THE JOURNAL OF
SEXUAL MEDICINE

ORIGINAL RESEARCH

PAIN

# Low-Level Laser Therapy for the Treatment of Provoked Vestibulodynia—A Randomized, Placebo-Controlled Pilot Trial

Ahinoam Lev-Sagie, MD,[1] Asia Kopitman, PT MA,[2] and Amnon Brzezinski, MD[1]

## ABSTRACT

**Background:** Low-level laser therapy (LLLT) is an emerging medical technology in which non-thermal laser irradiation is applied to treat pain. Because LLLT has been found effective in treating various pain syndromes without known side effects, we conducted a study evaluating the effect of LLLT on provoked vestibulodynia (PVD), a complex sexual pain disorder characterized by pain confined to the vulvar vestibule in response to contact or pressure.

**Aim:** To investigate the effectiveness of LLLT for PVD in a randomized, placebo-controlled, double-blinded trial.

**Methods:** Patients with PVD were randomly assigned to receive treatment with LLLT or sham treatment. Patients were treated twice weekly for 6 weeks, for a total of 12 LLLT or placebo sessions. Patients who showed improvement after LLLT were followed for 1 year by clinical pain report and Q-tip examination.

**Outcomes:** Change in pain scores obtained in response to the Q-tip test, clinical pain report, visual analog scale score, pain with tampon insertion, daily pain intensity, intercourse pain intensity, frequency of intercourse, and a battery of quality-of-life measures.

**Results:** Thirty-four patients with PVD participated, 18 received LLLT and 16 received placebo. In the clinical pain report at study completion, 14 of 18 patients (78%) receiving LLLT reported improvement compared with 7 of 16 (44%) in the placebo group ($P = .042$). This effect was not apparent in other outcome measurements. None of the patients reported side effects during the study. At 1-year follow-up, eight patients (57%) reported lasting improvement.

**Clinical Implications:** Larger studies with various treatment protocols are needed to define which patients can benefit from LLLT therapy.

**Strengths and Limitations:** Strengths include a placebo-controlled, double-blinded design, measurement of a large number of multidimensional end points, and a follow-up period of 1 year. Limitations include the small number of patients recruited, no improvement in measurable parameters, a high improvement rate in the placebo group, the absence of use of validated questionnaires, and the lack of evaluation of psychological and interpersonal factors that might have influenced the results.

**Conclusions:** Given the results of this pilot study, LLLT cannot currently be recommended as a treatment for PVD. Further studies with a larger population, various treatment protocols, and evaluation of LLLT in different subgroups of PVD are needed to define which patients can benefit from this therapy. **Lev-Sagie A, Kopitman A, Brzezinski A. Low-Level Laser Therapy for the Treatment of Provoked Vestibulodynia—A Randomized, Placebo-Controlled Pilot Trial. J Sex Med 2017;14:1403−1411.**



**Key Words:** Vulvar Pain; Provoked Vestibulodynia (PVD); Low-Level Laser Therapy (LLLT); Dyspareunia; Vulvar Vestibulitis

Received March 18, 2017. Accepted September 9, 2017.

[1]Department of Obstetrics and Gynecology, Hadassah Hebrew University Medical Center, Jerusalem, Israel;

[2]Department of Physical Therapy, Hadassah Hebrew University Medical Center, Jerusalem, Israel



http://dx.doi.org/10.1016/j.jsxm.2017.09.004

## INTRODUCTION

Provoked vestibulodynia (PVD) is defined as vulvar pain confined to the vestibule in response to contact or pressure.[1] Most patients with PVD present with dyspareunia and pain in response to non-sexual activities such as tampon insertion, gynecologic examinations, and even during sitting.[2] The diagnosis of PVD is made using the modified Friedrich criteria: a

history of vestibular pain upon touch or attempted penetration, tenderness to pressure localized within the vestibule on examination, and the exclusion of identifiable causes for the pain.[3]

The etiology of PVD remains unknown; proposed causes include chronic inflammation; peripheral neuropathy; genetic, immunologic, and hormonal factors; infectious processes; psychological disorders; sexual dysfunction; relationship factors; or disturbance in the central nervous system. However, given the varied presentation and individualized responses to treatment, the cause of PVD is most likely multifactorial. Because the exact mechanism of PVD remains unknown, many different treatment modalities have been proposed, including topical preparations (topical anesthetics, estrogen, compounded medications, and capsaicin), oral medications (tricyclic antidepressants and anticonvulsants), pelvic floor physical therapy, psychological interventions, and surgery ("vestibulectomy"), among others. There is a wide range of response to the various therapies, with 35% to 79% of women reporting some improvement in pain scores.[4] However, most published studies were case series, lacking a control or placebo group and lacking pretreatment pain and functional status evaluation, most used non-validated outcome measures of pain, and no long-term outcomes were reported.[4]

