

# Effects of Fractional CO<sub>2</sub> Laser Treatment on Patients Affected by Vulvar Lichen Sclerosus: A Prospective Study

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## Abstract

**Background:** Fractional carbon dioxide (CO<sub>2</sub>) lasers are today considered the most effective and efficient treatment for many vulvovaginal disorders, providing mini-invasive procedures without side effects. Previous studies demonstrated the efficacy of fractional CO<sub>2</sub> lasers in vulvar lichen sclerosus (VLS), a chronic skin disorder characterized by itching and painful lesions. Complications include pain, sexual and/or urinary dysfunction, with a negative quality of life, and an increased risk of squamous cell carcinoma. A definitive VLS treatment is still lacking.

**Objectives:** This is a prospective, single-center study aimed at evaluating the effect of fractional microablative CO<sub>2</sub> laser treatment on women affected by VLS.

**Materials and methods:** Patients with histologically confirmed VLS underwent three fractional microablative CO<sub>2</sub> laser treatments, 4 weeks apart, on the genital affected areas. Clinical and VLS-related symptoms, side effects, and patient satisfaction index were assessed and recorded for all the patients using the visual analog scale (VAS).

**Results:** Data from a total of 70 patients were included, paired at different time points and analyzed. VLS-related symptoms and other relevant parameters (pH, vaginal introitus discomfort, dyspareunia, vaginal dryness, itching, and burning) showed a statistically significant improvement ( $p < 0.001$ ) after the first laser treatment and kept improving after second and third sessions. According to VAS, the two most common symptoms, vaginal introitus discomfort and dyspareunia, went from (mean  $\pm$  standard deviation)  $8.2 \pm 2.3$  and  $8.3 \pm 2.2$ , respectively, at baseline, to  $3.6 \pm 2.6$  and  $3.8 \pm 2.6$ , respectively, 1 month after the last treatment. Vaginal dryness, itching, and burning were significantly improved as well. Most patients declared to be very satisfied with the results of the treatment. A total of 62.8% of the women expressed a satisfaction score  $\geq 8$  on a scale from 0 to 10.

**Conclusions:** Fractional microablative CO<sub>2</sub> laser treatment seems to be safe and effective to treat VLS and improve VLS-related symptoms.

**Keywords:** fractional CO<sub>2</sub> laser, CO<sub>2</sub> laser, vulvar lichen sclerosus, genital lichen sclerosus, vulvar disorders

## Introduction

VULVAR LICHEN SCLEROSUS (VLS) is a chronic inflammatory skin disease of the anogenital area. It can occur at any age, with a peak among premenarche and postmenopausal women.<sup>1</sup> VLS mostly involves the labia minora and the internal part of the labia majora, the interlabial sulcus, the clitoris, the vestibule, the perineum, and the perianal region, while rarely the vaginal mucosa is affected.<sup>2</sup> Clinically, the

most common features are represented by ivory white papules or plaques with a waxy consistency or epidermal wrinkles with a “cigarette paper” appearance. Scarring typically occurs later in the course of disease with bruising and ulceration.<sup>3</sup> Changes in anatomical morphology can lead to significant distortions of the architecture, resorption of the labia minora, phimosis of the clitoris, narrowing or stenosis of the introitus, and mechanical recurrence of the posterior fork.<sup>4</sup> Depigmentation or hyperpigmentation may also be present.

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The most common symptoms are itching, often intractable and manifesting mainly during the evening and night hours, burning, dysuria, pain during defecation, dyspareunia, and chronic vulvar pain.<sup>5</sup> Moreover, the scarring of the foreskin, through the decrease or loss of sensitivity of the clitoris and the significant reduction of vulvar tropism, negatively affects the quality of life (QoL) and sexual function, causes discomfort in the couple, compromises psychological well-being, and consequently leads to secondary anorgasmia.<sup>6</sup> Long-term persistent VLS has been also associated with a higher risk of vulvar cancer, particularly squamous cell carcinoma.<sup>7</sup> Therefore, diagnosis and treatment of VLS at the earliest possible stage are mandatory to reduce symptoms and complications.

