Efficacy of Non-ablative Laser Therapy for Lichen Sclerosus: A Randomized Controlled Trial

U. Bizjak Ogrinc

Urška Bizjak Ogrinc, MD, MSc;[1] Sabina Senčar, MD;[1] Boštjan Luzar, MD, PhD;[2] Adolf Lukanović, MD, PhD[3]

[1]Gynecology Clinic Juna, Ljubljana, Slovenia

[2]Institute of Pathology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

[3]Department of Gynecology, University Medical Centre Ljubljana, Ljubljana, Slovenia

ABSTRACT

Objective: The aim of this randomized controlled trial was to evaluate the safety and efficacy of neodymium: yttrium aluminum garnet laser treatment of lichen sclerosus (LS) by comparing it with topical corticosteroid treatment.

Methods: A total of 40 female patients with vulvar LS were randomized 1:1 into a study (laser) group and a control (topical corticosteroids) group. The laser group received three laser treatments. Blinded evaluators evaluated biopsies and graded improvement on clinical photographs at baseline and at 3 months. Patients graded the intensity of symptoms on a 0 to 10 visual analogue scale at baseline and 1-, 3-, and 6-month follow-up. Patients also rated the tolerability of laser treatments, and side effects were monitored. (Canadian Task Force classification I)

Results: Laser treatment discomfort was on average 1.5 of 10 on the visual analogue scale. At 1- and 3-month follow-up, patients in the laser group had significantly greater improvement in LS symptoms (burning, itching, pain, and dyspareunia), better patient satisfaction, and greater reduction of sclerosis than patients in the topical corticosteroid group. At 6-month follow-up, the improvement of symptoms in the laser group was still significant. The correct order of photographs (before and after treatment) was assigned significantly more often in the laser-treated patients compared with the control group.

Conclusion: Laser therapy for LS caused minimal patient discomfort during the treatment, with no adverse effects, and demonstrated better efficacy than in the control group, with significant improvement lasting up to 6 months. Laser therapy is a promising option for patients not responding to topical corticosteroid therapy or patients wishing to reduce long-term corticosteroid maintenance use.

Key Words: Vulvar lichen sclerosus, non-ablative laser therapy, histology, symptom assessment, treatment tolerability

Corresponding author: Dr. Urška Bizjak Ogrinc, Gynecology Clinic Juna, Ljubljana, Slovenia. urska.bizjak-ogrinc@juna.si

Competing interests: The authors declare that they have no competing interests. Each author has indicated that they meet the journal's requirements for authorship.

Received on November 14, 2018

Accepted on January 30, 2019

Résumé

Objectif : Cet essai clinique randomisé visait à comparer l'innocuité et l'efficacité du laser néodymium : YAG (grenat d'yttrium et d'aluminium) à celles des corticostéroïdes topiques pour le traitement du lichen scléreux (LS).

Méthodologie : Quarante femmes atteintes de LS vulvaire ont été réparties également dans un groupe expérimental (laser) et un groupe témoin (corticostéroïdes topiques). Le groupe expérimental a reçu trois traitements au laser. Des évaluateurs ignorant le traitement reçu ont examiné des tissus prélevés par biopsie et ont évalué l'amélioration selon des photographies cliniques prises au début de l'étude et après trois mois. Les patientes ont noté l'intensité de leurs symptômes sur une échelle visuelle analogue de 0 à 10 au début de l'étude, puis après un, trois et six mois. Elles ont également noté la tolérabilité des traitements au laser, et les effets secondaires ont été suivis (classification I du Groupe d'étude canadien).

Résultats : La douleur liée au traitement laser était en moyenne de 1,5 sur 10 à l'échelle visuelle analogue. Après un et trois mois, les patientes du groupe expérimental présentaient des résultats significativement supérieurs à celles du groupe témoin pour ce qui est de l'amélioration des symptômes de LS (sensation de brûlure, démangeaison, douleur, dyspareunie), du degré de satisfaction et de la réduction de la sclérose. Au suivi de six mois, l'amélioration des symptômes chez les femmes du groupe laser était toujours significative. L'identification correcte des photos (avant et après) était significativement plus fréquente pour les patientes du groupe expérimental que pour celles du groupe témoin.

Conclusion : Le traitement au laser du LS entraîne une douleur minime, n'est associé à aucun effet indésirable et a une meilleure efficacité que le traitement témoin; il est associé à une amélioration demeurant significative six mois plus tard. Il s'agit donc d'une option prometteuse pour les patientes ne répondant pas à la corticothérapie topique ou souhaitant éviter l'utilisation à long terme de corticostéroïdes.

J Obstet Gynaecol Can 2019;000(000):1–9
https://doi.org/10.1016/j.jogc.2019.01.023

INTRODUCTION

Lichen sclerosus (LS) is a chronic inflammatory skin disease mainly found in the anogenital area, predominantly in older (postmenopausal) women.[1] Risk factors include hormonal changes, trauma, and infections.[1] Twenty to thirty percent of women with LS have autoimmune diseases.[1] Initial whitish patches and nodules usually develop into large, white patches of atrophic skin.[1] Lacerations, ecchymosis, and scarring may develop, which may lead to fusion of labia minora, narrowing of the introitus, and burying of the clitoris.[1] The most common symptoms are itching, pain, and dyspareunia, interfering with sexual function and quality of life.[1,2] Untreated LS is associated with an elevated risk of cancer.[1,2]

The recommended initial treatment of LS is a 3-month application of potent to ultrapotent topical corticosteroids.[1] However, because the treatment is not curative, long-term maintenance treatment is required.[1] Patient noncompliance can considerably reduce treatment effectiveness.[1] Long-term steroid use can cause skin thinning, especially in children.[1] Effective treatment alternatives and/or adjuncts are therefore sought to reduce the need for long-term maintenance and to help in cases that do not respond to corticosteroids.

