Short running title: Low level laser therapy for Provoked Vestibulodynia

Low-level-laser therapy for the treatment of provoked vestibulodynia- A randomized, placebo-controlled pilot trial

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

[1]Department of Obstetrics and Gynaecology, [2]Department of Physical Therapy, Hadassah Hebrew University Medical Center, Jerusalem, Israel

Corresponding Author:
Ahinoam Lev-Sagie, MD
Department of Obstetrics and Gynaecology
Hadassah-Hebrew University Medical Center
Jerusalem, Israel
Email: levsagie@netvision.net.il
Telephone: +972-54-4327178
Fax: +972-8-9762666

Disclosures:
Research funding- Marinoff Vulvodynia Career Development Award, the National Vulvodynia Association (NVA).
Potential conflicts of interest – the authors report no potential conflicts of interest.

Abstract

Provoked Vestibulodynia (PVD) is a complex disorder that is difficult to treat. Low level laser therapy (LLLT) is an emerging medical technology where non-thermal laser irradiation is directly applied to treat pain.

The objective of this randomized, placebo controlled, double-blind trial was to investigate effectiveness of LLLT for PVD. Thirty four patients with PVD participated, 18 received LLLT and 16 received placebo. Treatment duration was twice weekly for 6 weeks.

Clinical response was assessed by multiple outcome measures including patient verbal report, visual analog scale (VAS), Q-tip test, tampon test, variable daily pain measures and sexual function parameters assessed using a daily 24-hour pain diary, quality-of-life questionnaires including the Brief Pain Inventory (BPI) and Neuropathic Pain Scale (NPS). Patients were followed for one year.

Groups were comparable in regards to demographic and clinical characteristics. Seventy eight percent of patients reported moderate to complete improvement following LLLT compared with 44% in the placebo group ($p=0.042$).

We conclude that treatment by LLLT safely and effectively reduced the symptoms of PVD. This effect was only apparent when patient verbal reports where evaluated. Further studies with a larger population and various treatment protocols are warranted.

ClinicalTrials Identifier: NCT01149031

Perspective: This clinical trial supports the benefit of LLLT for patients with PVD. LLLT was effective in reducing the symptoms of PVD in the one year follow up as well. Further testing should be performed on a larger population with more individualized treatment protocols.

Key words: vulvar pain, provoked vestibulodynia (PVD), low level laser therapy (LLLT), dyspareunia, vulvar vestibulitis

Introduction

Provoked vestibulodynia (PVD) syndrome is clinically defined as chronic, unexplained, vulvar pain or discomfort confined to the vestibule in response to contact or pressure. This pain may be in response to non-sexual activities such as tampon insertion, gynecological examinations, or recreational activities such as bicycle riding [10]. Most patients with PVD present with dyspareunia or a complete inability to have sexual intercourse. Once the syndrome develops, symptoms may last for years resulting in a profound effect on women's sexual and psychological well-being. The diagnosis of PVD is usually made by assessing if the patient meets the modified Friedrich's criteria, consisting of history of severe pain in the vulvar vestibule upon touch or attempted vaginal entry, tenderness to pressure localized within the vestibule when being touched with a cotton-tip applicator, and the exclusion of identifiable causes for the pain [2].

The etiology of PVD remains unknown; proposed causes include chronic inflammation, peripheral neuropathy, genetic, immunologic and hormonal factors, infectious processes, psychological disorders, sexual dysfunction, or disturbance in the central nervous system. However, given the varied presentation and individualized responses to treatment, PVD causation is most likely multifactorial. Because the exact mechanism of PVD remains unknown, many different treatment modalities have been proposed, including topical preparations (topical anaesthetics, estrogen, compounded medications, capsaicin), oral medications (tricyclic antidepressants, selective serotonin reuptake inhibitors and anticonvulsants), nerve blocks, pelvic floor physical therapy, complementary and alternative therapies, and surgery ("vestibulectomy") among others. There is a wide range of response to the various therapies for vulvar pain syndromes, with 35% to 79% of women reporting improvement in pain scores at 6 months. However, there is insufficient evidence to conclude that any of the nonsurgical therapies confer a net benefit for patients with PVD [1].

