

Solid State Vaginal Laser for the Treatment of Genitourinary Syndrome of Menopause: A Preliminary Report

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Abstract

Background: Genitourinary syndrome of menopause (GSM) is the new term for vulvovaginal atrophy (VVA). The condition is relevant in more than 50% of women, having an adverse impact on quality of life and sexual relationships. **Objective:** To assess the efficacy and safety of a new type of non-ablative laser, Solid State Vaginal Laser (SSVL), for vaginal tissue regeneration and rejuvenation. **Method:** Eighty participants with GSM symptoms were treated with a total of 4 treatments in about two months (every 15 - 20 days) of a non-ablative SSVL (LASEmaR 1500™-EUFOTON). A cumulative intensity of GSM symptoms using a 10-cm VAS (dryness and/or burning and/or dyspareunia), the vaginal health index (VHI), the Female Sexual Function Index (FSFI) were evaluated. Urinary Incontinence Short Form (ICIQ-UI SF) and vaginal bioptic samples were also collected. **Results:** Improvement following the SSVL was observed on VHIS, VVA symptoms and sexual female function. This finding was also ratified by the improvement of vaginal histological features. After the SSVL treatment, almost all patients (91%) affected by urinary incontinence obtained the complete remission of symptoms. **Conclusion:** The objective evaluation of VHIS, FSFI and ICIQ-UI SF scores and the histological results indicates a real favorable effect of SSVL on GSM and on urinary incontinence.

Keywords

Atrophic Vaginitis, Genitourinary Syndrome of Menopause, Urinary Incontinence, Fractional Laser

1. Introduction

Genitourinary syndrome of menopause (GSM) is a new term for vulvovaginal atrophy (VVA), an old condition occurring at menopause due to low levels of estrogen [1] [2]. However, GSM defines better than VVA all the possible symptoms and clinical signs from the lower genital (VVA) and urinary tract system (LUTS) during menopause [1]. Thus, women with GSM may present with one or more symptoms such as dyspareunia, dryness, itching/burning, sexual dysfunction, dysuria, urinary frequency, and urgency [1]. Common signs and symptoms in order of prevalence and degree of atrophy include vaginal dryness (in 75% postmenopausal women), dyspareunia (38%) and vaginal itching, discharge, and pain (15%) [3]. Topical hormonal treatment is considered the gold standard therapy for postmenopausal vaginal symptoms, promoting restoration of epithelial integrity, vaginal flora, and improving VVA symptoms [4]. This treatment is, however, associated with poor compliance due to multiple and inconvenient self-applications and increased vaginal discharge. The prescription of topical estrogens should also be avoided in women with history of breast cancer, estrogen-sensitive tumors, and thromboembolism, emphasizing the necessity for treatment alternatives. Lubricants and moisturizers are available options to help improve dryness, but often they are not enough to reduce vulvar pain and sexual discomfort [5] [6].

The role of lasers in gynecology has evolved from their initial use in the destruction and vaporization of lesions, to more recently promote revitalization or what is sometimes termed “rejuvenation” of vaginal and vulvar tissue in the hope of improving symptoms of vaginal atrophy, vaginal laxity, stress urinary incontinence, sexual dysfunction and vulvar lesions. The quality of data supporting the use of vaginal lasers varies, with the largest body of data surrounding its use being in the treatment of GSM [7]. The aim of our paper is to demonstrate the efficacy and safety of a new type of non-ablative laser, Solid State Vaginal Laser, for vaginal tissue regeneration and rejuvenation.

2. Methods

Study design. This prospective observational multicenter study included postmenopausal women (absence of menstruation for at least 12 months) presenting with symptoms of GSM (vaginal dryness, irritation, soreness, dyspareunia and urinary incontinence), and not responding/being unsatisfied with previous local estrogen therapies.

