatory phase after the surgery, suggesting that laser had positively modulated inflammatory cells, thus preventing incision-related complications. Esper et al.,[19] in a clinical trial, concluded that LED therapy showed a significant reduction in pain sensitivity after orthodontic tooth movement when compared with the control group. Leal Jr. et al.[20] concluded that a combination of super-pulsed laser, and red and infrared LED is effective in decreasing pain and improving the quality of life in patients with knee pain. Many studies have highlighted that coherent light therapy provided by laser sources is essentially monochromatic, and is expected to be more chromophore-specific than the broadband light emitted by non-coherent sources such as LED, which is believed to be able to excite multiple chromophores concurrently and, consequently, might trigger multiple biochemical responses.[21] However, recent studies have suggested that light coherence is not the main property involved in therapeutic and physiologic mechanisms of tissue photomodulation.

VAS has been proved to be one of the most reliable scales for evaluation of pain intensity.[22] In this study, groups treated with LED and LLLT (6 J/cm^2) after CABG surgery showed the same level of analgesic effects, characterized as reduction in pain during coughing. These effects were observed in both hyperglycemic and normoglycemic individuals. Table 3 shows a comparison between hyperglycemic and normoglycemic patients with respect to pain perception according to VAS. The data show that there was no statistical difference between them. Figure 1 shows that on the first four postoperative days, patients in all groups experienced the same pain severity; however, on postoperative days 6 and 8, both hyperglycemic and normoglycemic individuals in the LED and LLLT groups experienced an analgesic effect, with similar results. At 1 month postsurgery, the follow-up indicated that no patient reported pain on coughing.

Another important instrument used for pain assessment was the McGill Pain Questionnaire, which is the most widely used measures of pain intensity. There is much evidence supporting its validity and reliability.[23] Table 4, which compares pain perception between hyperglycemic and normoglycemic individuals using the McGill Pain Questionnaire, showed that there was no statistical difference between them ($p \geq 0.05$). These results are in line with those reported in Table 3, which leads to the conclusion that hyperglycemic and normoglycemic patients experience similar sternotomy-related pain when assessed at the same time points after CABG surgery. Figure 2 also shows that when comparing the LLLT and LED groups with the control and placebo groups with respect to the McGill Pain Questionnaire results, the former two showed an analgesic effect compared with the latter two on postoperative days 6 and 8; this was similar to the results of the comparison of the VAS scores. Therefore, laser and LED showed similar analgesic effects, which were observed in both hyperglycemic and normoglycemic patients.

Dall Agnol et al.[21] showed that red wavelengths of laser and LED have similar effects on tissue repair, similar to the results of our study. De Jesus et al.[24] showed that in rats with a partially injured Achilles tendon, LLLT probably modulated the proinflammatory agents by reducing interleukin (IL)-1β and cyclooxygenase (COX)-2 mRNA expression, consequently leading to reduced prostaglandin E2 (PGE2) levels, and also by reducing cell migration and the concentration of neutrophils, mast cells, and macrophages in the injured tissue. Further, similar results were obtained by Prianti Jr.[25] studying COX-2 mRNA expression in both subplantar and total brain tissues in a model of peripheral inflammation induced by administration of carrageenan. Xavier et al.[26] showed that LED, only in the initial phases of tissue damage, could decrease inflammatory cell influx and mRNA expression of IL-1β, IL-6, tumor necrosis factor-α (TNF-α), and COX-2, consequently reducing pain.

Studies suggest that LED therapy induces analgesia through activation of peripheral opioid receptors and the L-arginine/nitric oxide pathway.[27] Patients undergoing CABG surgery with a longitudinal sternotomy experience moderate to severe pain on the first postoperative day, mainly when moving the chest. The effects of LLLT and LED therapy on the modulation of inflammatory processes can possibly explain the analgesic effect our patients experienced between postoperative days 6 and 8, compared with the control and placebo groups. The irradiated groups described pain as low to intense (VAS 0–3), whereas the control and placebo groups described it as moderate (VAS 4–6) to severe (VAS 7–10).

Similar to the studies on LLLT, studies on LED therapy have suggested similar therapeutic mechanisms to control inflammation and pain. Nadur-Andrade et al.[28] demonstrated an analgesic effect of LED therapy on *Bothrops moojeni* venom-induced hyperalgesia. This snake venom has a characteristic effect of drastic local tissue damage involving hemorrhage, myonecrosis, and a prominent inflammatory and hyperalgesic response. Leal Jr. et al.,[20] in a clinical trial using a 905 nm super-pulsed laser and 875 and 640 nm LEDs, reported that both therapies are effective in decreasing pain and improving the quality of life in patients with knee pain. The present research also provides evidence that supports the use of LED therapy for the treatment of postoperative pain in CABG surgery, as well as contributing to the general knowledge about the endogenous mechanisms behind this effect.

Conclusions

In this study, we investigated the efficiency of a therapy protocol using LLLT and LED therapy, with 6 J/cm^2, for analgesic purposes in hyperglycemic and normoglycemic patients undergoing CABG surgery. With the current therapy parameters, it may be assumed from our data that both coherent (laser) and noncoherent (LED) light, as a phototherapeutic source, are effective in controlling pain, mainly after postoperative day 6. The analgesic mechanism is likely to be related to a decrease in inflammatory cell influx and mRNA expression of IL-1β, IL-6, tumor necrosis factor (TNF)-α, and COX-2. In addition, studies suggest that LED therapy induces analgesia through activation of peripheral opioid receptors and the L-arginine/nitric oxide pathway.

Further study is needed to clarify the influence of different protocols, dose-dependence, mechanisms, and effects on mediators and cell types in inflammatory models and clinical trials. Additional studies must also be performed comparing glycated hemoglobin (HbA1c) levels between the groups to verify the effectiveness of LLLT and LED in the healing process and pain control, once it can be used to reflect average blood glucose levels over 8–12 weeks, providing a useful longer-term gauge of blood glucose control.

Author Disclosure Statement

No competing financial interests exist.