Low level laser therapy (LLLT) is an emerging medical technology in which non-thermal laser irradiation (low levels of red and near infrared light) is applied directly to treat pain. It is referred to as "low level" since a low power laser is utilized in contrast to other forms of high power laser therapy that are used for ablation, cutting, and thermally coagulating tissue [8]. LLLT uses light energy to modulate cell and tissue physiology to

achieve a therapeutic benefit without a macroscopic thermal effect. Clinical applications that show potential benefit include soft tissue injury, chronic pain, and wound healing. LLLT was found to be effective in treating various pain syndromes and has no known side effects.

Exact mechanisms of action for LLLT-mediated pain relief are not fully understood, however, possible explanations for the clinical benefit include: anti-inflammatory effects of red and infrared laser irradiation with a reduction of specific inflammatory markers (prostaglandin E2, IL 1β and TNF α) [5], the ability to reduce oxidative stress and skeletal muscle fatigue [15,16], and the inhibition of transmission at the neuromuscular junction, thus having a direct effect on myofascial pain and trigger points [17]. Other proposed theory is that pain-relieving effects of LLLT are laser-induced neural blockade [3,7] and selective inhibition of nerve conduction, shown in Aδ and C fibers, which convey nociceptive stimulation [21,22]. These inhibitory effects could be mediated by disruption to fast axonal flow in neurons [7] or inhibition of neural enzymes.

LLLT is non-invasive, painless, and can easily be administered in primary-care settings. Incidence of adverse effects is low and similar to placebo, with no reports of serious events. Clinical applications that show some potential effectiveness include soft-tissue inflammation [4], neck pain [23], tendinopathies [6], rheumatoid arthritis and osteoarthritis.

Since inflammatory mechanisms and peripheral neuropathy have been proposed in the pathogenesis of PVD, we studied whether LLLT might be an effective therapy for PVD.

Methods

The pilot study was a placebo-controlled, double-blind, randomized, clinical trial. Patients were recruited from the oupatient clinic for Vulvovaginal Disorders at Hadassah University Medical Center, Jerusalem. The clinic population is comprised of patients referred primarily for the evaluation of chronic vulvovaginal symptoms, including dyspareunia. The study was conducted between January 2011 and December 2013 and was approved by Hadassah Medical Organization Institutional Review Board.

Non-pregnant women, between 18 and 50 years of age, were eligible to participate if they reported greater than 3 continuous months of insertional (entry way) dyspareunia, pain with tampon insertion, or both. Participants had to complain of tenderness, localized within the vestibule, when being touched with a cotton-tip applicator. After signing the informed consent form, all study candidates completed a self-administered intake questionnaire regarding demographics, general health, vulvovaginal symptoms, and sexual functioning. Patients were also asked to complete the Brief Pain Inventory (BPI) and Neuropathic Pain Scale (NPS). Each patient underwent a standard evaluation that included a detailed history, physical examination, vulvar and vaginal examination, pelvic floor musculature assessment, vaginal pH measurement, saline and 10% potassium hydroxide microscopy, and a yeast culture.

Vestibular tenderness was evaluated with the Q-tip test, performed on five defined points in the vestibule (1,5,6,7, and 11), with patients verbally reporting pain via a numeric rating scale of intensity, ranging from 0 to 10 at each point. The localization of the pain was confirmed by all remaining test points in the lower vagina, labia majora, and labia minora to be non painful. Additionally, no identifiable cause for pain, such as vulvovaginal candidiasis, vaginal atrophy, desquamative inflammatory vaginitis (DIV), herpes, dermatitis or vulvar dermatosis were found.

Study candidates who opted not to participate or who did not meet inclusion criteria were referred for appropriate clinical care.