Regarding long-term results, it was shown that although most patients reported improvement since diagnosis,[5,6] they continued to experience a high level of symptoms[5] and only a small number of women reported that they were cured.[6,7] This long-term course has a profound negative impact on women's sexual, relational functioning, and psychological well-being.

Low-level laser therapy (LLLT) is a medical technology in which non-thermal laser irradiation (low levels of red and near infrared light) is applied to treat pain. It is referred to as "low level" or "cold" because a low-power laser is used in contrast to high-power laser therapy that is used for thermally coagulating tissues.[8] LLLT is non-invasive and painless and can be administered in primary care settings. The incidence of adverse effects is low, with no reports of serious events. Clinical applications that show effectiveness include soft tissue inflammation,[9] neck pain,[10] tendinopathies,[11] rheumatoid arthritis, and osteoarthritis.

The exact mechanisms of action for LLLT-mediated pain relief are not fully understood. Possible explanations include anti-inflammatory effects with a decrease of inflammatory markers (prostaglandin $E_2$, interleukin-1$\beta$, and tumor necrosis factor-$\alpha$),[12] decrease of oxidative stress and skeletal muscle fatigue,[13,14] and inhibition of transmission at the neuromuscular junction, thus having a direct effect on myofascial pain and trigger points.[15] Another proposed theory posits a laser-induced neural blockade[16,17] and selective inhibition of peripheral nerve conduction, shown in A$\delta$ and C fibers, which convey nociceptive stimulation.[18,19] These inhibitory effects could be mediated by disruption to fast axonal flow in neurons[17] or inhibition of neural enzymes.

## AIMS

Because inflammatory mechanisms, peripheral neuropathy, and pelvic floor muscle dysfunction have been proposed in the pathogenesis of PVD, and LLLT is suggested to modify these factors, we studied whether LLLT might be an effective therapy for PVD.

## METHODS

This pilot study was a placebo-controlled, double-blinded, randomized, clinical trial. Patients were recruited from the clinic for vulvovaginal disorders at our institution. The study was conducted from January 2011 through December 2013 and was approved by the institutional review board.

Inclusion criteria included more than 3 months of insertional dyspareunia and/or pain with tampon insertion and confirmation of vestibular tenderness by cotton-swab test, performed at five defined points in the vestibule (1, 5, 6, 7, and 11). In addition, patients verbally reported provoked pain intensity using a numeric rating scale ranging from 0 to 10 at the five points. The score for all points was summed together, and a total rating equal or greater than 10 of 50 was required for participation. Subjects had to be 18 to 50 years old; not pregnant; have no identifiable cause for pain, such as vaginitis, atrophy, dermatitis or dermatosis; and not using antidepressants or antiseizure drugs at recruitment.

After signing the informed consent form, patients underwent a standard evaluation that included a medical history, vulvar and vaginal examination, a pelvic floor musculature assessment, a vaginal culture, vaginal pH measurement, and microscopy. Each participant completed a questionnaire on demographics, general health, symptoms, and sexual functioning.

Instructions concerning the performance and documentation of the daily 24-hour pain diary and intercourse pain log were given at the first visit by the principal investigator.

During the trial, patients were allowed to use acetaminophen or non-steroidal anti-inflammatory drugs as pain "rescue medication" for indications other than dyspareunia. The use of topical anesthetics during intercourse was not allowed and was considered a protocol violation. Patients were required to stop any other PVD treatment 2 months before study initiation. In patients undergoing physical therapy at recruitment, treatment was stopped during the trial.

After completion of the LLLT or placebo treatment, participants were evaluated with a vulvovaginal examination, Q-tip test, and a battery of outcome measurements (see below).

### Treatment With LLLT

Patients were randomly assigned to receive LLLT using the Omega XP diode laser system (Omega Laser Systems, Essex, UK) or placebo treatment. Treatment was performed with a pen-size probe transmitting irradiation applied to the vestibule for 20