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ORIGINAL ARTICLE

Low-level laser therapy improves pain in postcesarean section: a randomized clinical trial

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Abstract
This study aimed to evaluate the effect of low-level laser therapy (LLLT) on immediate postpartum pain relief during cesarean section. A randomized, parallel controlled trial was carried out. In total, 88 women with immediate postpartum were divided into 4 groups: control group ($n = 22$), placebo group ($n = 22$), experimental group I ($n = 22$, dose of 4 J/cm^2), and experimental group II ($n = 22$, dose of 2 J/cm^2). The pain measured by Numeric Rating Scale (NRS), algometry, and Global Change Perception Scale (GCPS) was assessed at 12, 20–24, and 44–48 h postpartum. Two LLLT sessions were performed at 12 and 24 h postpartum. A significant interaction was observed between time versus group for NRS $F(2.40) = 36.80$, $p < 0.001$ and algometry $F(1.70) = 27.18$, $p < 0.001$. GCPS revealed a significant difference between the groups during second ($p = 0.04$) and third evaluation ($p = 0.04$). The NRS and algometry presented a large effect size for the experimental groups. LLLT is an efficient method to reduce pain and enhance the GCP in postcesarean section. No significant clinical differences were found between the laser doses.

Keywords Low-level laser therapy · Cesarean section · Analgesia · Phototherapy

Introduction

Cesarean section has immensely increased in the industrialized and developing countries, such as Brazil, which presents the highest cesarean section rates worldwide, with 80–90% of births in private hospitals and 40% in the public health system [1, 2]. Women who undergo cesarean delivery prefer avoidance of pain during and after surgery; therefore, effective postoperative analgesia is crucial [3]. Severe postoperative pain is associated with persistent pain, rater opioid use, delayed functional recovery, and postpartum depression [4]. Moreover, acute postoperative pain has proven to be one of the most consistent and strongest predictors of chronic postsurgical pain after undergoing various surgical procedures including hernia repair [5], limb amputation [6], and coronary artery bypass [7]. Present evidence indicates a relatively low incidence of pain chronification after cesarean delivery, ranging between 1 and 18% [8, 9].

Women experiencing severe acute postpartum pain had a 2.5-fold increased risk of insistent pain and 3-fold augmented risk of postpartum depression compared with women with mild acute childbirth pain [10]. The pain after cesarean delivery can disrupt normal mother–infant physical contact and the care provided to the mother [11]. This situation may affect breast-feeding performance during the puerperium, thus impacting the mother's feed and care ability [12, 13].

It is essential to identify the patients at risk for high acute postpartum pain and address the need for more careful pain treatment after childbirth [13]. Multimodal analgesia includes scheduled nonsteroidal anti-inflammatory drugs and acetaminophen opioids to be administered for severe pain [14]. Studies suggest that nonpharmacological resources for optimizing postpartum pain management include hypnosis, transcutaneous electrical nerve stimulation, and low-level laser therapy (LLLT) [14–17].

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LLLT refers to a noninvasive, phototherapy, or photobiomodulation method that uses photons at a nonthermal irradiance in order to stimulate the biological activity and has been classified as a safe, noninvasive treatment modality [18]. It is used to treat numerous conditions that require healing stimulation, pain/inflammation relief, and function restoration [19]. Several mechanisms have been proposed for LLLT, including increased endogenous opioid neurotransmitter production, thermal pain improvement, increased adenosine triphosphate production, increased production of anti-inflammatory cytokines, and local neoangiogenesis [20–23]. One such LLLT mechanism includes photon absorption by cytochrome c oxidase in the mitochondrial respiratory chain that catalyzes oxygen reduction for energy metabolism, thereby leading to higher oxygen consumption and metabolic energy production via mitochondrial oxidative phosphorylation [24]. LLLT alters the cellular redox state, which further activates numerous intracellular signaling pathways and alters the affinity of transcription factors concerned with cell proliferation, survival, tissue repair, and regeneration [25–27]. These biological effects may prove efficient in various clinical settings including the treatment of acute and chronic pain [18].

LLLT could be an effective, economic, and deployable therapy to enhance functionality in postpartum patients, thus aiming to reduce pain and promote faster cesarean scar regeneration. Therefore, for the effective administration of LLLT, the optimal dosage should efficiently reach an enough volume of regenerative target tissue. Further studies are warranted to optimize its therapeutic value to determine if the effects of photobiomodulation can be made more reliable and extensive in treating postpartum pain.

Considering these assumptions, this study aimed to evaluate the effect of LLLT on immediate postpartum pain during cesarean section. We hypothesized that LLLT can significantly reduce the pain in postpartum women.

Methods

This is a randomized, double blind, controlled, and parallel clinical trial that followed the CONSORT's recommendations [28]. All women were informed about the study procedures, and that they could be randomized into any of the study groups and their participation would be voluntary as per resolution No. 466/12 of the National Health Council. This study was approved by the local institutional ethics committee from Federal University of Rio Grande do Norte (number: 1.998.386). The study was registered in the REBEC platform (Identifier: RBR-6B8HCC). All the participants signed the informed consent term, accepting to participate in the study. Data were collected from March 2017 to June 2018.

In total, 88 women in the immediate postpartum stage of cesarean section were included in this study. The participants were recruited by spontaneous demand in accommodation of Divino Amor Maternity located in the county of Parnamirim, state of Rio Grande do Norte and regarded as suitable to participate in this study, if they fulfilled the following criteria: (1) women over 18 years and absence of clinical or obstetric intercurrences (hypertension or diabetes) and (2) mean pain score of at least 3 on the Numeric Rating Scale (NRS). Exclusion criteria were (1) women with ineffective communication during the postpartum period, (2) hospital discharge before the end of intervention, and (3) those who presented intercurrences (as hemorrhage, postcesarean wound dehiscence, or sepsis).