Treatment with LLLT

Patients were randomly assigned to receive either treatment with LLLT using the Omega XP diode laser system (Omega laser systems, Essex, UK) or placebo. Subjects in the

LLLT group were treated with a pen-size probe, transmitting irradiation applied to the vestibule for 20 seconds at each point. The irradiation parameters chosen for the treatment were: wavelength - 820 nm, energy density of 32j/cm2, pulsed light (alternating 73 / 146 / 700 Hz). The placebo treatment was conducted in an identical manner as the LLLT treatment, using a placebo probe which could not emit irradiation, identical to the LLLT probe.

The treatment protocol chosen for the study was based on accepted protocols for musculoskeletal and neuropathic pain syndromes, using clinical experience regarding tissue penetration and response to various protocols (Recommended treatment doses for LLLT (revised 4/2010), WALT (world assoc. of laser therapy) [8,12,13].

Each painful location was treated by application of the probe, thus the number of treatment points was individualized, defined according to each woman's physical exam. For example, a patient with vestibular pain located between 4 to 8, had 5 treatment points (4,5,6,7,8), and so forth. Patients were treated twice weekly by the same certified pelvic floor physical therapist (AK), for 6 weeks, for a total of 12 LLLT/placebo sessions.

Outcome measurements

Clinical response to LLLT/placebo treatment was assessed by several outcome measures including a patient verbal report and change in the following parameters: visual analog scale (VAS) score, Q-tip test, tampon insertion pain (tampon test), daily pain intensity, intercourse pain intensity, frequency of intercourse and in a battery quality-of-life measures described below.

Verbal report - in the final study visit, after completion of the treatment, patients were asked to rate the change in their condition using percentage scaling: no or little improvement (<30%), moderate improvement (30-60%) and much improvement (>60%).

Visual analog scale (VAS) - a non numerical 13.5 centimeter rating scale measuring vulvar discomfort with the anchors "no discomfort at all" and "severe discomfort". The scale was then recalibrated from 0 to 100, with the worst pain being scored as 100. Patients were asked to separately rate the severity of discomfort in daily activities and sexual activity over the past week. Rating was performed at the baseline visit, weekly

during the trial, and at the follow-up appointment. The VAS score is presented as the absolute change from baseline (week 0), to the end of the trial (week 7).

Q tip test - every patient underwent a Q-tip test to estimate the intensity of pain, performed by the PI (ALS) at baseline and final visit. The exam was performed by touching the vestibule with a cotton-tip applicator in 5 defined points (1,5,6,7 and 11), while asking the patient to verbally rate the intensity of pain from 0 to 10 at each point. The reported pain in all 5 points was summed together for comparison before and after treatment. Patients were also assessed with the Q-tip test at 3 months, 6 months and 12 months post completion of treatment.

Tampon test [9] was used as an efficiency outcome measure. Patients were provided with original, regular Tampax Tampons, and were instructed to insert the tampon, using the applicator without lubrication, fully into the vagina above the level of the hymeneal ring, remove the applicator from the vagina, and immediately remove the tampon from the vagina by traction on the tampon string. Patients rated the degree of pain during the entire insertion-removal experience, on a 0-10 pain numeric scale (0 corresponding to no pain, and 10 corresponding to the worst possible pain). The Tampon-test was performed at baseline, weekly during the study period, and at the final visit. The participants recorded the level of pain in a logbook. The Tampon test is displayed as the change of mean tampon-test pain of weeks 6 and 7 from the mean of weeks 0 and 1, labelled as baseline.

A daily 24-hour pain measure and intercourse pain- patients were requested to report daily whether they experienced vesibular pain (on a 0-10 pain numeric scale); whether they attempted sexual intercourse-with possible responses: 1-“no, too painful”, 2-“no, not interested”, 3-“no, no opportunity” and 4-“Yes”. If intercourse was attempted, the patient was asked to rate her level of pain during sexual intercourse on a 0-10 pain numeric scale. The data presented for daily vulvar pain is the change of mean pain score at weeks 6 and 7 from the mean pain score at weeks 0 and 1, labelled as baseline. The frequency of sexual intercourse is presented as the change of total times per week at weeks 6 and 7 from the total times per week at weeks 0 and 1. The level of pain during intercourse is presented as the change of mean pain at weeks 6 and 7 from the mean pain at weeks 0 and 1.