Study exclusion were use of any hormone replacement therapies (either systemic or local) within the 6 months prior to inclusion in the study, use of vaginal moisturizers, lubricants or any other local preparation within the 30 days prior to inclusion in the study, acute or recurrent urinary tract and genital infections, serious or chronic illness that could interfere with the fulfillment of the study and psychiatric disorders precluding informed consent. The study protocol was approved by the Local Ethics Committee, and informed written consent was ob-

tained from study subjects.

Study protocol. All patients were treated with the non-ablative SSVL (LASEmaR 1500™-EUFOTON) with a wavelength of 1470 nm using a fluence (laser energy emitted per unit area) of 10 - 15 J/cm². The handpiece of the SSVL (LADYLIFT) used to perform the treatment is a vaginal internal probe developed for gentle introduction with a radial light emission in continuous mode working at 360° on the vaginal channel (**Figure 1**). Its spot size is larger than the spot size of the other vaginal laser (CO₂, Er: Yag spot size 150 - 300 micron) and this characteristic enables greater depth of penetration improving the absorption of energy at the target. Particularly this laser uses a laser wavelength with a proper mix between water absorption and tissue penetration without creating ablation. All eligible patients were submitted to vaginal biopsy before and after SSVL treatment to evaluate microscopic and ultrastructural modifications of vaginal mucosa.

According to our protocol, a treatment cycle included a laser application every 15 - 20 day for a total of 4 treatments in about two months. Time points of the study were at baseline (T0), at week 2 (T1), at week 4 (T2), at week 6 (T3), at week 8 (T4), and a follow-up after 4 weeks from the last laser application (T5). The procedure was performed in the outpatient clinic and did not require any specific preparation (e.g. analgesia/anesthesia). After each treatment the patients were advised not to have sexual activity and not to wear tight clothing and/or play sports that would rub the treated area for 1 week. We performed a bioptic vaginal sample before the start of the first treatment (T0) and after 4 weeks from the last treatment (T5).

Data assessments. Participants reported a cumulative intensity of GSM symptoms using a 10-cm VAS (dryness and/or burning and/or dyspareunia). The scale's left extremity indicates the complete absence of symptoms (0) and the



Figure 1. Vaginal probe.

right extremity indicates the worst possible symptom, and women rated the symptoms from 0 to 10. The vaginal health index (VHI), a quantitative assessment of vaginal health, was performed by the investigator to assess changes in vaginal elasticity, fluid volume, vaginal pH level, and epithelial integrity and moisture after treatment and at follow-ups after the final treatment (6, 12, and 24 weeks) compared to baseline. Each parameter was graded from 1 to 5, being atrophic a total score ≤ 15 [8]. The Female Sexual Function Index (FSFI) questionnaire was also administered. The FSFI is a 19-item, multidimensional self-report instrument for assessing the key dimensions of sexual function in women [9]. The secondary outcome was to analyze the efficacy of SSVL in patients affected by urge/stress incontinence using International Consultation on Incontinence Questionnaire–Urinary Incontinence Short Form (ICIQ–UI SF). The ICIQ–UI SF provides a brief and robust measure to assess the impact of symptoms of incontinence on quality of life and outcome of treatment [10].

It is a four diagnostic items questionnaire about frequency of urinary incontinence, amount of leakage, overall impact of urinary incontinence and self-diagnostic items that is used to screen for incontinence, to obtain a brief yet comprehensive summary of the level, impact and perceived cause of symptoms of incontinence. The scoring system consists in 0 - 21 overall score with greater values indicating increased severity and self-diagnostic item unscored. The test is considered normal when the ICIQ–UI SF score is <11 . Vaginal bioptic samples for each patient at baseline (T0) and after 4 weeks from the last treatment (T5) were also analyzed.

Differences between values at baseline and follow-up were analyzed with Wilcoxon signed-rank test for paired data. Statistical significance was set at $P < 0.05$. First, confirm that you have the correct template for your paper size. This template has been tailored for output on the custom paper size (21 cm * 28.5 cm).

3. Results

Eighty participants (mean age 57.2 ± 5.4 years) were enrolled in this study, their baseline characteristics are presented in **Table 1**. All participants completed the study protocol without any serious side effects. Only a temporary mild irritation of the introitus was noted that started immediately after the laser treatment, lasted up to 2 hours and resolved spontaneously.