To date, the first-line treatment of VLS is represented by topical ultrapotent steroids,<sup>8–10</sup> aimed at alleviating symptoms and delaying relapses of the disease. Subdermal injection of steroids has also proved to be a valid alternative to topical steroids, with the advantage of injecting the steroid directly into the dermis, knowing precisely the amount of drug administered in the target tissue.<sup>8</sup> However, chronic use of high-potency topical steroids tends to worsen skin atrophy over time, exacerbating lichen symptoms, manifesting contact sensitization, and creating a greater risk of secondary infection.<sup>11</sup> Further, resistance to treatment usually occurs in severe disease, manifesting itself with signs of hyperkeratosis. In these cases, ultrapotent corticosteroid therapy may be ineffective.

Recently, many alternative treatment options have been proposed.<sup>12</sup> Among them, fractional carbon dioxide (CO<sub>2</sub>) lasers seem to be a promising successful treatment for VLS.<sup>13</sup> The delivery of CO<sub>2</sub> laser energy in a controlled way has proven to promote neoangiogenesis, to induce the formation of glycogen and to increase the production of collagen in the lamina propria, thus improving the sclerosis and atrophy typical of VLS.<sup>14,15</sup>

Accordingly, the purpose of this prospective study is to assess the efficacy of the fractional CO<sub>2</sub> laser on the life of women diagnosed with VLS, evaluating parameters, including extension, symptoms, and clinical VLS signs, patient satisfaction, and treatment tolerance.

## Materials and Methods

### Patient selection

This was a prospective study on adult women affected by VLS, clinically suspected and histologically confirmed, conducted at the Department of Obstetrics and Gynecology of State Hospital of the Republic of San Marino, in the period between May 2013 and September 2020. Information was collected using an electronic database and included the following: demographic data, clinical features and severity of VLS, medical history, presence of comorbidities, previous treatments, and current therapies.

Exclusion criteria included the following: female <18 years of age; pregnancy or breastfeeding; active urinary infection; presence of genital tract infection, lesion, or abscess; vaginal and/or vulvar neoplasia; use of topical or systemic drugs in the previous 2 months before or during the study period; contraindications to the use of laser (e.g., active viral, bacterial, or fungal infections); decompensated psychiatric disorders; alcohol or drug addiction; chronic

systemic diseases; unsigned informed consent; or uncertain diagnosis of vulvar disease.

The study was carried out according to the Declaration of Helsinki and an informed consent was signed by all the enrolled patients.

### Study protocol

The study protocol consisted of three sessions of fractional CO<sub>2</sub> laser treatment, 4 weeks apart, using a device equipped with a scanning system and appropriate probes for vulvovaginal treatment (SmartXide2 V2LR by DEKA, Florence, Italy).<sup>13</sup>

According to the extension and severity of the condition, treated areas included external genitalia (such as vulva and clitoris), internal genitalia (especially at the level of the vaginal intake), and the perianal area.

Laser settings were chosen based on the target area; for vaginal treatment, parameters included the following: power 40 W, dwell time 1000  $\mu$ s, spacing 1000  $\mu$ m, smart stack 2, corresponding to a fluence of 113 J/cm<sup>2</sup>, which averages an ablation depth of 250  $\mu$ m; for vaginal introitus treatment, power 25–30 W, dwell time 1000  $\mu$ s, spacing 1000  $\mu$ m, smart stack 1, corresponding to a fluence of 35–42 J/cm<sup>2</sup>, which averages an ablation depth of 75–100  $\mu$ m; for the vulva, clitoris, and perianal area, power 20–25 W, dwell time 1000  $\mu$ s, spacing 1000  $\mu$ m, smart stack 1, corresponding to a fluence of 35–42 J/cm<sup>2</sup>, which averages an ablation depth of 75–100  $\mu$ m.

The SmartStack function represents an energy multiplier. A number of emissions are therefore repeated on the same microablation zone (Dermal Optical Thermolysis, DOT) before the scanner moves to the next zone. The dwell time is the time in which the laser emission is delivered over each single microzone of thermal damage (DOT) before moving on to the next, while the spacing is the distance between two adjacent microzones (DOTs).