Non-ablative lasers with wavelengths of 810 to 1210 nm improved skin healing and scar prevention after surgery in randomized clinical trials.[3,4] The controlled elevation of skin temperature induced by laser activates overexpression of heat shock protein 70.[3] These chaperone proteins shorten the inflammatory phase of the wound healing process and hasten scar maturation and tissue regeneration.[3] Furthermore, in recent years, non-ablative lasers have been applied in gynaecology for improvement of symptoms of genitourinary syndrome of menopause and stress urinary incontinence, with the mechanism relying on thermally induced collagen remodelling.[5] The safety and efficacy of such application have been demonstrated in a randomized controlled trial.[6]

Histological examination before and after laser stress urinary incontinence treatment showed signs of neocollagenesis, neoangiogenesis, elastogenesis, reduction of epithelial degeneration and atrophy, and an increase in the fibroblast population in the vaginal wall.[7] LS is characterized histologically by orthohyperkeratosis, epidermal atrophy, basal cell degeneration, a bandlike lymphocytic infiltrate, and a dermal collagen hyalinization zone.[2] Therefore, patients with LS may benefit from irradiation with a non-ablative laser.

The aim of this randomized controlled pilot study was to provide the first assessment of the efficacy and safety of non-ablative neodymium: yttrium aluminum garnet (Nd:YAG) laser treatment of LS in comparison with standard treatment with topical corticosteroids. The Nd:YAG 1064-nm laser wavelength has adequate penetration depth to induce a heat response in the affected dermis. Nd:YAG pulse durations, much longer than the thermal relaxation time of the epidermis, do not cause high initial epidermal temperature peaks[8] and thus avoid causing discomfort or damage to the epidermis of the sensitive vulvar area.