The severity and the presence of GSM-symptoms decreased significantly, while the sexual function (as assessed by the FSFI) improved significantly (**Table 2** and **Figure 2**). At T4 70% of patients no longer complained of any symptoms; 15% declared a clear improvement; 10% claimed to have achieved a partial improvement; 5% said to have little benefit. No patients declared to be worse.

These results were also overlapping to four weeks after the last laser (T5).

The number of patients that at the beginning of the study had an FSFI score ≤ 26.55 (corresponding to sexual dysfunction) is dropped dramatically from 92%

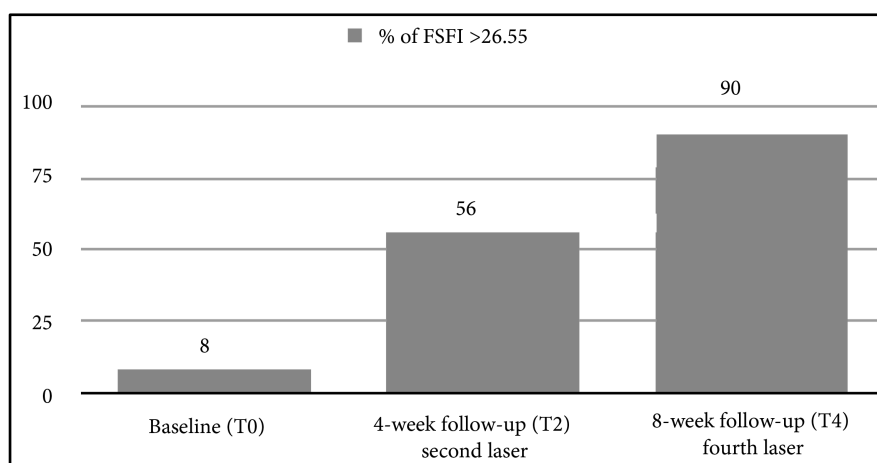


Figure 2. Changes in FSFI at baseline and after laser sessions.

Table 1. Patients demographics and baseline characteristics.

	Patients n. 80
Age (y)*	54.2 (\pm 5.2)
BMI (kg/m ²)*	25.3 (\pm 1.2)
Smoke: Yes-No	38 (47.5%) - 42 (52.5%)
Patients with previous breast cancer	4 (5.0%)
Parity	2 (1 - 3)
Sexual active women	72 (90.0%)
Previous systemic HRT	33 (41.0%)
Previous local HRT	50 (63.0%)
Duration of previous HRT (months)	33 (6 - 60)

* Mean values standard \pm deviation. HRT, Hormone Replacement Therapy; BMI, Body Mass.

Table 2. GSM symptoms (dryness and/or burning and/or dyspareunia) using a 10-cm VAS at baseline and after laser-sessions (T2-T4).

VAS	Baseline (T0)	4-week follow-up (T2) second laser	8-week follow-up (T4) fourth laser
0 - 1	--/--	15/80 (19)	56/80 (70)
2 - 3	4/80 (5)	5/80 (6)	12/80 (15)
4 - 5	8/80 (10)	12/80 (15)	8/80 (10)
6 - 7	11/80 (14)	25/80 (31)	--/--
8 - 9	37/80 (46)	17/80 (21)	4/80 (5)
10	20/80 (25)	6/80 (8)	--/--

Number (%).

to 44% after the second laser treatment. At the end of the study, after the last treatment, 10% of women showed an FSFI score \leq 26.55, demonstrating that SSVL is effective in 90% of the treated cases.

The VHIS increased significantly after the completion of the study protocol

(Table 2). At the baseline (T0), 90% of patients had a VHIS score <15 (atrophic epithelium). After three treatments, 74% of patients present a VHIS score >15. After the fourth last treatment, VHIS measures were further improved, demonstrating a restoration of vaginal epithelial tropism in 95% of treated women (Figure 3). Two of the patients who achieved inferior results on vaginal atrophy were in advanced age (76 and 79-years old) and the other two had had an early menopause before 40 years.

