

6 ORIGINAL SCIENTIFIC RESEARCH

Low-Level Laser Therapy Effectiveness for Reducing Pain After Breast Augmentation

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1 **Introduction:** The purpose of this Institutional Review Board (IRB)-approved, placebo-controlled, randomized, double-blinded parallel-grouped, multicenter trial was to determine the effectiveness of low-level laser therapy (LLLT) in decreasing patients' postoperative pain 24 hours post breast augmentation surgery.

Materials and Methods: The Erchonia EML, 630–640 nm, (Erchonia Medical, Inc., McKinney, Texas) with 2 7-mw laser-emitting diodes was used within 10 minutes of the start of the procedure over each breast for 4 minutes at a distance of 6 inches. This was repeated within 10 minutes of completion of the procedure with the same methodology. One hundred and four (104) patients participated in the study, 50 test subjects and 54 controls. Primary investigator and patient were blinded with respect to treatment group.

Results: The success criteria for this study using the standardized Visual Analogue Scale (VAS) was a self-reported degree-of-pain rating of less than 30 at 24 hours after the implant procedure. At this time the patient had not taken pain medication for 4 hours. Overall study success criteria were defined as at least 30% difference between treatment groups with respect to proportion of successes. At the 24-hour time interval 37 (74%) of the test subjects and 20 (37%) of the control subjects met the success criteria, a difference of 37% ($p < .0002$). The amount of pain medication used over the first 7 days post operatively was measured as a covariant. The test subjects used less medication 848 versus 932 total doses ($p < .01$).

Conclusion: Low-level laser therapy is effective at significantly decreasing postoperative pain and the amount of pain medication needed after breast augmentation at 1 day and 1 week respectfully. All other covariants studied including, implant type, implant size, incision size, implant

location, test site location, amount of swelling measurements, hydration level, and adverse events were found to be negligible.

Low-level laser therapy (LLLT) stimulates cell activation processes that intensify physiologic activity at the cellular level.¹ It is thought that laser energy facilitates reactions between the cell membrane through the cytoplasm to the cell nucleus in a process called cellular amplification, the demonstration of which earned the 1994 Noble Prize in Physiology.²⁻⁴ It has been revealed in several studies that LLLT possesses the ability to stimulate the respiratory chain located in the mitochondrion; specifically, it is believed that near-infrared light stimulation targets *cytochrome c oxidase*, a terminal enzyme whose role it is to transfer electrons between complex III and IV within the respiratory chain.⁵⁻⁷ It is believed that *cytochrome c oxidase* stimulation accelerates the transfer of electrons and promotes an up-regulation of oxidative phosphorylation, producing more adenosine triphosphate molecules (ATP).^{8,9} This stimulation promotes intracellular signaling as well as extracellular signaling, which it is believed to reduce edema and pain.¹⁰⁻¹²

Many studies have been performed to show the use of LLLT in wound healing, control of inflammation, and pain management.^{4,13} LLLT has received US Federal Drug Administration (FDA) approval for pain therapy (2002), liposuction (2004), and acne treatment (2005). The time to recovery is extremely important in terms of lost time from work for the patient. Decreasing the time to recovery decreases the overall cost of medical care and improves patient satisfaction.

Low-energy lasers stimulate tissue but have no thermal effect in contrast to high energy lasers that vaporizes tissue. The low-level laser emits a visible light at 630–640 nm that easily passes through the

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dermal layers.^{14,15} Low-intensity laser irradiation has been shown to increase the amount of growth factors which in turn cause an increase in cellular matrix production, angiogenesis, and cytokine release.^{16,17} Numerous related studies showed fibroblasts and keratinocytes activation which is critical to wound healing with low-level laser irradiation. The wavelength used is very important to the benefits of LLLT. Cell processes such as DNA replication, proliferation of cell lines, and promotion of microcirculation occur between 630–640 nm. Lyosomal stimulation can start at 670 nm so band width is to be tightly controlled.^{18–20} The purpose of this clinical study was to determine the effectiveness of the LLLT in decreasing the patient's degree of postoperative pain at 24 hours after breast augmentation surgery. The FDA and the Institutional Review Board (IRB) approved the study-design protocol.