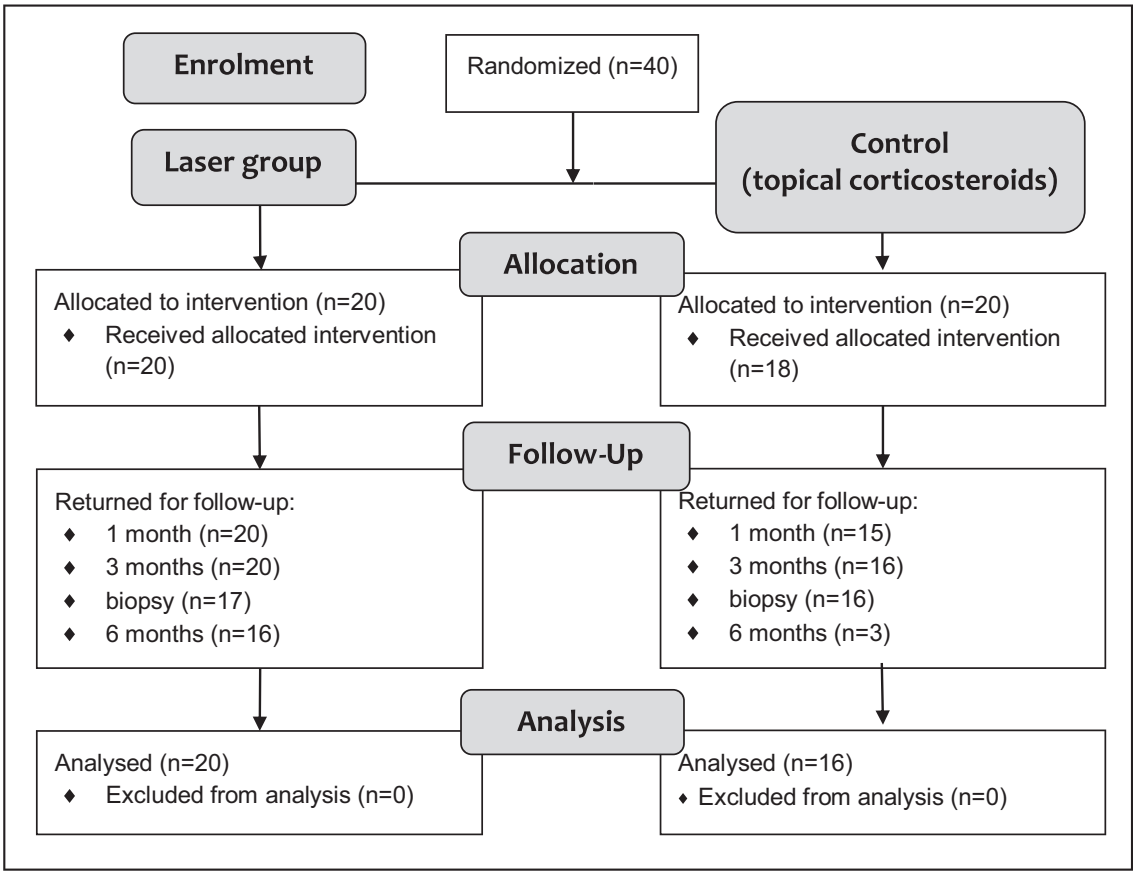
METHODS

The study protocol was approved by the National Medical Ethics Committee of the Republic of Slovenia (No. 121/12/15) and registered at ClinicalTrials.gov (Nd: Yttrium Aluminum Garnet Laser Treatment for Lichen Sclerosis; NCT03525522). From January 2016 to January 2017, female patients presenting with LS at two centres in Slovenia (Division of Gynecology and Obstetrics, University Medical Centre Ljubljana, and Juna Gynaecological Clinic, Ljubljana) were screened for inclusion in the study (Figure 1). Patients aged >18 with a histologically confirmed diagnosis of LS who signed informed consent forms were included in this study. Exclusion criteria were pregnancy, use of photosensitizing medication, presence of pathology (other than lichen) or tissue damage in the treatment area, or other inflammation. Patients were asked to discontinue any hormone contraception, local hormone therapy, or topical therapy used before the study.

Power analysis was based on the primary outcome measure: the sum symptom score at 3-month follow-up. Because no previous study existed to provide effect size data for power analysis, we assumed a large expected effect size of 1 for this pilot study. We calculated that 17 patients per group would be needed to have 80% power to detect such a difference with a test at two-sided $\alpha = 0.05$. Six additional patients were recruited to account for uncertainties in effect size estimation and loss during follow-up.

A total of 40 patients were included in the study and were randomized (1:1) into the laser group or control group by random drawing of sealed envelopes. The personnel

Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram of the progress of patients through the phases of this randomized controlled trial.



conducting outcome measurements were blinded to group allocation. The gynaecologist preforming the treatment and the patients could not be blinded.

The patients in the study (laser) group received three Nd: YAG laser (SP Dynamis, Fotona, Slovenia) treatments every 14 days, using the R33 non-contact handpiece with a 9-mm spot size, Piano pulse mode (5 seconds), and 90 J/cm^2 fluence. These parameters were previously recommended for wound healing and scar prevention.[8] Six passes were performed over the affected whitish or reddened areas and borderline granulations. One week before the first laser treatment, the patients in this group started pre-treatment with topical corticosteroid betamethasone (Diprosone) to alleviate symptoms and increase treatment comfort. This therapy lasted 3 weeks with decreasing dosage: twice daily during the first week, once daily during the second week, and every second day during the third week. After laser treatment, the patients were prescribed betamethasone-gentamicin ointment (Diprogenta) to use twice daily over the treated area for 2 days. They were advised to avoid sexual intercourse and swimming pools for at least 3 days, maintain their usual hygiene, keep the area dry, and use cotton underwear. Follow-up was performed 1 month after the start of therapy and at 3 and 6 months after the last treatment.

The control group received the topical corticosteroid betamethasone (Diprosone) for 4 weeks with decreasing dose: twice daily during the first 2 weeks, once daily during the third week, and every second day during the fourth week. Follow-up was performed after the end of therapy and at 3 and 6 months after the end of treatment.

The effect observed in the laser group is a combination of corticosteroid pre-treatment and laser sessions. Comparison against the control group, in which corticosteroid therapy was used alone, allows the difference in efficacy to be attributed to the effect of laser.

Outcome Assessment

Outcome assessment included the following:

- Patients rated symptoms (burning, itching, and pain) on a 0–10 visual analogue scale (VAS) scale at baseline and every follow-up visit. The improvement in

the sum of scores of all three symptoms at 3-month follow-up was the primary outcome measure.
- Patients reported whether they were sexually active and answered yes or no questions about lack of sensation during intercourse, anorgasmia, and dyspareunia at baseline and during every follow-up visit.
- Patients rated their satisfaction with the results of treatment (0: very unsatisfied; 1: unsatisfied; 2: satisfied; 3: very satisfied).
- Histological evaluation was performed by a blinded assessor at baseline and 3 months after the end of treatment. Formalin-fixed and paraffin-embedded punch biopsies of the vulva were cut into 4-µm thick sections and stained with hematoxylin and eosin.
- Measurement of the thickness of epidermis and sclerosis and assessment of inflammation on a four-point scale (none, mild, moderate, severe) were performed in only one of the two pathology centres used in the study, including seven patients from the laser group and five patients from the control group.
- Evaluation of clinical photographs of the affected area taken at baseline and 3 months after the end of treatment was performed by three independent blinded evaluators unaware of group assignment and unaware which of the pair of photos was taken before and which was after treatment. The evaluators assigned the order and rated the improvement (0: no improvement; 1: poor improvement; 2: partial improvement; 3: complete improvement). If they incorrectly assigned the order of photographs, their score was given a negative value. The interrater reliability was assessed by using a two-way, consistency, average-measures intraclass correlation as implemented in the R statistical software (R Foundation, Vienna, Austria) package "irr".[9] The intraclass correlation coefficient obtained was 0.745 (95% confidence interval [CI] 0.56−0.86; $F_{36,72} = 3.92$; $P < 0.001$) and is considered good to excellent.[10]
- For the laser group only, patients evaluated the tolerability of every laser treatment on a 0 to 10 VAS scale.