After the SSVL treatment almost all patients (91%) affected by urinary incontinence obtained the complete remission of symptoms: 97% were affected by urge-incontinence and 85% stress-incontinence (Figure 4). All vaginal tissue samples analyzed in T0 showed signs of atrophic vulvo-vaginitis of different severity, characterized by thinning of vulvo-vaginal epithelium with reduction or absence of papillae marked fibrosis of chorion. The reduction of collagen activity and the increase of inflammatory infiltrate, predominantly lymphocytic with or

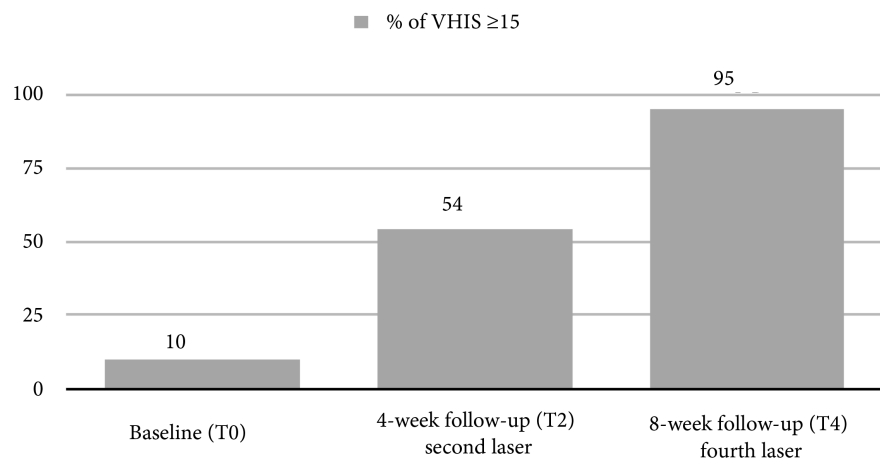


Figure 3. Changes in VHIS at baseline and after laser sessions.

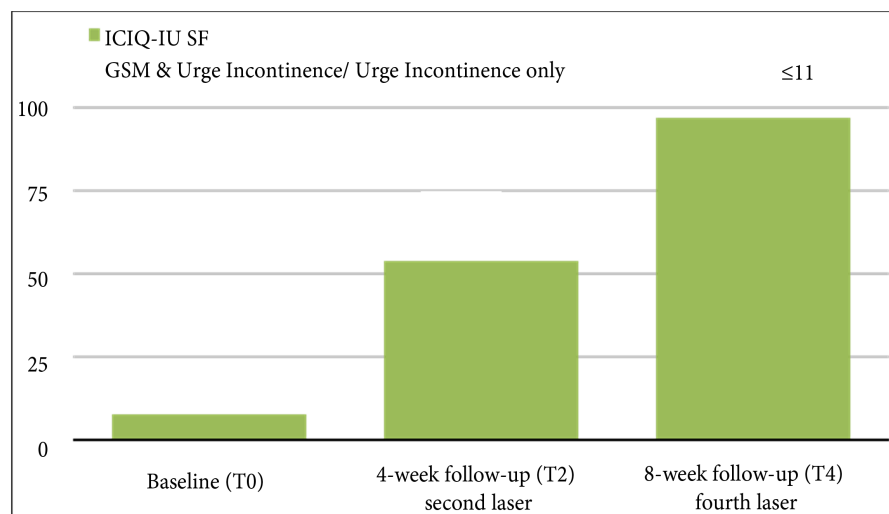


Figure 4. Changes in ICIQ-IU SF at baseline and after laser sessions.

without lichenoid “band” arrangement, can be observed. After four laser treatments (T4) the histological samples showed a coating epithelium that has regained its normal thickness a sort of “glycogenization” (glycogenic acanthosis). In the chorion we observed reduction of fibrosis and the increase of collagenic and angioblastic fibroblastic activity, “angioblastic granulation tissue-like”. Inflammation was also visibly reduced.