Device Description

The Erchonia EML laser (Erchonia Medical, Inc., McKinney, Texas) used in the study is equipped with two 7 mw red (630–640 nm) laser emitting diodes manufactured by Coherent (Coherent Inc., Santa Clara, Calif) and classified as a Class IIIb laser diode by the FDA's Center for Devices and Radiological Health (Silver Spring, MD). It is a hand-held device that uses rechargeable batteries or a separate AC power adapter. For safety and eye injury protection Laser Gard Helium-Neon (He-Ne) spectacles with Spectral Examination Protection Minimum OD of 5X for the 630–640 nm range were used in this study.

Procedure

Each patient was prepared for surgery in accordance with the American Academy of Cosmetic Surgery "Guidelines for Breast Augmentation Surgery." The patients were placed under general anesthesia as per the American Society of Anesthesiologists (ASA) Guidelines. Within 10 minutes of the start of surgery the patient received the preimplant LLLT procedure with the Erchonia EML laser using either device A or B as per randomized group assignment. The laser was administered by a study investigator wearing protective eyewear. Each breast was scanned for 4 minutes across its entire length and width approximately 6 inches above the breast. Breast augmentation was then performed. The LLLT procedure was repeated within 10 minutes of completion of surgery prior to the final dressing placement. Postoperative care after the patient

arose from anesthesia was performed per ASA guidelines. At 24 hours and 1 week postoperatively all patients received the exact same treatment protocol again with the same laser A or B.

Study Population

All qualifying patients came from the general population to each investigator's office seeking breast augmentation. Qualifying patients were neither compensated nor charged for their participation in this study in any way other than the standard fees associated with having elective breast augmentation surgery. One hundred and four (104) patients qualified and were enrolled in this study of which 50 were placed in the test group and 54 in the control group. Sixty three (63) were enrolled at test site #1 and forty one (41) at test site #2. No patient who was evaluated failed to qualify, refused to enroll, or withdrew prior to the completion of the 24-hour postprocedure study success evaluation point.

Inclusion criteria included:

- a patient who signed the informed consent,
- suitability for breast augmentation or need for augmentation to correct a congenital deformity,
- indication for bilateral surgery,
- between 18–55 years old,
- female,
- willing to refrain from consuming over the counter (OTC) or prescription medications for pain or swelling relief 48 hours prior to the procedure,
- agreed to refrain from OTC medications and non-study prescribed medications other than rescue medication for the first week postoperatively.

The exclusion criteria included:

- any patient who was having augmentation related to breast reconstruction or trauma,
- a connective tissue disorder,
- inadequate tissue to cover the implant,
- consumption of any narcotics or steroids,
- inability to consume the prescribed postoperative study medications due to allergy or adverse reaction,
- a developmental disability,
- a cognitive impairment that would impact the ability to understand informed consent,
- pregnancy,
- any significant psychiatric disorder,
- any active infection,
- prior breast surgery,

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- any person involved in litigation or receiving disability, or
- participation in any research study in the last 90 days.

Study Design

The LLLT breast implant study was a placebo-controlled, randomized, double-blinded parallel group two-center design. There was a test and control group in this study where the test group received the test protocol with the laser, and the control group received a sham red light. Both devices, A and B, appear identical to the investigator and no differences can be seen or felt by the study participants since LLLT emits no heat to the patient's skin. Randomization of patients was performed in successive groups of ten. In each group of ten, five patients were randomly selected to the test and control groups. This randomization was repeated as necessary for all study participants. The investigator performed the pre and postoperative measurements and the laser treatment with either device as specified per protocol and the surgery. Results were sent to the test monitor and the IRB.

Study Outcome Measures

The study outcome measures were taken for 4 weeks postoperatively. The study measured VAS Degree of Pain Rating just prior to the procedure, at 24 hrs, 1 week, 2 week, and 4 week intervals. The use of rescue medication (Vicodin ES, Percocet 5/325 Lortab 10/500, Dolacet) was documented for the first 7 days. Breast diameter (vertical and horizontal breast measurement using calipers) and hydration level indicators (presence of pitting edema and measurement of bilateral ankle circumference) were evaluated immediately postoperative, at 24 hours, and at one week. Wounds were examined for signs of infection at 24 hours and 7 days postoperative. A Modified Hollander Cosmesis Scale used to evaluate wound healing at the surgical sites was performed at 7 days postoperative. All nonstudy medications were documented from the time of surgery to day 7. All potential adverse reactions or events were evaluated by the site investigator and immediately reported to the test monitor (Regulatory Insight, Inc., Littleton, CO) from the time of surgery through day 28.