Portable low-intensity gallium-aluminum-arsenide (GaAlAs) laser device, Laserpulse IBRAMED®, was used during the interventions. The laser was previously evaluated by an independent researcher to confirm its power emittance. LLLT was performed in two sessions: at 12 and 20–24 h postpartum. The interventions were carried out via two different protocols: in the experimental group I, an LLT dose of 4 J/cm^2 and 0.24 J/point in 8 s was used. In the experimental II group, the LLLT dose of 2 J/cm^2 and 0.12 J/point in 4 s was used. Spot diameter was 0.06310 cm^2 and irradiance was 0.47 W/cm^2. In the placebo group, LLLT was performed in presence of electricity, but without energy emission of energy. Furthermore, as the device produces insufficient heat, the patients will be unable to understand whether active or placebo PBMT was administered. Besides that, patient and researcher used the same protection glasses. Details of LLLT parameters are described in Table 1. This protocol was preferred due to its feasibility and was be previously established for wound healing in other surgical scars including healing after episiotomy and to relieve pain after fracture surgery [16, 35].

An expert physiotherapist performed the technique. The application form was punctual, non-contact, and with spot laser positioned perpendicular to the skin in the line of the cesarean incision. The number of points applied depended on the surgical wound extension, considering the distance of 1 cm between the application points (Fig. 1). The laser source tip was cleaned between the sessions of irradiation with 70% alcohol and was wrapped with a flexible plastic material (polyvinyl chloride). The physiotherapist and the patient used specific glasses for further protection in the placebo, experimental I, and experimental II groups. The positioning of the patient was in neutral supine position. For the placebo laser, all sites were treated with the lasers in turn-off mode with the same duration.

The study presented three phases: first phase (I): 12 h after cesarean: includes gynecological and obstetric history and primary and secondary outcomes (first evaluation); second phase (II): interventions were performed in 2 consecutive days; third phase (III): two evaluations were performed between 20 and 24 h postpartum (second evaluation) and 44–48 h postpartum (third evaluation). The overview of all procedures is presented in Fig. 2.

Table 1 Parameters of the LLLT used in the study

Groups	Parameters	Values
	Laser active	GaAlAs
	Mode	Continuous
	Wavelength	660 nm
	Power	30 mW
Experimental I	Dose	4 J/cm^2
	Energy/point	0.24 J
	Energy/session	2.4 J
	Total energy	4.8
	Irradiation time/point	8 s
	Number of points	10
	Area	1 cm^2
	Laser active	GaAlAs
	Mode	Continuous
	Wavelength	660 nm
	Power	30 mW
Experimental II	Dose	2 J/cm^2
	Energy/point	0.12 J
	Energy/session	1.2 J
	Total energy	2.4
	Irradiation time/point	4 s
	Number of points	10
	Area	1 cm^2

J Joules, *J/cm*^{2} Joules per centimeter square

Pain was defined as the primary outcome evaluated by numeric rating scale (NRS) and algometry. The NRS is a segmented numeric version of the visual analog scale, in which the respondents select a whole number (0–10 integers) that best reflects the intensity of their pain. The pain NRS is a single 11-point numeric scale with 0 representing one pain extreme (e.g., "no pain") and 10 representing the other pain extreme (e.g., "pain as bad as you can imagine") [30].

The digital algometry (Force Gage model Wagner FDM®) was used to assess the pain threshold. The equipment had a rubber disk of a 1 cm^2 connected to a pressure gage (values in kgf/cm^2). The rubber disk was coated with PVC plastic wrap and was sanitized with 70% alcohol. The volunteer was encouraged to stop the process when the pressure with the tip of the equipment evoked pain. The threshold record was measured at the time of the "stop" report. Three measurements of algometry were recorded at the extremities and midpoint of the operative wound. For calculating the algometry, the average of the 3 points was considered [31].

Fig. 1 Laser therapy target points with a distance of 1 cm between them. The number of points was determined based on the cesarean incision size

The secondary outcome was measured using the Global Change Perception Scale (GCPS). The evaluation occurred at 20–24 h and 44–48 h postpartum. The scale is a one-dimensional measure in which the individuals can classify the improvement of pain symptomatology by associating the intervention to seven factors, distributed as follows: 1 = no changes, 2 = almost the same, 3 = slightly better, 4 = with certain improvements, 5 = moderately better, 6 = better, 7 = considerably better. This instrument is validated in the Portuguese version and is easy and quick to apply. It is often used in individuals undergoing interventions to determine the clinically important minimal differences during pain assessment, physical function, and quality of life [32].

The sample calculation was performed according to the Miot [33] formula based on the stage of pain in the region of the surgical incision (as a reference the visual analog scale of the pain graded from 0 to 10 and presented a reduction of 3 points in the graded pain score). The alpha error was 0.05 and test power was 80%. The sample size calculation indicated that 72 participants were necessary. We decided to add 16 additional patients to account for attrition. Thus, 88 patients were recruited and randomized into 4 groups of 20 patients.

Randomization was performed through by using the software originated by the site www.randomization.com in a 1:1:1:1 sequence by an independent researcher who was not involved with either stimulation or assessments. All volunteers were randomized and divided into four groups: control group (no LLLT, n = 22), experimental I (n = 22), experimental II (n = 22), and placebo group (equipment turned on without irradiation emission, n = 22) (see Fig. 3). Both participants and evaluator researcher involved in the assessments were blinded to the group allocation throughout the trial. Moreover, all participants were blinded to the intervention group, with no information of the applied dose.

Data were analyzed using SPSS software 20.0 (Statistical Package for the Social Sciences) for Windows, and in all statistical analyses, p values < 0.05 were considered as statistically significant. We performed Shapiro–Wilk test and Levene for normality of the data distribution and equality of variances. Descriptive statistics were presented using the measures of central tendency. Mauchly's test of sphericity was used to validate the correlation of the repeated measures, and if the assumption of sphericity was violated, the Greenhouse–Geisser correction was applied. A two-way repeated measures ANOVA was used to compare the effects of LLLT between groups over time on a primary outcome. The independent fixed variables were time (1st, 2nd, and 3rd evaluations), stimulation groups (control, placebo, experimental I, and experimental II), and the interaction term. When appropriate, post hoc comparisons were carried out using Tukey's post hoc correction for multiple comparisons. The one-way ANOVA