Questionnaires- patients were asked to complete a questionnaire evaluating extent to which PVD interfered with social activities, frequency of sexual intercourse, sexual desire, difficulty in becoming lubricated, frequency of discomfort or pain during sex, overall level of discomfort or pain with intercourse and satisfaction with overall sexual life between initial to final visit using a 5-point numerical rating scale. Patients were also asked to report side effects of the treatment. Data is presented as the change from baseline (week 0), to the end of the trial (week 7) and was assessed in the final appointment.

Instructions concerning the performance and documentation of the weekly tampon test, the daily 24-hour pain diary, and intercourse pain log were given to each participant on the first visit by the PI.

During the initial and final study visits, participants were evaluated with a physical examination, a Q-tip test, and a battery of health-related quality-of-life measures. All components of the examination were routinely performed by the same examiner (ALS) in identical fashion.

Long term follow-up

All the patients in the placebo group were offered LLLT after the completion of the study. Patients who did not improve following LLLT were offered other treatments. Patients that improved following LLLT (both those that were in the LLLT arm and those in the placebo arm, who received the LLLT following the placebo) were followed for one year by verbal report and Q-tip examination.

Statistical Analysis

In order to compare quantitative variables between the two study groups, a two-sample t-test was applied. The association between two qualitative variables was tested using either the Chi-square or the Fisher's exact tests. The paired t-test was used for assessing the significance of change within each of the study groups. The repeated measures ANOVA model was used in order to simultaneously test the time effect, treatment effect, and the interaction between them. All tests applied were two-tailed, and a p-value of 0.05 or less was considered statistically significant.

Results

Thirty four patients completed the study, 18 received LLLT and 16 received placebo. Participants ranged from 19 to 46 years of age (mean, LLLT 27.4/ placebo 25.4) and the duration of pain prior to enrolment in the study ranged from 5 months to 20 years (mean, 7.1/5.2 years). All but one woman reported being heterosexual, and most of the participants were married or partnered (83%/69%). The chief complaint was pain with intercourse (100%/100%), however, patients also complained of discharge (22%/6.3%), itch (44%/44%) and burning (50%/56%). When asked what preceded the onset of dyspareunia, the most common response was "it began after intercourse" (50%/56%). The second most common response was "do not know" (17%/44%), followed by "yeast infection" (17%/0%) and use of hormonal contraception (17%/0%). The two groups were comparable in relation to age, duration of pain, parity, contraception method, symptoms and type of PVD (primary or secondary) (Table 1).

When questioned regarding previous treatments, patients reported receiving zero to ten different regimens (Table 2). The most common treatment was estrogen cream (73%), followed by pelvic floor physical therapy (70%), topical anaesthetics (62%), anti-fungals (62%) topical steroids (38%), topical antibiotics (32%), probiotics (26%), acupuncture (9%), low oxalate diet (9%), amitriptyline 2%-baclofen 2% cream (9%) and vestibulectomy (6%).

On verbal report at study completion, in the treatment group 10 women reported "significant improvement" (>60%), 2 reported "moderate improvement" (30-60%), 2 reported "complete improvement" (total, 14/18, 78%), and 4 patients reported "no improvement" (<30%). In the placebo group, 5 patients reported "significant improvement", 2 patients reported "moderate improvement" (7/16, 44%), and 9 patients (56%) reported "no improvement" (p=0.042) (Table 3).

In contrast to the patient verbal report, measurable parameters did not show a difference between the LLLT and the placebo. Comparison of the Q tip test (22% pain reduction for LLLT and 24% pain reduction for the placebo, p=0.954), intercourse pain on the VAS (28% pain reduction for LLLT and 26% pain reduction for the placebo, p=0.467) and tampon test (36% pain reduction for LLLT and 22% pain reduction for the placebo, p=0.395) before and after the study found similar reduction of pain in both groups. There

was no significant influence on frequency of intercourse in both groups (reduction of frequency by 4% in the LLLT group compared to 7% reduction in the placebo group, p=0.871).