The primary efficacy outcome measure was defined as the difference between test and placebo subjects ratings for overall degree of pain experienced in the

breast area 24 hours after their surgery. Individual success criteria was defined as a self-reported VAS Pain Rating of less than 30 24 hours after the implant procedure at which time the patient had not taken any pain medication for 4 hours. Overall success criteria were defined as at least a 30% difference between treatment groups in the proportion of those patients meeting individual success criteria.

Results

The individual success criteria met by the treatment group was 37 of 50 patients (74%) versus 20 of 54 control group patients (37%) that report a pain level less than 30 on the VAS at 24 hours after the procedure Table 1. The difference was 37% between groups, which exceeded the target of 30% defining study success ($p < .0002$).

The average VAS score postprocedure was 15.3 points lower in the test group vs. the placebo group ($p < .001$) at 24 hours. A series of covariate analyses were performed on a number of variables which could influence the breast augmentation procedure. Using ANOVAs for the two independent samples on the primary outcome measure it was determined that in all variables (incision size, amount of fluid given, and volume of augmentation of the left and right breast) that if the individual differences were removed the adjusted means would still differ significantly ($p < .005$) indicating efficacy of the LLLT.

The degree of pain was measured at all time points (1 day, 7 days, 14 days, 28 days) using the VAS pain ratings. At all points the test group was lower than the placebo group. The difference was only significant at the 24 hour mark via *t*-tests for independent samples (Table 2).

From the immediate postoperative period through the end of the first week the patients were instructed to record the time and dosage of their rescue medication usage (Table 3). All medications were in the same combination narcotic analgesic drug category described

Table 1. Comparison of Test vs Placebo Groups

Comparison	Test Patients	Placebo Patients	All Patients
Total number	50	54	104
Number success criteria	37	20	
Success criteria %	74	37	55
Average VAS score	21.4	36.7	29.3
Standard deviation	20.6	24.6	23.9

Table 2. VAS Pain Rating Over Time Points

Time	Test Group		Placebo Group		p-value
	Number	Average	Number	Average	
24 hours	50	21.40	54	36.78	0.001
7 days	50	9.90	54	13.09	0.245
14 days	50	10.64	54	12.19	0.632
28 days	50	3.32	54	6.70	0.060

Table 3 Rescue Medication Usage by Treatment Group

Comparison	Test (n = 46)	Placebo (n = 46)	All (n = 96)
Total possible doses	1932	1932	3864
Actual doses	848	932	1780
% doses	43.89	48.24	46.07
Average # doses	18.43	20.26	19.33
Standard deviation	10.03	8.89	9.47

previously. All subjects were instructed to not take any medication 4 hours prior to any VAS pain recording. Of the total 104 patients in this study 92 patients (46 in each arm) recorded their rescue medication usage over the first 7 days. There were 42 possible medication dosages over the 7 days. The difference between the treatment groups was significant with respect to total amount of dosages taken of rescue medication ($p < 0.01$) in the first 7 days post procedure.

A one-way ANOVA analysis of variance was performed on 3 time samples (postoperative, 24 hours, 7 days) for the factor of breast diameter swelling in a vertical and horizontal fashion by treatment group. The only significant finding was right breast vertical measurement for the placebo group size increased significantly ($p < 0.05$) between the postoperative period to the 7 days measurement. No difference was seen in pitting edema, infection, or cosmesis for any data points. There was a significant finding for left ankle decreased swelling between 24 hours and the seven days time interval ($p < 0.05$) in the test group. The significance of these two findings out of the numerous measurements performed over multiple time intervals on both treatment groups for breast swelling and ankle circumference is unknown. Two potential adverse events were recorded during the study. There was one each in the test and placebo groups. The test subject stated increased pain in the left breast versus the right but after review by the investigator it was

determined to be within the normal postoperative variance of pain experienced by patients after surgery which resolved with no effect on the end result. The placebo subject reported separation of the wound edges with drainage but upon review by the investigator there was no notable wound complication and the patient was reassured.

Conclusion

The LLLT significantly decreased postoperative pain and the amount of post-operative pain medication rescue dosages used by patients at 1 day and 1 week respectfully in the test group vs the placebo group. None of the other covariants significantly altered these findings including implant size, incision size, test location, hydration level, implant location, swelling indicators, and number of adverse effects. The LLLT was found to be easily and safely administered by the investigators with no adverse reactions noted.

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