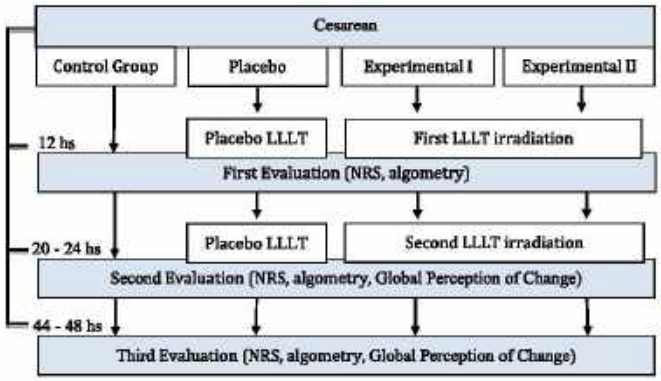

Fig. 2 Stages of data collection and groups of intervention. Low-level laser therapy. NRS: numeric rating scale

was used to assess the pain outcome at each assessment and the overall perception of change (secondary outcome) in the reassessments along with the Tukey's post hoc test to identify the difference between groups. The minimum clinically significant difference was demonstrated by calculating the effect size with Cohen's *d* formula. For the missing data, intention to treat analysis was used.

Results

A total of 1320 individuals were screened for eligibility and 1232 were excluded as they did not meet the inclusion criteria. In this study, 88 patients were divided into 4 groups and 11 volunteers abandoned the study. The reasons for exclusion included discontinued intervention due to bleeding, painless, withdrawal, and difficult communication. No significant differences were observed in the sociodemographic and clinical variables in the baseline values between groups (Table 2). LLLT did not reveal any side effects during the study.

A significant interaction between time versus group was found for NRS $F(2,140) = 36.80$, $p < 0.001$ and algometry $F(1,70) = 27.18$, $p < 0.001$ (Table 3). A significant difference was observed between groups in the third evaluation of NRS ($p = 0.03$) and algometry ($p = 0.04$). GCP was evaluated at 20–24 h (first evaluation) and 44–48 h (second evaluation) postpartum and revealed a significant difference between groups in the first ($p = 0.04$)

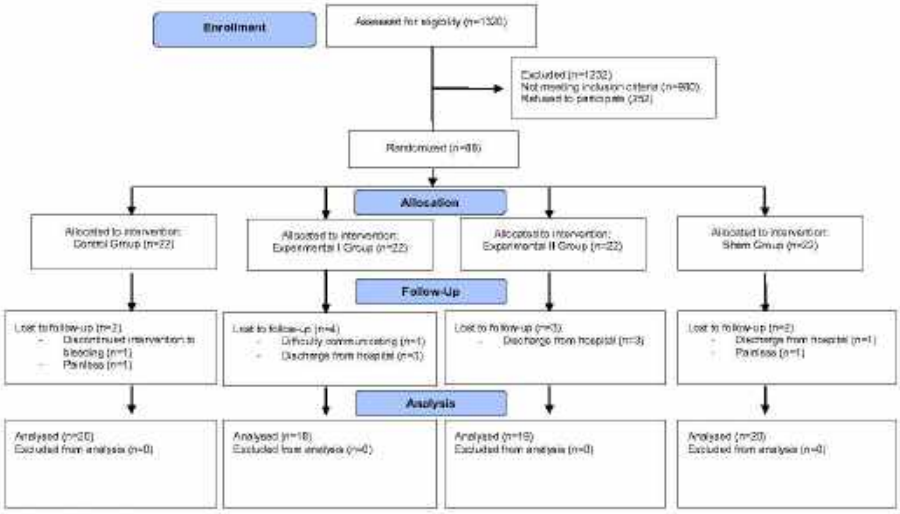

Fig. 3 Flowchart of the study

Table 2 Comparison of baseline characteristics between groups

Variables	Control ($n = 20$)	Placebo ($n = 20$)	Experimental I ($n = 18$)	Experimental II ($n = 19$)	p value
Numeric rating scale	5.75 ± 1.44	3.90 ± 2.40	5.24 ± 2.42	5.47 ± 2.00	0.06
Pain threshold (kgf/cm^2)	0.77 ± 0.47	0.72 ± 0.54	0.58 ± 0.30	0.67 ± 0.33	0.08
Number of pregnancies	1.63 ± 0.83	2.08 ± 1.28	2.10 ± 1.11	1.79 ± 0.82	0.17
Gestational age (week)	39.00 ± 1.44	39.17 ± 1.47	38.80 ± 2.04	38.47 ± 2.31	0.21
Age groups (years)					0.42
18–28	25% ($n = 5$)	40% ($n = 8$)	33.33% ($n = 6$)	31.58% ($n = 6$)	
29–39	65% ($n = 13$)	40% ($n = 8$)	38.89% ($n = 7$)	47.37% ($n = 9$)	
30–39	10% ($n = 2$)	20% ($n = 4$)	27.78% ($n = 5$)	21.05% ($n = 4$)	
Marital status					0.65
With partner	90% ($n = 18$)	95% ($n = 19$)	100% ($n = 18$)	94.74% ($n = 18$)	
Without partner	10% ($n = 2$)	5% ($n = 1$)	0% ($n = 0$)	5.26% ($n = 1$)	
Educational level (%)					0.77
Illiterate	0% ($n = 0$)	0% ($n = 0$)	0% ($n = 0$)	0% ($n = 0$)	
4 years of study	0% ($n = 0$)	0% ($n = 0$)	5.55% ($n = 1$)	10.52% ($n = 1$)	
8 years of study	10% ($n = 2$)	10% ($n = 2$)	11.12% ($n = 2$)	10.52% ($n = 1$)	
11 years of study	90% ($n = 18$)	90% ($n = 16$)	77.78% ($n = 14$)	78.96% ($n = 15$)	
More 11 years of study	0% ($n = 0$)	10% ($n = 2$)	5.55% ($n = 1$)	0% ($n = 0$)	

Experimental group I (LLLT with dose of 4 J/cm^2). Experimental group II (LLLT with dose of 2 J/cm^2)

and second ($p = 0.02$) evaluation (Table 3). Pain intensity indicated a significant difference at 44–48 h between groups in the third evaluation ($p = 0.04$; Fig. 4).