Severity of discomfort in daily activities (everyday VAS) was reduced by 35% in the placebo group as compared to 11% reduction in the LLLT group (p=0.386), while daily pain intensity was similarly reduced in both groups (27% in the LLLT group, 24% in the placebo group, p=0.912).

The extent to which PVD interfered with social activities, frequency of sexual intercourse, libido, lubrication, and sexual satisfaction (data not shown) did not differ before and after the study in both groups.

Among the 14 patients in the LLLT group who reported an improvement, the long term follow-up (1 year after completion of the study) revealed that 8 patients (57%) reported a consistent improvement after one year. The "complete improvement" that was reported by two women at the end of the study was maintained at the one year follow up. Four patients who reported "significant improvement" remained satisfied with the results while the remaining 6 (33%) reported recurrence of vestibular pain and requested additional treatment. Two women who reported "moderate improvement" following LLLT, eventually underwent a vestibulectomy.

All of the patients in the placebo group were offered LLLT after study completion. Nine out of 16 (56%) declined the LLLT; of those who received it, 5 (71%) reported improvement which persisted for one year (4 reported "significant" or "complete improvement" while 1 reported "moderate improvement"). One patient had improvement immediately after the treatment but reported recurrence of symptoms after several months and one patient had no improvement.

None of the patients reported side effects during the study.

Discussion

Vulvodynia, including the PVD subtype, is reported by up to 16% of women in the general population [2]. Its pathogenesis is not clearly understood, and, therefore, treatment is generally predicated on a trial and error basis. Thus, many different forms of treatment modalities have been used, with variable response rates, while results of clinical trials and research studies remain largely inconclusive. There is also evidence suggesting that the symptoms of PVD fluctuate considerably over time, further blurring interpretation of success or failure of available treatment options.

Despite the limited number of participants, our study stands out from most previously published PVD clinical trials as we utilized a placebo-controlled, double blind design, measured a large number of multidimensional end points, and included a year follow-up period.

According to patients' verbal report, LLLT effectively reduced the symptoms of PVD in the majority of the treatment group as compared to the placebo group (78% vs 44%). This difference was statistically significant. However, this effect was not apparent when measurable parameters (Q tip test, sexual pain VAS, and tampon test) where evaluated. This difference is not understood. Furthermore, 57% of the patients who reported improvement following LLLT experienced a consistent reduction in symptomatology during the year follow up, as most of them did not seek further treatment, thus supporting an actual improvement. Of note, patients' report did not show improvement in the parameters of sexual function (frequency of sexual intercourse, libido, lubrication, and satisfaction from sexual life). It has been reported that although a proportion of patients report improvement in pain scores, there is no increase in sexual activity [19]. Reed et al. [18] found that women with vulvodynia have different attitudes about sexually related issues when compared with controls, including lower levels of sexual interest, more negative feelings about themselves as sexual people, equal level of sexual satisfaction despite the fact that their sexual experiences are considered of inferior quality, and decreased frequency as compared with controls. These characteristics may explain why patients do not report improvement in sexual function despite reduction in sexual pain. From a therapeutic point of view, the hypothesis that sexual functional problems will be improved as the result of pain reduction is not obvious. We believe that improvement in

pain scales does not necessarily correspond to improved quality of life, and therefore, the psychological issues and sexual dysfunction must be assessed and treated in combination with pain treatment.

The initial verbal report improvement rate of 78% with LLLT is comparable to the median improvement effect of vestibulectomy surgery reported in PVD trials [1]. In addition, 57% of the patients reported consistent improvement after one year, while 33% reported recurrence of vestibular pain.