All patients were evaluated at baseline (pretreatment), after each laser session and 1 month after the last session of treatment, assessing pH, dyspareunia, vaginal introitus pain, vaginal dryness, burning, and itching. Patients assessed the severity of their symptoms using the visual analog scale (VAS), from 0 (no pain/discomfort) to 10 (maximum pain/discomfort).

A questionnaire assessed the satisfaction of patients concerning treatment results after each laser session and at follow-up, based on a 10-point scale ranging from 0 to 10 (0—totally unsatisfied; 10—totally satisfied).

### Statistical analysis

A paired Student's *t*-test was used to compare the paired data collected at different time points. The Wilcoxon signed-rank test was also performed for confirmation. A *p*-value <0.05 was considered statistically significant.

## Results

### Study population

A total of 70 females were enrolled. Mean age [ $\pm$ standard deviation (SD)] at baseline was 60.2  $\pm$  8.2 years (range, 41–84 years). Most subjects were already on menopause (*n* = 64, 91.4%).

The most common comorbidity was found to be hypertension ( $n=18$ , 25.7%), followed by hypercholesterolemia ( $n=17$ , 24.3%) and hypothyroidism ( $n=15$ , 21.4%). Subjects also reported gastrointestinal disorders ( $n=25$ , 35.7%), insomnia ( $n=16$ , 22.9%), mood swings ( $n=11$ , 15.7%), recurrent vaginitis ( $n=5$ , 7.1%), and hemorrhoids ( $n=5$ , 7.1%). Nine patients (12.9%) had a previous cancer diagnosis (four breast ductal carcinomas, three lymphomas, one meningioma, and one rhinopharyngeal cancer), out of whom one was still under hormonal therapy (Table 1).

Previously, VLS treatments included the following: topical corticosteroids ( $n=70$ , 100%), topical vitamin E ( $n=35$ , 50%), retinoids ( $n=26$ , 37.2%), and antihistamines ( $n=5$ , 7.1%).

Based on clinical evaluation, VLS most commonly involved the clitoris ( $n=43$ ; 61.4%), followed by the anal area ( $n=23$ ; 32.9%), vagina ( $n=19$ ; 27.1%), and vestibular-vulvar area ( $n=11$ ; 15.7%); two patients presented dystrophy and two hyperkeratosis in the vulvar area. The most frequent lesions were represented by atrophy (70%,  $n=49$ ), erythema (20%,  $n=14$ ), and fissures (10%,  $n=7$ ).

Genitourinary syndrome affected 69 patients (98.6%), stress urinary incontinence was referred by 21 patients (30.0%), and 8 subjects (11.4%) presented vaginal prolapse, out of whom one case was classified as grade 2 and the other seven as grade 1.

Among reported symptoms, the most common was vaginal introitus discomfort ( $n=66$ , 94.3%), followed by dyspareunia ( $n=61$ , 87.1%), vaginal dryness ( $n=63$ , 90.0%), itching ( $n=45$ , 64.3%), and burning ( $n=44$ , 62.9%) (Table 2).

TABLE 1. DEMOGRAPHIC AND ANAMNESTIC DATA OF FEMALE SUBJECTS ( $n=70$ ) INCLUDED IN THE STUDY

Age (average $\pm$ SD, years)	60.2 $\pm$ 8.2
Age range (years)	41–84
Menopause ( $n$ , %)	64; 91.4
Comorbidities ( $n$ , %)	
Hypertension	18; 25.7
Hypercholesterolemia	17; 24.3
Hypothyroidism	15; 21.4
Osteoporosis	5; 7.1
Gastroenteric disorders	3; 4.3
Diabetes	1; 1.4
Migraine/headache	1; 1.4
Von Willebrand	1; 1.4
Previous cancer diagnosis	9; 12.9
Other disorders ( $n$ , %)	
Insomnia	16; 22.9
Mood swings	11; 15.7
Vaginitis	5; 7.1
Hemorrhoids	5; 7.1
Gastrointestinal disorders, including:	25; 35.7
Colitis	7; 10.0
Gastritis	6; 8.6
Reflux	5; 7.1
Constipation	4; 5.7
Diarrhea	2; 2.9
Hiatal hernia	1; 1.4

SD, standard deviation.