The effect sizes for NRS in placebo and control groups were 0.11 and 0.43, respectively. Experimental I presented an effect size of 0.71, and for experimental II, it was 0.69. Algometry revealed an effect size of 0.26 and 0.27 for the placebo and control groups, respectively. The experimental I and experimental group II presented large effect sizes of 0.91 and 0.88 for algometry, respectively.

Tenoxican, scopolamine butylbromide, dipyrone, and simethicone were administered. In the placebo group, 5% patients ($n = 1$) were administered tenoxicam and scopolamine butylbromide and 25% ($n = 5$) were given simethicone. In the control group, 5% ($n = 1$) were administered tenoxicam and dipyrone and 10% ($n = 2$) were given scopolamine

Table 3 Comparison of means and standard deviation in pain and clinical perception between groups

	Evaluation	Control ($n = 20$)	Placebo ($n = 20$)	Experimental I ($n = 18$)	Experimental II ($n = 19$)	p value
Numerical rating scale	12 h	5.47 ± 2.00 (4.44–6.50)	3.90 ± 2.40 (2.77–5.02)	5.23 ± 2.41 (3.99–6.47)	5.75 ± 2.00 (5.07–6.42)	0.12
	20–24 h	6.05 ± 2.07 (4.99–7.13)	4.75 ± 1.55 (4.02–5.48)	4.17 ± 1.74 (3.28–5.07)	4.10 ± 1.86 (3.22–4.97)	0.23
	44–48 h	3.94 ± 1.91^{b} (2.74–4.55)	3.65 ± 1.92^{a} (2.74–4.55)	1.88 ± 2.08^{a,b} (0.81–2.95)	2.70 ± 1.38 (2.05–3.34)	0.03*
Pressure pain threshold (kgf/cm^2)	12 h	0.61 ± 0.19 (0.54–0.88)	0.72 ± 0.54 (0.47–0.98)	0.57 ± 0.31 (0.41–0.73)	0.66 ± 0.33 (0.50–0.84)	0.07
	20–24 h	0.61 ± 0.74 (0.46–0.77)	0.61 ± 0.36 (0.44–0.78)	0.90 ± 0.48 (0.65–1.15)	0.89 ± 0.40 (0.68–1.10)	0.07
	44–48 h	0.76 ± 0.14^{b,d} (0.46–1.07)	0.84 ± 0.22^{a,c} (0.74–0.95)	1.49 ± 1.11^{a,b} (1.01–1.82)	1.45 ± 0.75^{c,d} (1.03–1.80)	0.04*
Global change perception	20–24 h	2.60 ± 1.28^{a,b} (1.87–3.01)	3.95 ± 1.93 (2.93–5.01)	5.11 ± 1.31^{a} (4.75–6.37)	5.52 ± 1.21^{b} (4.44–6.54)	0.04*
	44–48 h	1.40 ± 1.60^{b,c} (1.15–3.16)	3.70 ± 2.22^{a,d} (2.89–4.96)	6.18 ± 0.90^{a,b} (5.99–6.91)	6.00 ± 0.69^{c,d} (5.32–6.68)	0.02*

*Significant, $p < 0.05$—ANOVA one-way and Tukey's post hoc. Data is presented in means, standard deviation, and 95% confidence interval. The same letters indicate significant difference between the groups

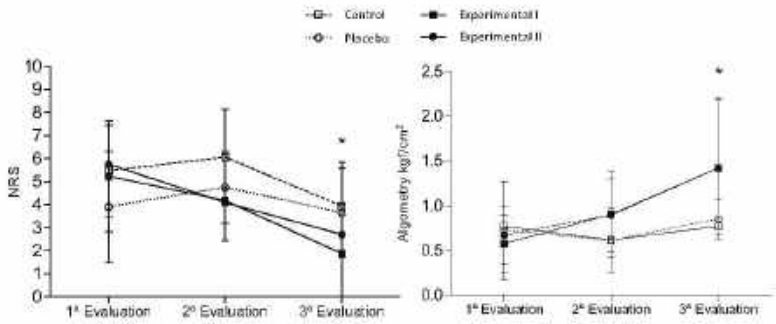

Fig. 4 Pain intensity after 12 h (1st evaluation), 20–24 h (2nd evaluation), and 44–48 h (3rd evaluation) post cesarean. Numeric rating scale (NRS). *Significant difference between groups

butylbromide. In experimental I and II, 10.53% were administered simethicone ($n = 2$) and 5.55% were given dipyrone ($n = 1$).

Discussion

The primary objective of this study was to evaluate the effect of continuous GaAlAs laser with wavelength of 660 nm on immediate postpartum pain in cesarean incision. The secondary aim was to assess the GCP after the intervention. The results revealed that LLLT improved pain and GCP after cesarean incision. No significant difference was observed between the dosimetry of 2 J and 4 J.

LLLT is clinically a well-accepted tool in rehabilitation and has been used to restore functionality in various clinical conditions, thus aiming to improve pain, enhance wound healing, and promote tissue regeneration with more quality [18, 34]. Studies suggest LLLT for tissue regeneration in postoperative surgery, periodontal treatment, pain and inflammation control [35–37]. Pain relief promoted by LLLT is related to reduced E2 prostaglandin, which prevents the onset of pain by stimulating compounds and also controls inflammation process [34]. Analgesia is caused by the release of endogenous endorphins and hyperpolarization of nerve endings, which inhibit the transmission of painful stimuli to the central nervous system. Additionally, the biological effects produced due to the energy absorption by the tissues allow the light of the photons to interact with the cellular structure [25]. An increase in cellular energy is observed, which alters the permeability of the cell membrane, causes reduction in the interstitial fluid, wound healing, muscle relaxation, modulation of the immune system, and nerve regeneration [25]. Only one clinical trial was reported in literature regarding the use of LLLT in pain after elective cesarean section [29].

Poursalehan et al. (2018) [29] studied 80 patients after an elective cesarean with an objective to investigate the effect of low power laser on acute pain. The authors used two different wavelengths (GaAlAs: 804 nm and GaAlInP: 650 nm) applied in the surgery room postsurgery and before the bandage. The incisions were treated by the red laser (1 J/cm^2 for 10 s) and IR laser (2 J/cm^2 for 10 s). Thereby, only one LLLT session was performed and pain was measured at 1, 4, 8, 12, 16, and 24 h after the end of cesarean section. The authors found that the pain significantly reduced at 1, 4, 8, 12, 16, and 24 h after surgery [29].