Statistical Analysis

Analysis of covariance with baseline value as covariate was used to compare the two groups. The significance of change from baseline was determined by repeated measures *t* test. The McNemar test was used to compare the proportion of women reporting difficulties in their sex life at baseline and each follow-up. The Fisher exact test was used to compare the frequency distributions between the two groups. Stepwise Bonferroni correction was used to account for multiple comparisons throughout the analysis. Uncorrected *P* values are reported, with those that are significant after correction is applied printed in bold.

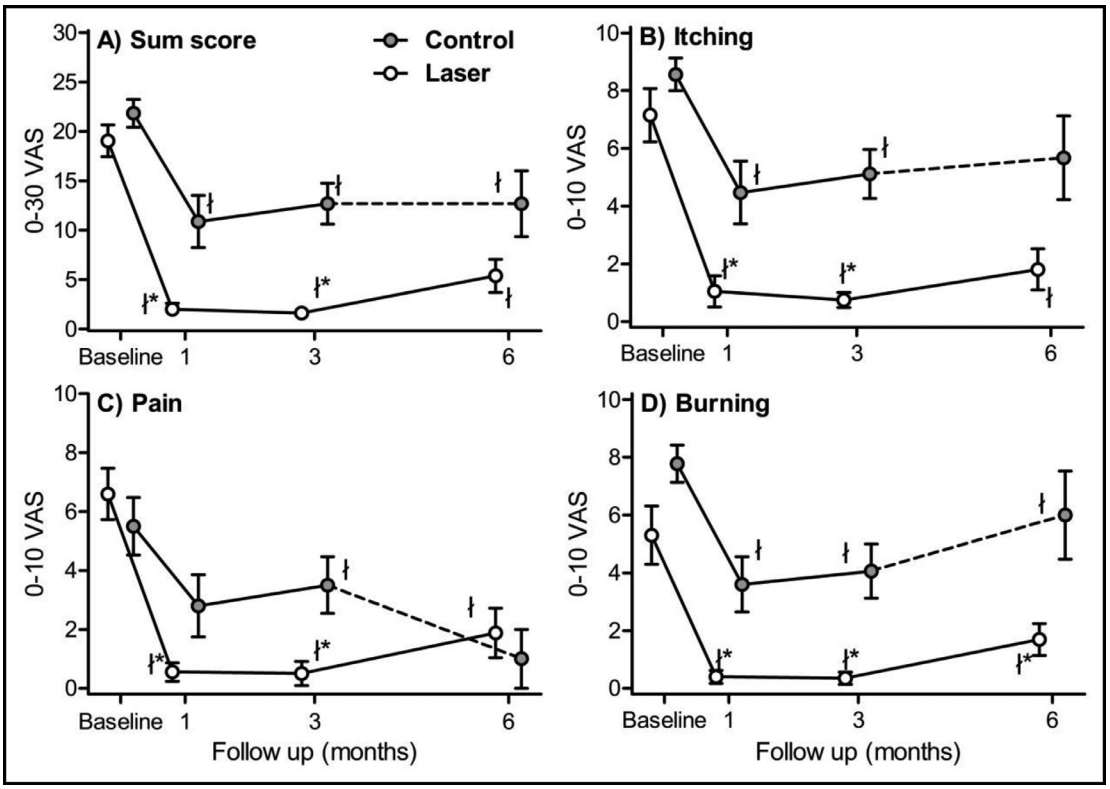
RESULTS

The flow of patients through the trial is presented in Figure 1. Demographic characteristics and baseline values of the outcome measures are shown in Table 1. The mean duration of the laser procedure was 15 to 20 minutes. Patients in the laser group reported minimal treatment discomfort, mostly described as a sensation of warmth. Sixteen of 20, 17 of 20, and 20 of 20 patients reported "no discomfort" at first, second, and third laser treatment, respectively. No adverse effects were observed or reported, and there was no new disease on follow-up local gynaecological examination.

Table 1. Characteristics of laser and topical corticosteroid control groups at baseline

Characteristics	Laser group (n = 20)	Corticosteroid group (n = 18)
Age, mean ± SD	59 ± 10	57 ± 14
Parity, mean ± SD	1.9 ± 0.9	1.9 ± 1.1
Duration of symptoms, n (%)		
<1 year	2 (10)	5 (28)
1–5 years	10 (50)	6 (33)
>5 years	8 (40)	7 (39)
Symptoms, n (%)	20 (100)	18 (100)
Burning	12 (60)	17 (94)
Itching	16 (80)	17 (94)
Tingling	5 (25)	8 (44)
Pain	16 (80)	13 (72)
Sexually active, n (%)	12 (60)	10 (56)
Responded to questions regarding their experience during intercourse, n (%)	16 (80)	14 (78)
Lack of feeling (% of respondents)	10 (63)	5 (36)
Anorgasmia	8 (50)	7 (50)
Dyspareunia	11 (69)	8 (57)
Corticosteroid treatment, n (%)	16 (80)	14 (78)
Hormone replacement therapy, n (%)	10 (50)	13 (72)
Personal history, n (%)		
Autoimmune disease	12 (60)	9 (50)
Malignant disease	1 (5)	1 (6)
Neurological disease	0 (0)	2 (11)
Diabetes	3 (15)	3 (17)
Gynaecological surgery	6 (30)	4 (22)
Infections	5 (25)	6 (33)

Figure 2. Symptom assessment (mean visual analogue scale [VAS] ± standard error) before and after treatment in the control (topical corticosteroid) and laser-treated groups. See Figure 1 for the number of patients in each group at each follow-up. Note that only three patients were left in the control group at 6-month follow-up, and results obtained at this time point should be interpreted with caution. (A) Sum score. (B) Itching. (C) Pain. (D) Burning.