#### Lichen sclerosus-related and other genitourinary symptoms

Both pH and all lichen sclerosus-related symptoms analyzed in the study (dyspareunia, vaginal introitus discomfort, vaginal dryness, itching, and burning) showed a statistically significant improvement ( $p<0.001$ ) at follow-up, as shown in Figs. 1–4.

Mean ( $\pm$ SD) pH measured before laser treatment was  $6.9\pm 1.0$  and decreased to  $6.1\pm 0.7$  after three laser treatments. Using VAS, the vaginal introitus discomfort went from  $8.2\pm 2.3$  at baseline to  $3.6\pm 2.6$  at follow-up, and dyspareunia went from  $8.3\pm 2.2$  to  $3.8\pm 2.6$  after the completion of treatment. Vaginal dryness, itching, and burning were significantly improved as well: the vaginal dryness score lowered from  $7.7\pm 2.2$  to final  $3.3\pm 2.4$ ; itching improved from  $6.8\pm 2.6$  to  $2.3\pm 2.6$ ; and burning reduced from  $6.9\pm 2.4$  to  $2.3\pm 2.3$ . Scores recorded at baseline and after each treatment for the abovementioned parameters and symptoms are shown in Table 3.

#### Side effects

No significant discomfort or side effect was reported, neither during laser treatment nor immediately after or at the follow-up visit.

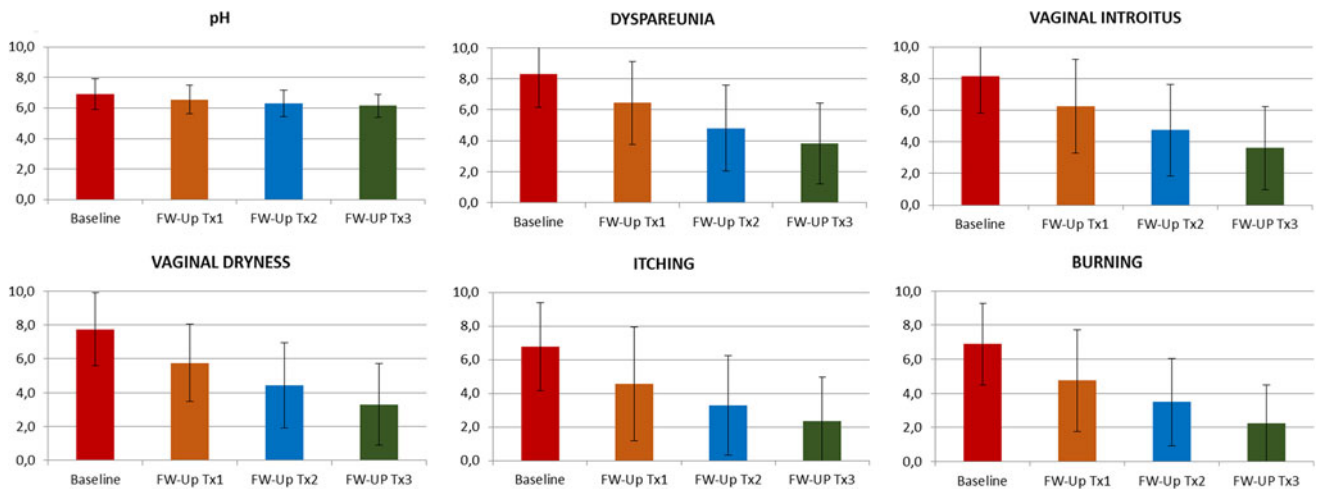
#### Subject satisfaction

The mean final satisfaction index was  $8.0\pm 1.3$  and 62.8% of the subjects giving a score  $\geq 8$ . Only two patients declared to be slightly unsatisfied (score: 5) because of higher expectations. The satisfaction index improved with the number of received laser treatments: after one single laser session, the mean satisfaction index reported was  $6.5\pm 2.0$ , while after two sessions it was raised to  $7.3\pm 1.6$ .