Another study evaluates the LLLT (5 J/cm^2) on pain and perineal healing after episiotomy [16]. Fifty-four postpartum women who had a spontaneous birth with a right mediolateral episiotomy were subjected to three sessions of irradiation. No significant difference was observed between the groups regarding perineal healing and pain scores after LLLT [16]. Similar results from a previous study indicated that after LLLT irradiation, no difference was seen between the scores of episiotomy healing and perineal pain up to 2 h, 20–24 h, and 15–20 days after normal birth [16, 37]. These results indicate that the anatomical area and the type of surgery could influence pain and healing.

Reduction of pain should have interfered positively in improving the health status among the treatment of episiotomies [38]. Our study showed similar effects. LLLT has a positive acceptance by patients for promoting physical improvement and emotional well-being after surgical procedures [38].

In this study, it is clear that pain not showed significant difference between groups in baseline, but p value is close to 0.05. Therefore, one proof that this does not interfere is the significant intragroup and post-experiment intergroup effect and also by the effect measure (Cohen's d) that reveals clinical impact effects between interventions. This study had certain limitations, wherein, the population losses occurred throughout the study, despite all the exclusions had being considered to intention to treat analysis; moreover, the reduced period for pain assessment, which was limited to the discharge from hospital. The thermal measurement was not quantified or calibrated in this study, and future investigations should consider this for more accurate LLLT effects [39]. The LLLT can easily be routinely applied in postpartum patients with an aim to reduce pain and to help restore functionality.

Conclusion

This study suggests that LLLT was effective in relieving surgical wound pain after cesarean section. Laser therapy seems to be a good nonpharmacological resource for pain improvement after cesarean section; however, different protocols and long-lasting effects need to be investigated in future trials.

Authors' contributions AMPHA: conceptualization, planning, data collection, and writing of the manuscript. KRRS: data collection and planning. EMSF: writing of the manuscript, supporting data analysis, and proofreading. RP: conceptualization, planning, data analysis, and writing of the manuscript. MTABCM: conceptualization, planning, data analysis, and writing of the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interests The authors declare that they have no conflict of interests.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (include name of committee + reference number) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the local institutional ethics committee from Federal University of Rio Grande do Norte (number: 1.998.386). The study was registered in the REBEC platform (Identifier: RBR-6B8HCC).

Informed consent Informed consent was obtained from all individual participants included in the study.

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Effect of preoperative ibuprofen in controlling postendodontic pain with and without low-level laser therapy in single visit endodontics: A randomized clinical study

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Abstract

Aim: The aim of this study is to evaluate the effect of low-level laser irradiation and ibuprofen in reducing the onset and severity of postoperative pain following single visit endodontics. **Materials and Methods:** One hundred and twenty patients were recruited for this study. Group A (*n* = 30) patients were administered 400 mg of ibuprofen orally 1 h before the institution of an endodontic procedure. Group B (*n* = 30) patients were given irradiation of a low-level laser at 50 Hz for 3 min after the standard endodontic procedure at the periapical region on both buccal and lingual aspect. Group C (*n* = 30) patients were given preoperative ibuprofen followed with a low-level laser at 50 Hz for 3 min after endodontic treatment. Group D (*n* = 30) patients were administered no preoperative ibuprofen nor low-level laser irradiation after the endodontic procedure. The patient immediately recorded his/her pain perception on the Heft Parker pain survey after completion of the appointment and at 4, 8, 12, 24, and 48 h postoperatively. Inter group analysis was carried out using the analysis of variances with "least significant difference" *post hoc* test. For intra group analysis, Students *t*-test was used. Chi-square test was applied for nonparametric data. **Results:** Pain was significantly reduced in all the treatment groups postoperatively. Ibuprofen showed significant pain reduction at 4 h and 8 h period. The combination of low-level laser and ibuprofen showed the best results in terms of postoperative pain reduction. **Conclusion:** This study proved that low-level laser therapy can be an effective alternative for conventional use of nonsteroidal anti-inflammatory drugs in controlling postendodontic pain thereby eliminating the adverse effects of such drugs on the patients.

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Full Text

Introduction

Single-visit root canal offers several advantages, including a reduced flare-up rate, decreased number of operative procedures, and no risk of inter-appointment leakage through temporary restoration.[1] The major concern regarding single appointment endodontics has been a postoperative pain. Recently, Mulhem *et al*.[2] and DiRenzo *et al*.[3] in their studies and in a study conducted by Wang *et al*.[4] on 100 vital teeth, found no statically significant difference between pain levels of single and multiple visit groups. Certain factors influence the progression of postoperative pain:[5],[6] which includes the history of preoperative pain and the need for re-treatment. Microorganisms are usually regarded as the most common cause of postoperative pain, other causes include mechanical or chemical injury to pulpal or peri-radicular tissues.[7] Many clinical studies have reported varying degrees of postendodontic pain, ranging from 25% to 40%.[8],[9] Postoperative endodontic pain is linked to inflammatory mediators prostaglandins, leukotrienes, bradykinin, and serotonin that activate sensitive nociceptors, leading to both peripheral and central mechanisms of hyperalgesia. Prostaglandins play a critical role in the pathogenesis of pulpal and periradicular disease.[10] Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed analgesics for preventing postoperative pain.[11] The most commonly investigated is ibuprofen it is safe, widely prescribed, inexpensive and has effective analgesic and anti-inflammatory action for postoperative pain.[12]

Rapid developments in laser technology and a better understanding of bio interactions of different laser systems have broadened the clinical use of laser in contemporary endodontics. A low-level laser also called a soft or a cold laser has no thermal effect on tissues and produce a reaction in cells through light, called photobiostimulation or photochemical reaction. These lasers have an average output power range between 5 and 500 mW. Low-level laser therapy (LLLT) is well established in clinical dentistry because of its anti-inflammatory, regenerative, and tooth etching effects.[13],[14] LLLT has also shown nonthermal, and bio-stimulatory effects as the energy output of the device are low enough not to exceed an irradiated tissue temperature of 36.5°C.[15] LLLT is considered as an adjunct to alleviate postdental procedure pains [16],[17] and no study has compared the effect of preoperative ibuprofen with the combination of LLLT in reducing postendodontic pain.