4. Discussion

This study assesses the efficacy of SSVL therapy in postmenopausal women with clinical signs and symptoms of GSM, focusing not only in the genital tract but also in the lower urinary tract. This efficacy was assessed in both principles of treatment (improvement of local pathophysiology and alleviation of symptoms) and it was independent to the participants’ baseline characteristics (*i.e.* years since last period). Improvement following the SSVL was observed on VHIS, VVA symptoms and sexual female function. This finding was also ratified by the improvement of vaginal histological features. Research has demonstrated the tissue remodeling properties of fractional lasers in aesthetic medical applications for body regions such as the skin of the face, neck, and chest, with the effect of stimulating the production of new collagen and elastin, bolstering the extracellular matrix [11]. Improvement of vulvovaginal symptoms after fractional laser has been demonstrated in multiple case series, though there is a need for larger-scale studies to assess the risk/benefit profile of this treatment in patients with GSM [12].

This study is the first to assess the effects of a new SSVL treatment on GSM symptoms, sexual function and bladder-related issues in postmenopausal women who had failed to respond to estrogen therapy or didn’t want to use it. In the short term (4 - 8 weeks after the initial treatment), we observed significant improvements in sexual function, dyspareunia, sexual issues, bladder function, vaginal sensation and lubrication. From baseline to 4 months follow-up, we recorded maintenance in improvement in all above mentioned variables.

Our findings are similar to those of different reports on the use of the fractional CO₂ laser and Er: YAG laser that revealed the capability to improve GSM symptoms [13].

The main contribution of this study is the use of a new type of SSVL. This SSVL is based on a non-ablative procedure like to the radiofrequency effect. Its handpiece is characterized by a larger spot that doesn’t focus the beam on surface, but deeply penetrates vaginal tissues, thus reaching that layers in which collagen fibers are more represented with greater effectiveness. It also avoids damaging mucosal surface, in opposition to what it happens using ablative and fractional ablative systems. Moreover, the VHIS increased significantly indicating the positive effect of the SSVL on vaginal health. This effect was in accordance to the findings of previous studies regarding the use of lasers in GSM patients. In addition, in our study, we demonstrated after four laser treatments

histological modifications that can be interpreted as tissue remodeling in a rejuvenating sense. Looking specifically at each single effect produced by SSVL, we observed a reduction of fibrosis and the increase of collagenic and angioblastic fibroblastic activity (angioblastic granulation tissue-like). To the best of our knowledge, only one study demonstrated histological changes in the vaginal wall of postmenopausal women irradiated with laser. In this trial according to our results, five women treated with microablative fractional CO₂ laser obtained neocollagenesis and restoration of the trabecular architecture of the collagen itself, which resembled what appeared in premenopausal women [14]. The VSSL equipment used in this study is based on a specific protocol, called Ladylift, performed with a laser with a wavelength of 1470 nm (Eufoton-Trieste-Italy) transmitted with a specific probe and parameters customized according to the patient.

The common mechanism of UI is pelvic floor dysfunction due to loss of its supportive function. The mechanical stability of the urethra and bladder neck is largely provided by intact pelvic muscles and connective tissue of the pelvis. Thus, the majority of therapeutic approaches aim at strengthening the support of the pelvic floor, either conservatively or surgically [15] [16].

The mechanism of action of laser treatment for SUI is largely due to thickening and strengthening of the vaginal wall with an emphasis to the anterior wall, which supports the bladder and urethra.

Our results suggest that VSSL working with sub necrotic temperatures, aim to influence collagen remodelling restoring the natural composition of a content pelvic floor [17].

However, this multicenter observational study has several limitations: lack of long-term follow-up, lack of randomization with a sham treatment and/or standard treatment, and absence of a comparator (placebo or other active treatment).

Nevertheless, the objective evaluation of VHIS, FSFI and ICIQ-UI SF scores and the histological results, however, indicates a real favorable effect of SSVL on GSM and on urinary incontinence.

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