TABLE 2. GENITOURINARY EVALUATION AT BASELINE ( $n$ ; %)

VLS	70; 100
Genitourinary syndrome	69; 98.6
Stress urinary incontinence	21; 30.0
Prolapse	8; 11.4
Recurrent cystitis	7; 10.0
VLS-related alterations	
Clitoris (itching, burning)	43; 61.4
Anal area (itching, fissures)	23; 32.9
Vaginal disorders or fissures	19; 27.1
Vestibulo-vulva disorders	11; 15.7
VLS lesions	
Atrophy	49; 70
Erythema	14; 20
Fissures	7; 10
VLS-associated symptoms	
Vaginal introitus discomfort	66; 94.3
Dyspareunia	61; 87.1
Vaginal dryness	63; 90.0
Itching	45; 64.3
Burning	44; 62.9

VLS, vulvar lichen sclerosus.



**FIG. 1.** Lichen sclerosis-related symptoms at baseline and at follow-up.

**Discussion**

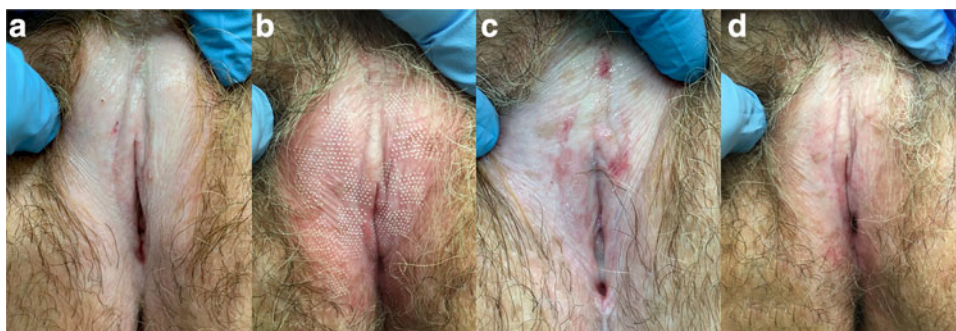
VLS is a chronic inflammatory condition whose etiopathogenesis is still unknown, although evidence suggests a multi-factorial disease.<sup>16</sup> A genetic predisposition, as well as hormonal and immunological alterations, has been implicated.<sup>17</sup> Moreover, many systemic disorders have also been associated with VLS,<sup>18</sup> including cardiovascular diseases and thyroid dysfunction,<sup>19</sup> as confirmed by our study.

VLS is difficult to treat, as the involution of the tissues of the genitalia is full thickness, involving the dermoepidermal structures, the corpora cavernosa, blood vessels, and connective tissue. Consequently, women progressively manifest disabling signs and symptoms, which negatively affect the QoL as well as sexual activity. The goal of treatment is to relieve symptoms, reduce anatomical alterations due to complications, and avoid malignant transformation.<sup>13</sup> The topical medical therapy recommended by all the guidelines is represented by steroids.<sup>8-10</sup> However, the relapsing and refractory nature of the disease has led to the search of alternative or complementary treatments to control signs and symptoms for longer period. Among them, fractional CO<sub>2</sub> laser has shown promising results in women who do not respond to traditional management with steroids, who do not want to take medical therapy for too long, who have side

effects or complications, or who are unable to continue taking it.<sup>13</sup> In the past, lasers were niche procedures due to their costly nature and the need for dedicated surgical facilities. However, advances in microfractionated laser technology, with minimal surface ablation, together with the thermal effect on cells, have increased the potential use of this therapeutic approach, becoming an outpatient practice.