Therefore this study randomized out to evaluate the effect of preoperative analgesics and LLLT for postendodontic pain reduction.

Materials and Methods

Subjects and patients

The study involved one hundred and twenty patients who required conventional root canal therapy.

The patients were selected according to the following criteria.[18]

Inclusion criteria

Permanent teeth with fully formed apex, teeth with vital pulp, teeth with no periapical radiolucency, patients having preoperative pain.

Exclusion criteria

Teeth with incompletely formed apex, teeth requiring secondary endodontic treatment, patients having complicating systemic disease such as diabetes, malignancy, pregnancy, central nervous system disorders, Cardiovascular system (CVS) disorders, respiratory disorders, asthma patients, psychiatric disorders, immunocompromised patients, patients taking anti-inflammatory or antibiotics, patients giving history of analgesic or antibiotic intake 1 week before treatment, patients below 18 years of age, patients above 65 years of age, patients having history of peptic ulcer or gastrointestinal bleeding, teeth having calcified canals, teeth having multiple canals or multirooted teeth, teeth affected with periodontal disease. Teeth tender on percussion, teeth having procedural errors such as transportation, perforation, missed canals.

A thorough history was recorded from the patients. Informed consent was obtained, and a clinical examination was administered. The examination included cold pulp testing, heat testing, electric testing, percussion and palpation evaluation, periodontal probing, mobility assessment, and a periapical radiograph. All past and present symptoms of the involved tooth were recorded. A pulpal diagnosis was determined from the data collected in the examination and was recorded. Only those patients with a diagnosis of symptomatic irreversible pulpitis were included in the study. Patients were randomly assigned into four treatment groups. Group A (n = 30) patients were administered 400 mg of Ibuprofen orally 1 h before the institution of an endodontic procedure. Group B (n = 30) patients were given irradiation of a low-level laser at 50 Hz for 3 min after the standard endodontic procedure at the periapical region on both buccal and lingual aspect. Group C (n = 30) patients were given preoperative ibuprofen followed with a low-level laser at 50 Hz for 3 min after endodontic treatment. Group D (n = 30) patients were administered neither preoperative ibuprofen nor low-level laser irradiation after endodontic procedure.

Endodontic procedure

Before treatment, the patient filled out his/her initial perception of pain on the pain survey. For ibuprofen group patients took 400 mg ibuprofen (Brufen, Abbot, India Ltd.,) orally 1 h before the procedure. Local anesthetic (1:80,000 Arcaine, Aarge Pvt Ltd., India) was administered, and endodontic access was achieved under rubber dam isolation. Cleaning and shaping of the canal systems were achieved in the following manner; early negotiation and cleaning and shaping was completed with Flex-O-Files (Malleffer Switzerland) #8, #10, #15, #20. An initial working length reading was taken with the apex locator root ZX mini (J Morita Japan) and a confirmatory radiograph was taken. The working length was estimated to be 0.5 mm short of the radiographic apex.

Canals were prepared using engine driven rotary nickel titanium pro taper files (Dentsply Maillefer, Ballaigues Switzerland) following manufacturer's instructions. RC prep (Premier Dental Products Co., Philidelphia, PA, USA) was used as a lubricant. Irrigation was performed with 5.25% sodium hypochlorite after each file change. Apical enlargement was accomplished with using finishing files which ranged from F1 to F5 depending upon the initial diameter of the canal. Canals were filled with protaper universal Gutta percha (Dentsply Maillefer) and AH plus sealer (Dentsply De Trey, Gmbh, Konstanz, Germany) using a lateral compaction technique and restored with composite (Ceram X Duo Dentsply India Ltd.,). All cases were completed in one appointment (access, cleaning/shaping, and obturation). For patients in laser groups, low-level laser irradiation (Quanta Pulse Pro Jsc "Milta-Humanitarian-Information Technologies Design and Production Company" Moscow, Russia) was given at the periapical area [Figure 1]. Laser tip was placed in contact mode perpendicular to the periapical region of the teeth both bucally as well as lingually for 3 min [Figure 2].{Figure 1}{Figure 2}

Patients were then given the Heft and Parker [18] pain rating scale and were instructed to mark the individual pain level at 4, 8, 12, 24, and 48 h after root canal therapy. Patients then recorded postoperative pain using the pain rating scale and returned 48 hours after treatment.

Statistical analysis

Parametric data were analyzed with the help of means and standard deviations. Inter group analysis was carried out using the analysis of variances with "least significant difference" post hoc test. For intra group analysis, Student's t-test was used. Chi-square test was applied for nonparametric data. The value of $P < 0.05$ was considered statistically significant.

Results

Fifty-two female patients and 68 male patients participated in the study [Table 1]. The gender distribution was not significant among the groups ($P = 0.965$). The age of the patients ranged from 18 to 64 years [Table 2]. There was no statistically significant age difference between the four groups ($P = 0.973$). All groups showed significantly less postendodontic pain levels as compared to preoperative pain levels.{Table 1}{Table 2}

Result at 4 h [Table 3] a significant difference was observed between Group A and Group D, Group B and Group C, Group B and Group D, and Group C and Group D. The ibuprofen laser combination showed the least mean pain score of 3.8 and was the most effective in controlling pain at this time interval. This was followed by the ibuprofen group and then by the laser group. The most pain was seen in the control group.{Table 3}

Result at 8 h a significant difference was observed between Group A and Group D, Group B and Group C, Group B and Group D, Group C and Group D. The results were similar to the results at 4 h interval with the laser ibuprofen combination proving to be most effective in controlling pain.

Result at 12 h a significant difference was observed between Group A and Group B, Group A and Group C, Group B and Group D, Group C and Group D. The lowest pain score was given by laser ibuprofen group with a mean pain score of 3.1. It was followed by laser group at 7.4. Ibuprofen showed no significant pain relief as compared to control.