†Statistically significant difference from baseline; *Statistically significant difference between the laser and control groups.

Both laser and corticosteroid treatments reduced the intensity of symptoms (itching, burning, pain) compared with baseline (Figure 2). The reduction was statistically significantly better in the laser group for all symptoms at 1- and 3-month follow-up (Figure 2, Table 2). Too few patients were left in the control group at 6 months (only three) for a valid between-group comparison at this time point. In the laser group, the effect was still significant at 6 months (Figure 2, Table 2). Eight of 20 patients in the laser group were free of symptoms at 3-month follow-up (sum score: 0) compared with none of 16 patients in the control group. Four of 16 patients in the laser group were free of symptoms at 6-month follow-up.

The effect of LS on the quality of the patient's sex life was reduced significantly only in the laser group (Figure 3). The problems recurred at 6-month follow-up.

Patient satisfaction was significantly higher in the laser group than in the control group 3 months after treatment (chi-square = 36.4; $P < 0.001$). All 20 patients in the laser group were "very satisfied," whereas only two of 16 control patients were "very satisfied," five of 16 were "satisfied," five of 16 were "unsatisfied," and four of 16 were "very unsatisfied." At 6 months, 11 of 16 patients in the laser group were still "very satisfied" with the effect of treatment, four of 16 were "satisfied," and one of 16 was "unsatisfied."

At least two of the three blinded evaluators determined the order of photographs correctly in 15 of 20 cases in the laser group and in only four of 11 cases in the control group. The difference was statistically significant (chi-square = 4.47; $P = 0.035$). The mean improvement score was 0.58 ± 1.25 in the laser group and −0.27 ± 1.27 in the control group. The difference between treatments was not significant ($F_{1,29} = 3.28$; $P = 0.80$; effect size 0.856 ± 0.472; 95% CI −0.110 to 1.822).

Biopsy samples taken before and after treatment were analyzed histologically (Figure 4). All patients had LS at baseline. At 3-month follow-up, nine of 17 and six of 16 biopsy samples in the laser and control group, respectively, were negative for lichen. The difference was not significant. The thickness of sclerosis was reduced significantly after laser treatment (−0.67 mm; 95% CI −0.99 to −0.34 mm; $P = 0.009$) but not after corticosteroid treatment (−0.10

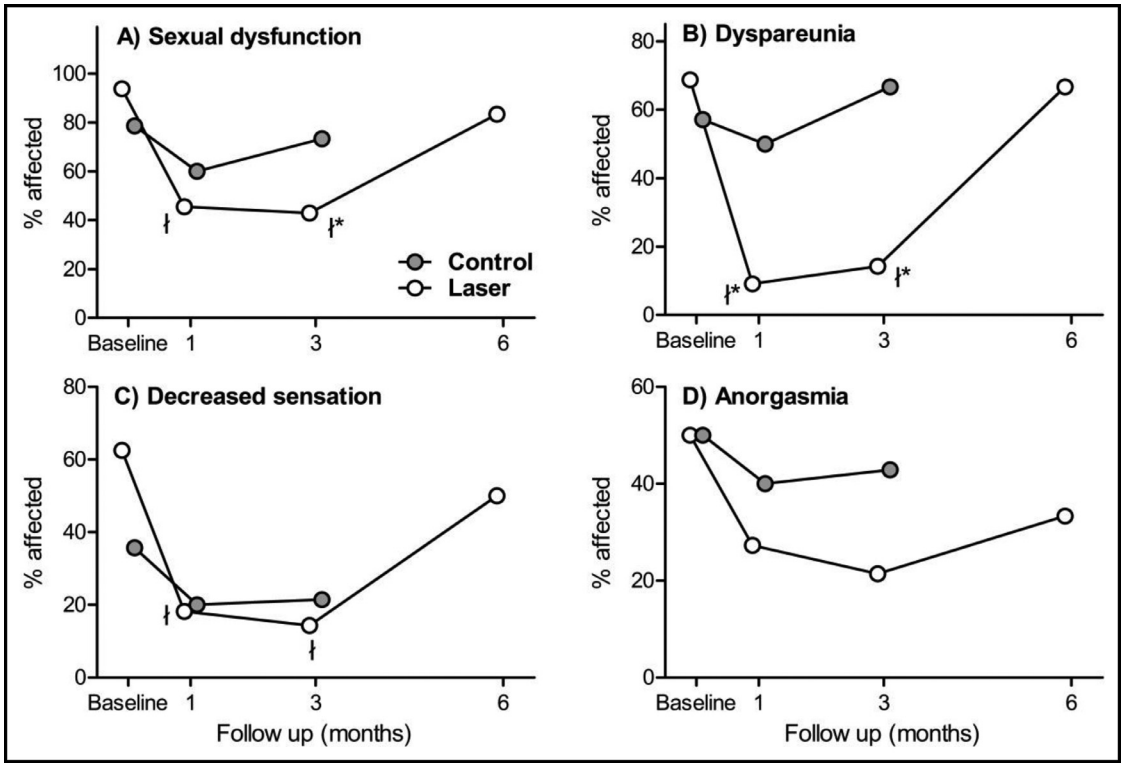
Table 2. Effect size[a]