The LLLT/placebo treatment regimen chosen for the study was based on accepted protocols for musculoskeletal and neuropathic pain syndromes, using clinical experience regarding tissue penetration and response. Data regarding LLLT is largely empirical, its physiological mechanisms are not well-understood and tend to be very broad [14]. One hypothesis is that LLLT increases the nociceptive threshold, specifically an inhibition of A and C nerve-fibres, by alteration of the axonal flow [7] or by inhibition of neural enzymes [20]. In clinical practice, a large number of parameters such as the wavelength, fluence, power density, pulse structure, and timing of the applied light must be chosen for each treatment [8]. Reduced response or ineffective treatment may be the result of an inappropriate light source and dosage. Commonly, parameters are altered according to the patient's response, thus allowing a more individualized treatment for every patient. Due to the placebo-blinded design of the study, we instituted a universal treatment protocol where the same parameters were used for all treatments on all participants. It is possible that a flexible protocol, with changing technical parameters, may allow for an improved response rate. In addition, it is common to re-treat patients with attenuation of the LLLT response; repeated treatment usually includes fewer interventions than in the primary program, and may be required as needed. In fact, after completion of the study, some patients who reported recurrence of vestibular provoked pain opted to repeat LLLT treatment with a marked improvement.

Another possible explanation for the partial response rate is due to the premise that PVD is a group of distinct disorders that have been classified together because they produce the same clinical syndrome [11]. It is possible that differences in response represent different etiologic factors or diverse pain mechanisms; LLLT might only alleviate one subset of patients, thus resulting in a partial lack of effect, secondary to dilution of the

patient subpopulation. When the exact etiology of PVD is identified or better classified, perhaps there can be better allocation of patients to specific treatment modalities, including LLLT, thereby increasing the response rate.

In summary, treatment with LLLT safely and effectively reduced the symptoms of PVD. Given an initial response rate of 78%, comparable to the improvement effect of vestibulectomy surgery, its long-term effect, low cost, and good safety profile, we recommend using LLLT prior to other treatment modalities. Further studies with a larger population and varied treatment protocols are warranted.

Acknowledgment: The Low Level Laser was provided by OMEDIC, Raanana, ISRAEL

References

[1] Andrews JC. Vulvodynia interventions-Systemic Review and Evidence Grading. 2011;66:299–315.

[2] Bachmann GA, Rosen R, Pinn VW, Utian WH, Ayers C, Basson R, Binik YM, Brown C, Foster DC, Gibbons JM, Goldstein I, Graziottin A, Haefner HK, Harlow BL, Spadt SK, Leiblum SR, Masheb RM, Reed BD, Sobel JD, Veasley C, Wesselmann U, Witkin SS. Vulvodynia: a state-of-the-art consensus on definitions, diagnosis and management. The Journal of reproductive medicine.2006, Vol. 51. pp. 447–456.

[3] Baxter GD, Walsh DM, Allen JM, Lowe AS, Bell AJ. Effects of low intensity infrared laser irradiation upon conduction in the human median nerve in vivo. Exp. Physiol. 1994;79:227–34. Available: http://www.ncbi.nlm.nih.gov/pubmed/8003306. Accessed 26 Oct 2013.

[4] Bjordal JM, Johnson MI, Iversen V, Aimbire F, Lopes-Martins RAB. Low-level laser therapy in acute pain: a systematic review of possible mechanisms of action and clinical effects in randomized placebo-controlled trials. Photomed. Laser Surg. 2006;24:158–68. doi:10.1089/pho.2006.24.158.

[5] Bjordal JM, Lopes-Martins RAB, Iversen V V. A randomised, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E2 concentrations. Br. J. Sports Med. 2006;40:76–80; discussion 76–80. doi:10.1136/bjsm.2005.020842.

[6] Childress MA, Beutler A. Management of chronic tendon injuries. Am. Fam. Physician 2013;87:486–90. Available: http://www.ncbi.nlm.nih.gov/pubmed/23547590. Accessed 26 Oct 2013.