Result at 24 h a significant difference was observed between Group A and Group B, Group A and Group C, Group D and Group B, Group C and Group D. The laser ibuprofen combination was most effective followed by the laser group.

Result at 48 h the results were similar to that observed at the 24 h interval. The laser ibuprofen combination was most effective followed by the laser group. [Table 4] shows the inter group comparison.{Table 4}

Discussion

Results from the present study indicate that pain was significantly reduced in all the treatment groups postoperatively [Figure 3]. Ibuprofen showed significant pain reduction at 4 h and 8 h period as compared to control group. A prophylactic dose of 400 mg was used in this study. These results are consistent with that found by Dionne et al.,[20],[21] and Winter et al.[22] More recently, Arslan et al.,[23] also found that ibuprofen was more effective in reducing postendodontic pain at 6 h period. Prophylactic administration of ibuprofen before RCT can block the Cox pathway and by this application, pain sensation can be blocked. Laser group showed significant pain reduction at 12, 24, and 48 h, posttreatment as compared to ibuprofen group. While it was nonsignificant at 4 and 8 h when compared to ibuprofen group. Furthermore, pain was significantly reduced at all-time intervals when compared to control. A significant difference was also found at 4 and 8 h when compared to laser ibuprofen combination with the combination showing increased pain control.{Figure 3}

Only one study has previously evaluated the effect of low-level laser irradiation on postendodontic pain. Asnaashari et al.,[24] found that low-level laser significantly reduced postendodontic pain at 4, 8, 12, and 48 h. Lizarelli,[25] reported a significant reduction of pain following irradiation of low-level laser pre- and post-implant surgeries. Sakurabe et al.,[26] showed LLLT diminished pain in sensitive pulps using a semiconductor low-level laser unit. Kreisler et al.,[27] demonstrated more pain reduction in laser group than the placebo group in the 1st day after endodontic surgery. In one study, application of low-level red and infrared laser was significantly effective in the treatment of dentin hypersensitivity.[28] Enwemeka et al., [29] in their meta-analysis represented low-level laser was significantly effective in pain control and tissue repair. They concluded that insignificant results of some studies were due to small sample size.

In this study, a number of patients was enough which did not pose such a problem. Roi et al.,[30] reported less pain perception in pediatric patients in laser treatment. In addition, other

researchers showed the same results for LLLT in orthodontic treatment procedures.

The combination of low-level laser and Ibuprofen showed the best results in terms of postoperative pain reduction. The difference was significant at all-time intervals as compared to control while it was significantly better at 12, 24, and 48 h's period as compared to Ibuprofen.

When compared to laser alone the difference was significant at 4 and 8 h. The low-power lasers showed a significant analgesic effect in the present study. The wavelength of laser unit was 905 nm for laser irradiation (power 12–16 mw, 875 nm for broadband infra-red irradiation (power 60 mw) and 640 nm for visible red irradiation (power 7 mw) which conformed to the optimal optical range.

Currently the following analgesic effects are recognized, low-level laser inhibit the release of mediators from injured tissues, decrease concentration of chemical agents such as histamine, acetylcholine, serotonin, H+ and K+, all of which are pain mediators, inhibit concentration of acetylcholine, a pain mediator, through increased acetylcholine esterase activity, cause vasodilatation and increase blood flow to tissues, accelerating excretion of secreted factors, better circulation leads to a decrease in tissue swelling, decrease tissue edema by increasing lymph drainage, remove the pressure on nerve endings, resulting in stimulation decrease, decrease sensitivity of pain receptors as well as transmission of impulses, decrease cell membrane permeability for Na+ and K+ and cause neuronal hyperpolarization, resulting in increased pain threshold, the production of β-endorphin, injured tissue metabolism is increased by electromagnetic energy of laser. This is induced by ATP production and cell membrane repolarization.[31]

Conclusion

This study suggests that LLLT can be an effective alternative for conventional use of NSAIDs in controlling postendodontic pain thereby eliminating the adverse effects of such drugs on the patients. Further research is needed for assessing the required intensity and time intervals of the laser irradiation in treating postendodontic pain.

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Conflicts of interest

There are no conflicts of interest.

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Therapeutic laser for pain relief after tonsillectomy

Analgesia com laser terapêutico após tonsilectomia

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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.

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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 2mm². Each surgical wound was irradiated for 3 minutes and 20 seconds, at an energy density of 4 J/cm²[12,15]. 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[3-6]. 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

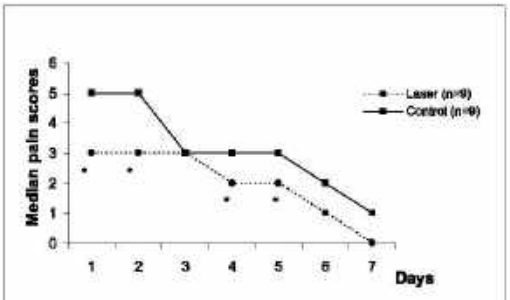

Figure 1 – Median of visual analog scale pain scores in laser and control groups throughout the seven-day follow-up period after tonsillectomy. The number of patients in each group is indicated in parentheses.

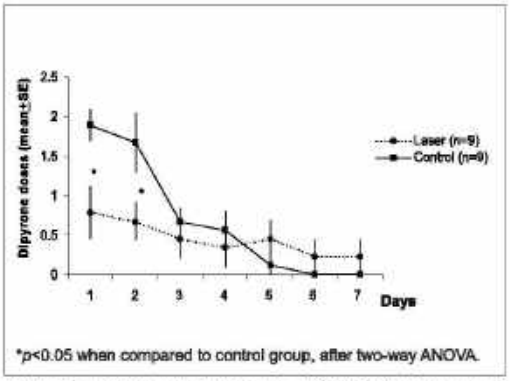

Figure 2 – Mean and standard error (SE) for the number of dipyrone doses used in laser and control groups throughout the seven-day follow-up period after tonsillectomy. The number of patients in each group is indicated in parentheses.

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[9,25,27].

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.

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