Symptom	FU (months)	Laser vs. baseline			Control vs. baseline			Laser vs. control		
		df	Change (95% CI)	*P*	df	Change (95% CI)	*P*	df	Effect size (95% CI)	*P*
Burning	1	19	4.9 (2.9–6.9)	**<0.001**	14	3.7 (1.8–5.7)	**0.001**	1,32	2.8 (1.1–4.6)	**0.003**
	3	19	5.0 (3.0–6.9)	**<0.001**	15	3.6 (1.5–5.6)	**0.002**	1,33	3.3 (1.5–5.1)	**0.001**
	6	15	4.4 (2.4–6.5)	**<0.001**	2	1.7 (0.2–3.1)	0.038	1,16	3.9 (1.2–6.6)	**0.008**
Itching	1	19	6.1 (4.2–8.1)	**<0.001**	14	3.8 (1.7–5.9)	**0.002**	1,32	3.1 (0.8–5.3)	**0.009**
	3	19	6.4 (4.6–8.3)	**<0.001**	15	3.4 (1.7–5.0)	**0.001**	1,33	4.1 (2.5–5.7)	**<0.001**
	6	15	4.9 (2.4–7.4)	**0.001**	2	3.0 (−1.3–7.3)	0.095	1,16	3.5 (−0.3–7.3)	0.066
Pain	1	19	6.1 (4.3–7.8)	**<0.001**	14	1.8 (−0.1–3.7)	0.056	1,32	2.9 (1.1–4.8)	**0.003**
	3	19	6.1 (4.3–7.9)	**<0.001**	15	2.2 (0.1–4.2)	0.037	1,33	3.3 (1.4–5.1)	**0.001**
	6	15	5.4 (3.3–7.5)	**<0.001**	2	2.0 (−3.0–7.0)	0.225	1,16	0.6 (−4.0–5.1)	0.793
Sum	1	19	17.1 (14.3–19.8)	**<0.001**	14	9.3 (4.0–14.7)	**0.002**	1,32	8.4 (3.8–13.1)	**0.001**
	3	19	17.5 (14.4–20.5)	**<0.001**	15	9.1 (5.0–13.2)	**<0.001**	1,33	10.2 (6.5–14.0)	**<0.001**
	6	15	14.7 (10.5–18.9)	**<0.001**	2	5.7 (0.5–10.8)	0.042	1,16	7.6 (−1.0–16.1)	0.080

CI: confidence interval; df: degrees of freedom; FU: follow-up.

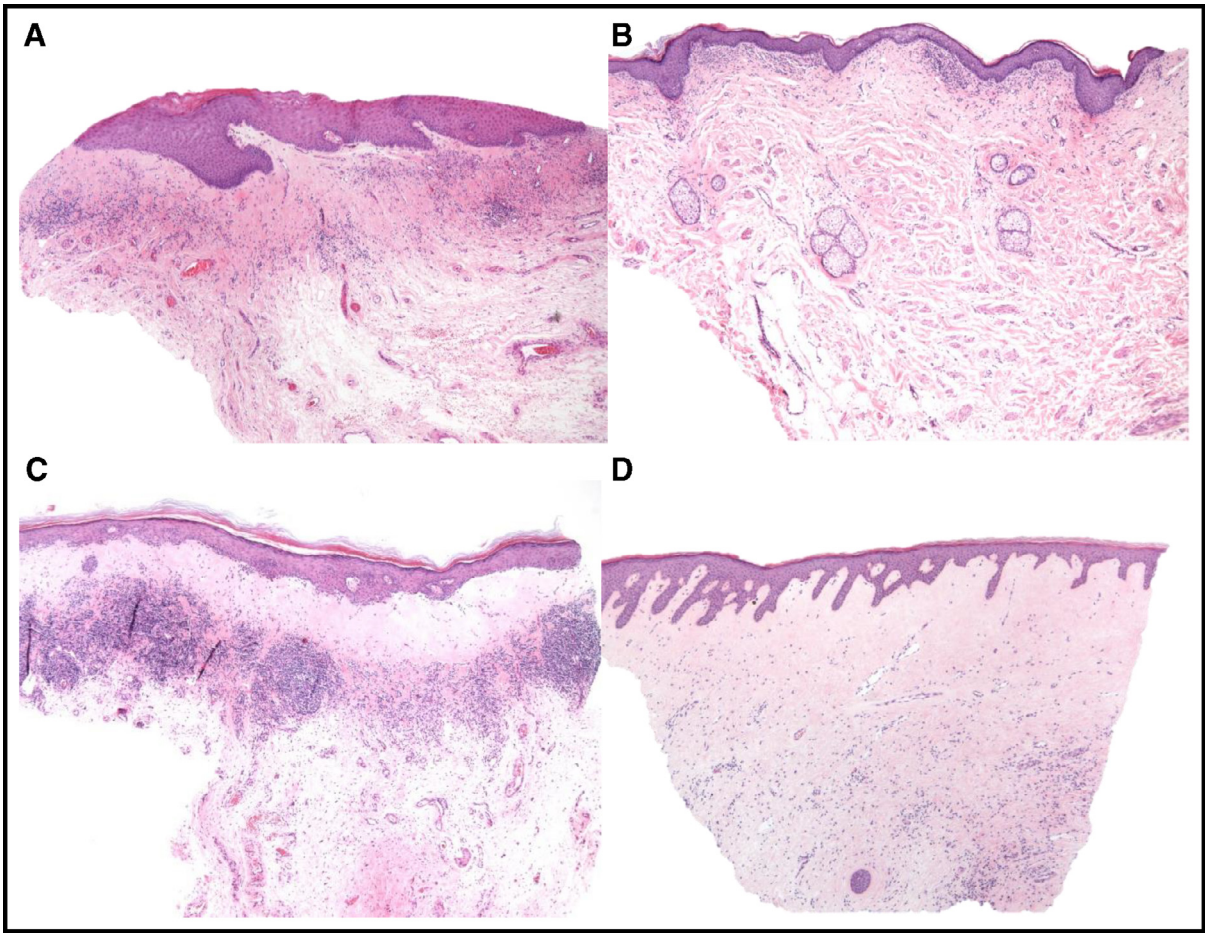
[a] Decrease in visual analogue scale (VAS) scores from baseline and 95% confidence interval in laser and control groups at 1 to 6 months follow-up. *P* value from paired *t* test. Effect size of laser versus control group (decrease in mean VAS in laser group compared with control and 95% confidence interval) and *P* value from analysis of covariance with baseline value as covariate. Sum symptom score at 3 months was the main outcome measure. Note that individual symptoms were scored on a 0−10 VAS, and the sum score has a range of 0−30 VAS. *P* values still significant after stepwise Bonferroni correction are bold.