[7] Chow RT, David MA, Armati PJ. 830 nm laser irradiation induces varicosity formation, reduces mitochondrial membrane potential and blocks fast axonal flow in small and medium diameter rat dorsal root ganglion neurons: implications for the analgesic effects of 830 nm laser. J. Peripher. Nerv. Syst. 2007;12:28–39. doi:10.1111/j.1529-8027.2007.00114.x.

[8] Chung H, Dai T, Sharma SK, Huang Y-Y, Carroll JD, Hamblin MR. The Nuts and Bolts of Low-level Laser (Light) Therapy. Ann. Biomed. Eng. 2012;40:516–533.

[9] Foster DC, Kotok MB, Huang L-S, Watts A, Oakes D, Howard FM, Stodgell CJ, Dworkin RH. The tampon test for vulvodynia treatment outcomes research: reliability, construct validity, and responsiveness. Obstet. Gynecol. 2009;113:825–32. doi:10.1097/AOG.0b013e31819bda7c.

[10] Friedrich EG. Vulvar vestibulitis syndrome. J. Reprod. Med. 1987;32:110–4. Available: http://www.ncbi.nlm.nih.gov/pubmed/3560069. Accessed 20 Sep 2013.

[11] Gunter J. Vulvodynia: new thoughts on a devastating condition. Obstet. Gynecol. Surv. 2007;62:812–9. doi:10.1097/01.ogx.0000290350.14036.d6.

[12] Hamblin MR, Demidova TN. Mechanisms of Low level light therapy. Proc. SPIE 6140.2006, Vol. 6140. pp. 614001–614001–12. doi:10.1117/12.646294.

[13] Hashmi JT, Huang Y-Y, Sharma SK, Kurup DB, De Taboada L, Carroll JD, Hamblin MR. Effect of pulsing in low-level light therapy. Lasers Surg. Med. 2010;42:450–466.

[14] Kingsley JD, Demchak T, Mathis R. Low-level laser therapy as a treatment for chronic pain. Front. Physiol. 2014;5:306. doi:10.3389/fphys.2014.00306.

[15] Leal Junior ECP, Lopes-Martins RAB, Baroni BM, De Marchi T, Taufer D, Manfro DS, Rech M, Danna V, Grosselli D, Generosi RA, Marcos RL, Ramos L, Bjordal JM. Effect of 830 nm low-level laser therapy applied before high-intensity exercises on skeletal muscle recovery in athletes. Lasers Med. Sci. 2009;24:857–63. doi:10.1007/s10103-008-0633-4.

[16] Lopes-Martins RAB, Marcos RL, Leonardo PS, Prianti AC, Muscará MN, Aimbire F, Frigo L, Iversen V V, Bjordal JM. Effect of low-level laser (Ga-Al-As 655 nm) on skeletal muscle fatigue induced by electrical stimulation in rats. J. Appl. Physiol. 2006;101:283–8. doi:10.1152/japplphysiol.01318.2005.

[17] Nicolau RA, Martinez MS, Rigau J, Tomàs J. Neurotransmitter release changes induced by low power 830 nm diode laser irradiation on the neuromuscular junctions of the mouse. Lasers Surg. Med. 2004;35:236–41. doi:10.1002/lsm.20087.

[18] Reed BD, Advincula AP, Fonde KR, Gorenflo DW, Haefner HK. Sexual activities and attitudes of women with vulvar dysesthesia. Obstet. Gynecol. 2003;102:325–31. Available: http://www.ncbi.nlm.nih.gov/pubmed/12907108. Accessed 26 Jul 2014.

[19] Sadownik L a. Clinical profile of vulvodynia patients. A prospective study of 300 patients. J. Reprod. Med. 2000;45:679–84. Available: http://www.ncbi.nlm.nih.gov/pubmed/10986689.

[20] T KCIKOKMMO. Effects of 830nm Gallium Aluminium Garsenide diode laser radiation on rat saphenous nerve sodium-potassium-adenosine triphosphatase activity: a possible pain attenuation mechanism examined. Laser Ther 1989;1:63–67.