According to our study, fractional CO<sub>2</sub> laser significantly reduced all the symptoms reported by our patients, for example, dyspareunia, vaginal introitus discomfort, vaginal dryness, itching, and burning, thus representing an alternative effective treatment for VLS patients. Many of the patients we recruited, together with VLS, had also associated genitourinary syndrome of menopause, but this latter condition was not an exclusion factor for the study. Indeed, the improvement of both the diseases demonstrated a further advantage and confirmation of the effectiveness of the treatment.

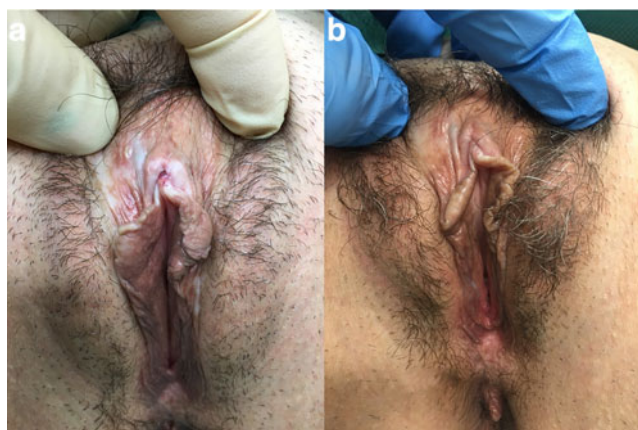
Recently, Gardner and Aschkenazi<sup>20</sup> reported satisfactory results in 31 patients affected by VLS using vulvovaginal fractional microablative CO<sub>2</sub> laser. Moreover, in a prospective study on 27 symptomatic postmenopausal women diagnosed with VLS, Baggish<sup>21</sup> also reported pain and itching cessation in 88.9% of women and improvement in skin color, elasticity, and vascularity in 96.3% of them after



**FIG. 2.** A 67-year-old female with severe VLS with itching and burning lesions (a). The patient performed three fractional microablative CO<sub>2</sub> laser treatments, 4 weeks apart (b) with improvement of vulvar skin lesions after the last session of treatment (c) and maintenance of the results 3 months later (d) with an increase in superficial vascularity and reduction of ivory white lesions. CO<sub>2</sub>, carbon dioxide; VLS, vulvar lichen sclerosis.



**FIG. 3.** A 54-year-old female with VLS before (a) and after (b) fractional microablative CO<sub>2</sub> laser treatments. The labia minora and majora fusion as well as the hooding of the clitoris was still present, but the painful and burning symptoms solved.



**FIG. 4.** A 57-year-old female with VLS before (a) and after (b) fractional microablative CO<sub>2</sub> laser treatments: a great reduction of the ivory plaques in the paraclitoral area, with resolution of itching, was obtained.

three sessions of fractional CO<sub>2</sub> laser treatment at intervals of 4–6 weeks. None of the patients had previously undergone any other treatments.

Pagano et al.<sup>22</sup> showed a significant improvement in vulvar itching, dryness, superficial dyspareunia, and sensitivity after two microablative CO<sub>2</sub> fractional laser cycles in 40 VLS women and suggested it as an alternative strategy to relieve pain and sexual discomfort in women with resistant VLS.

Balchander and Nyirjesy<sup>23</sup> demonstrated a reduction in itching, dyspareunia, vaginal pain, and dysuria in 72.5% of 40 women with refractory VLS, not responding to standard treatment protocols, treated with fractional CO<sub>2</sub> laser. They also found a need for fewer corticosteroid applications to keep the obtained results.

Other studies regarding the use of CO<sub>2</sub> lasers in women with VLS showed conflicting data and results. Lee et al.<sup>24</sup> obtained improvement in five patients with severe, symptomatic, and hyperkeratotic VLS patients, resistant to topical corticosteroids: four patients underwent fractional CO<sub>2</sub> laser treatment and one ablative CO<sub>2</sub> laser therapy. However, the treatment was reported as painful and needed prophylactic analgesia; moreover, all the patients continued to apply clobetasol 0.05% ointment to maintain clinical remission. Origoni<sup>25</sup> also underlined that Lee's findings were questionable since patients' symptoms were not measured objectively and the patients had not stopped steroid treatment.