Figure 3. Proportion of patients reporting a negative effect of lichen sclerosis on their sex life before and after treatment in the control (topical corticosteroid) and laser-treated groups. (A) Proportion reporting any negative effect. (B) Proportion reporting dyspareunia. (C) Proportion reporting decreased sensation. (D) Proportion reporting anorgasmia. Twelve of 20, 11 of 20, 11 of 20, and seven of 16 patients in the laser group were sexually active at baseline and at 1-, 3-, and 6-month follow-up, respectively. Ten of 18, nine of 15, 11 of 16, and one of three patients in the control group were sexually active at baseline and at 1-, 3-, and 6-month follow-up, respectively.



†Statistically significant difference from baseline; *statistically significant difference between the laser and control groups.

Figure 4. (A) Laser group at baseline; a broad band of dermal sclerosis is apparent, accompanied by moderately intense inflammatory cell infiltrate and acanthosis of the epidermis. (B) Three months after laser treatment; significantly lower degree of dermal sclerosis is seen, associated with mild inflammatory cell infiltrate and normal epidermis. (C) Corticosteroid group at baseline; broad band of dermal sclerosis is accompanied by moderately intense inflammatory cell infiltrate and slight acanthosis of the epidermis. (D) Three months after corticosteroid treatment; although the inflammatory cell infiltrate has diminished significantly after treatment, broad band of dermal sclerosis is still apparent. Epidermis displays mild acanthosis.



mm; 95% CI −0.48 to 0.20 mm; $P = 0.577$). The improvement was statistically significantly better in the laser group (by 0.57 mm; 95% CI 0.01−1.13 mm; $P = 0.46$). No statistically significant differences were observed for the changes of thickness of the epidermis and the degree of inflammation either within or between groups.

DISCUSSION

At 1- and 3-month follow-up, patients in the laser group had significantly greater improvement of LS symptoms (burning, itching, pain, and dyspareunia) than patients in the topical corticosteroid group. At 6-month follow-up, the effect was only significant for burning, which was more greatly reduced in the laser group. Although other scores were also better in the laser group, the difference was not significant because there was high loss to follow-up in the control group.

We found it very difficult to motivate patients in the control group to adhere to the study protocol. This was in part because of the recurrence of symptoms and in part because of the negative attitude of the patients to the control treatment. Most of the recruited patients had used topical corticosteroids before and came to us looking for a better or more permanent solution. With the chosen study design, it was impossible to blind the patients. In the future, designs in which blinding is possible would be recommended (e.g., including sham laser treatment in the control group). In this way the placebo effect, which can be significant for patient-reported subjective symptoms,[11] would be better controlled, and loss

to follow-up resulting from problems with motivation could possibly be reduced.

Objective outcome measures (blinded histological evaluation and photograph assessment), which are less influenced by the placebo effect,[11] were also included in this study. During blinded assessment of photographs, evaluators take into account such vulvar clinical signs as erythema, pallor, atrophy (revealed by wrinkled skin and textural change), purpura, erosions, hyperkeratosis, and fissuring.[12] In our case, assessment was complicated by the quality of the available photographs. Improvement in signs was nevertheless more obvious in the laser-treated group. Clinical signs improved less readily than symptoms. For example, in a case series of over 200 women with LS treated mostly with topical corticosteroids, complete resolution of symptoms was observed in 65% of patients, whereas complete resolution of clinical signs, including return to normal colour and texture, occurred in only 23% of patients.[12]

In this study, sclerosis was more greatly reduced with laser than with corticosteroid treatment, whereas other histological variables did not differ between the two treatments. A negative finding for LS on post-treatment biopsy did not correlate with a lack of patient-reported symptoms. In a recent attempt to develop a consensus standard severity scale for adult vulvar LS,[13] 66 members of the International Society for Study of Vulvovaginal Disease voted for symptoms and signs to be included in the scale. Histological and immunohistochemical markers were not proposed for inclusion by any of the experts throughout the consensus exercise. The authors concluded that it may be objective to look at biopsy changes in response to treatment, but it is unclear whether this outcome is important to patients and it likely should be used as an adjunct to other measures.[13]

The control corticosteroid in this study was less effective in reducing symptoms compared with results reported in the literature.[12] A shorter course of topical corticosteroid therapy than is common practice was used in this study. This was done out of concern that prolonging the trial duration in the control arm would increase loss to follow-up. Consequently, the treatment period was shortened to match that in the laser arm (1 month). Furthermore, a high proportion of patients (78%) had already received topical corticosteroid treatment before this study, and the fact that they sought further treatment would indicate that they were among poor responders, a factor that could also account for our results.