[21] Tsuchiya K, Kawatani M, Takeshige C, Matsumoto I. Laser irradiation abates neuronal responses to nociceptive stimulation of rat-paw skin. Brain Res. Bull. 1994;34:369–74. Available: http://www.ncbi.nlm.nih.gov/pubmed/8082027. Accessed 26 Oct 2013.

[22] Tsuchiya K, Kawatani M, Takeshige C, Sato T, Matsumoto I. Diode laser irradiation selectively diminishes slow component of axonal volleys to dorsal roots from the saphenous nerve in the rat. Neurosci. Lett. 1993;161:65–8. Available: http://www.ncbi.nlm.nih.gov/pubmed/8255549. Accessed 26 Oct 2013.

[23] Verhagen AP, Schellingerhout JM. Low-level laser therapy for neck pain. Lancet 2010;375:721; author reply 722. doi:10.1016/S0140-6736(10)60296-6.

Table 1: Patients' characteristics

	LLLT (n=18)	Placebo (n=16)	P value
Age	27.4±5.8	25.4±4.6	0.296
Duration of Pain (months)	86±62.8	62.8± 54.9	0.217
Currently married/partnered	83.3%(15)	69%(11)	0.429
Nullipara	83% (15)	94% (15)	0.604
Symptoms			
Discharge	22%(4)	6.3%(1)	0.34
Itch	44%(8)	44%(7)	0.968
Burning	50%(9)	56%(9)	0.716
Dyspareunia	100%(18)	100%(16)	
Most bothering symptom			
Dyspareunia	100%(18)	87.5 %(14)	
Constant irritation	0	6.3% (1)	
Itch	0	6.3% (1)	
Pain start after			0.125
Intercourse	50% (9)	56% (9)	
Yeast infection	16.6% (3)	0% (0)	
Oral contraception	16.6 % (3)	0%	
Do not know	16.6 %(3)	44%(7)	
Primary PVD	61.1% (11)	68.8%	0.642
Contraception method			.488
Hormonal contraception	39%(7)	56% (9)	
Condoms	33%(6)	19% (3)	
Other	11%(2)	6% (1)	
None	17%(3)	19%(3)	

Table 2: Previous treatments

	LLLT	Placebo	Total of study group
Total of treatments before the study	4.52±2.5	4.56±2.6	P=.971
Anti fungal	9	12	62%
Estrogen cream	14	11	73.5%
Topical antibiotics	7	4	32%
Steroid cream	7	6	38%
Pelvic floor physical therapy	11	11	70%
Topical anesthetises	10	11	62%
Probiotics	7	2	26%
Oral antidepressants	1	2	9%
Vestibulectomy	1	1	6%

Table 3: Study's outcomes

	LLLT before	LLLT after	LLLT group, difference	Placebo before	Placebo after	Placebo group, difference	P value
Verbal report-improvement		14 (78%)			7 (44%)		.042
Q tip	28.50±10	22.18±13.6	6.3±2.8 (22%)	29.06±11.5	22.06±13.4	7±9.1 (24%)	.954
Sex pain-VAS	90.1±8.3	64.7±26.8	25.4±22.7 (28%)	83.5±19	61.5±30	21.9±27.3 (26%)	.467
Tampon Test	4.4±2.7	3.2±2.1	1.16±1.81 (36%)	3.4±2.6	2.6±2.6	0.75±1.02 (22%)	.395
Everyday VAS	9.5±14.97	7.9±19.82	1.12±5.7 (11%)	27.58±32.5	19.3±29.09	8.3±25.17 (35%)	.386
Daily pain intensity	1.39±1.63	1.01±1.51	0.386±0.24 (27%)	2.48±3.53	2.02±3.18	0.6±0.91 (24%)	.912
Intercourse frequency	2.5±2.09	2.39±1.72	0.11±0.43 (-4%)	2.57±2.03	2.39±2.79	0.18±2.13 (-7%)	.871