Based on our experience,<sup>26,27</sup> the effectiveness of a fractional CO<sub>2</sub> laser treatment depends on the chosen parameters: different anatomical sites show different thicknesses and textures; thus, modulating the parameters (power, dwell time, spacing, and smart stack) is essential to obtain the best results, avoiding side effects.

In agreement with most of the literature data,<sup>20–23</sup> in our study, the laser treatment was tolerated by almost all the women and significantly improved their QoL, through amelioration in color, elasticity, and moisture of the skin and mucosa after three cycles of laser treatment.

The mechanism of action of microfractionated CO<sub>2</sub> laser treatment in VLS is still unclear. One of the hypothesized mechanisms is the capability of microfractional laser to induce the absorption of light energy by the water molecules

**TABLE 3.** pH AND VULVAR LICHEN SCLEROSUS-RELATED SYMPTOM SCORES AT BASELINE AND AFTER FRACTIONAL CARBON DIOXIDE LASER TREATMENT (MEAN ± STANDARD DEVIATION)

	pH	p	Vaginal introitus discomfort	p	Dyspareunia	p
Baseline	6.9 ± 1.0		8.2 ± 2.3		8.3 ± 2.2	
FW-UP Tx1	6.6 ± 0.9	<0.001	6.2 ± 3.0	<0.001	6.4 ± 2.7	<0.001
FW-UP Tx2	6.3 ± 0.9	<0.001	4.7 ± 2.9	<0.001	4.8 ± 2.8	<0.001
FW-UP Tx3	6.1 ± 0.7	<0.001	3.6 ± 2.6	<0.001	3.8 ± 2.6	<0.001
	Vaginal dryness	p	Itching	p	Burning	p
Baseline	7.7 ± 2.2		6.8 ± 2.6		6.9 ± 2.4	
FW-UP Tx1	5.8 ± 2.3	<0.001	4.6 ± 3.4	<0.001	4.8 ± 3.0	<0.001
FW-UP Tx2	4.4 ± 2.5	<0.001	3.3 ± 2.9	<0.001	3.5 ± 2.6	<0.001
FW-UP Tx3	3.3 ± 2.4	<0.001	2.3 ± 2.6	<0.001	2.3 ± 2.3	<0.001

FW-UP Tx1, follow-up after first laser treatment; FW-UP Tx2, follow-up after second laser treatment; FW-UP Tx3, follow-up after third laser treatment.

present in the epidermis, thus determining the ablation of the epidermis and the superficial dermis. Consequently, the laser could improve the processes of epithelial repair and re-epithelialization reducing atrophy.<sup>26–28</sup> At the same time, the subsequent transfer of energy to the underlying connective tissue could induce biostimulation mechanisms that stimulate neoangiogenesis, induce the formation of glycosaminoglycans, and increase the production of collagen in the lamina propria, as it has been shown in many scleroatrophic conditions.<sup>29–31</sup> Low-dose fractional CO<sub>2</sub> laser has also been involved in remodeling the collagen fiber through the activation of procollagen I and III and the induction of cytokines such as tumor necrosis factor (TNF) alpha, TNF beta-1, interleukin 1-beta, and metalloproteinases.<sup>32,33</sup>

The limitations of our study, despite the number of patients treated being rather representative, comprise the lack of a control group, a nonrandomized design, a subjective evaluation of symptoms, and above all the possibility of generating a placebo effect. In fact, the results obtained regarding the reduction of the impact on the life of the patients could be attributed to some biases since not being a double-blinded study, and given a strong dependence on subjective scores, it could have induced the patients to increase the desire to cooperate knowing they were about to be cured. However, we made a careful selection of the patients with a scrupulous clinical evaluation.

### Conclusions

The fractional microablative CO<sub>2</sub> laser can provide a treatment option for women with VLS who do not respond to traditional management with steroids. Further studies could be useful to assess the best physical parameters of the laser treatment, for example, the most effective energy dose, the interval and frequency between the various sessions, and the therapeutic effect of any additional treatments, to better treat our patients.

### Author Disclosure Statement

No competing financial interests exist.

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