A 3-month application of topical corticosteroid reportedly induces remission of symptoms in 80% to 90% of patients.[12] In a large retrospective case series, response of symptoms to topical treatment at the end of treatment period was available for 219 women; response was graded as symptom-free in 142 women (65%), partial (improvement and/or partial resolution of individual symptoms) in 67 women (31%), and poor (no change or worsening) in 10 women (5%).[12] In comparison, 50% of laser-treated patients in this study were symptom-free after two treatment sessions, and the remaining patients had at least a 67% reduction in the total symptom score. No woman had a poor response to laser treatment. Non-ablative laser treatment can thus be an important additional treatment option for patients with poor response to topical treatment. Furthermore, significant relief from symptoms was still observed 3 and 6 months after laser treatment. Incorporating laser treatment could thus reduce the need for long-term maintenance corticosteroid therapy, thereby lowering the possibility of side effects of long-term use.

Ablative lasers (carbon dioxide laser) have previously been used for recalcitrant vulvar LS,[14–16] but as far as we know, this is the first study examining the use of non-ablative lasers. Because of the minimally invasive non-ablative approach, Nd:YAG laser therapy for vulvar LS demonstrated minimal treatment discomfort with no serious adverse effects. The laser-treated group showed significantly better results than the control group 3 months after treatment. Improvement of symptoms in the laser group was still significant at 6 months. Parameters previously recommended for wound healing and scar prevention[8] were used in the study, with protocol details (number of treatments, time interval) based on our previous clinical experience. Clinical studies comparing different protocols would help establish clear optimal treatment guidelines.

CONCLUSION

If further studies with longer follow-up and patient blinding confirm the promising results of this pilot study, non-ablative laser treatment may become a valuable alternative for patients not responding to topical corticosteroid therapy or patients wishing to avoid long-term corticosteroid maintenance use.

REFERENCES

1. Kirtschig G. Lichen sclerosus-presentation, diagnosis and management. Dtsch Arztebl Int 2016;113:337–43.

2. Kirtschig G, Becker K, Günthert A, et al. Evidence-based (S3) guideline on (anogenital) lichen sclerosus. J Eur Acad Dermatol Venereol 2015;29:e1–43.

3. Casanova D, Alliez A, Baptista C, et al. A 1-year follow-up of post-operative scars after the use of a 1210-nm laser-assisted skin healing (LASH) technology: a randomized controlled trial. Aesthetic Plast Surg 2017;41:938–48.

4. Capon A, Iarmarcovai G. Scar prevention using laser-assisted skin healing (LASH) in plastic surgery. Aesthetic Plast Surg 2010;34:438–46.

5. Gambacciani M, Palacios S. Laser therapy for the restoration of vaginal function. Maturitas 2017;99:10–5.

6. Blaganje M, Scepanovic D, Zgur L, et al. Non-ablative Er:YAG laser therapy effect on stress urinary incontinence related to quality of life and sexual function: a randomized controlled trial. Eur J Obstet Gynecol Reprod Biol 2018;224:153–8.

7. Lapii GA, Yakovleva AY, Neimark AI. Structural reorganization of the vaginal mucosa in stress urinary incontinence under conditions of Er:YAG laser treatment. Bull Exp Biol Med 2017;162:510–4.

8. Lukac M, Vizintin Z, Pirnat S, et al. New skin treatment possibilities with PIANO mode on an Nd : YAG Laser. LA&HA - J Laser Heal Acad 2011;2011:22–32.

9. Gamer M, Lemon J, Fellows I, et al. Various coefficients of interrater reliability and agreement. XXX 2010;XX:xx–x .

10. Hallgren KA. computing inter-rater reliability for observational data: an overview and tutorial. Tutor Quant Methods Psychol 2012;8:23–34.

11. Hróbjartsson A, Gøtzsche PC. Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. N Engl J Med 2001;344:1594–602.

12. Cooper SM, Powell JJ, Wojnarowska F. Does treatment of vulvar lichen sclerosus influence its prognosis? Arch Dermatol 2004;140:702–6.

13. Sheinis M, Selk A. Development of the adult vulvar lichen sclerosus severity scale - a Delphi consensus exercise for item generation. J Low Genit Tract Dis 2018;22:66–73.

14. Lee A, Lim A, Fischer G. Fractional carbon dioxide laser in recalcitrant vulval lichen sclerosus. Australas J Dermatol 2016;57:39–43.

15. Origoni M. Fractional carbon dioxide laser in recalcitrant vulvar lichen sclerosus [letter]. Australas J Dermatol 2017;58:e157–8.

16. Stuart GC, Nation JG, Malliah VS, et al. Laser therapy of vulvar lichen sclerosus et atrophicus. Can J Surg 1991;34:469–70.