

Sexual function after fractional microablative CO₂ laser in women with vulvovaginal atrophy

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ABSTRACT

Objective To investigate the effects of fractional microablative CO₂ laser on sexual function and overall satisfaction with sexual life in postmenopausal women with vulvovaginal atrophy (VVA).

Method This prospective study included 77 postmenopausal women (mean age 60.6 ± 6.2 years) treated for VVA symptoms with the fractional microablative CO₂ laser system (SmartXide² V²LR, Monalisa Touch, DEKA, Florence, Italy). Sexual function and quality of life were evaluated with the Female Sexual Function Index (FSFI) and the Short Form 12 (SF-12), respectively, both at baseline and at 12-week follow-up. A 10-mm visual analog scale was used to measure the overall satisfaction with sexual life and the intensity of VVA symptoms (vaginal burning, vaginal itching, vaginal dryness, dyspareunia and dysuria) before and after the study period.

Results We observed a significant improvement in the total score and the scores in each specific domain of the FSFI at 12-week follow-up compared to baseline ($p < 0.001$). After concluding the laser treatment, the overall satisfaction with sexual life significantly improved ($p < 0.001$). Seventeen (85%) out of 20 (26%) women, not sexually active because of VVA severity at baseline, regained a normal sexual life at the 12-week follow-up. Finally, we also found a significant improvement in each VVA symptom ($p < 0.001$) and in quality-of-life evaluation, both for the scores in the physical ($p = 0.013$) and mental ($p = 0.002$) domains.

Conclusions Fractional microablative CO₂ laser treatment is associated with a significant improvement of sexual function and satisfaction with sexual life in postmenopausal women with VVA symptoms.

INTRODUCTION

Vulvovaginal atrophy (VVA) defines a progressive age- and estrogen-dependent condition that may lead to the occurrence of symptoms, such as dryness, burning, itching, irritation, discharge and dysuria^{1,2}. VVA symptoms can affect up to 50% of postmenopausal women^{3–8} with a significant impact on quality of life and sexual function^{9,10}. The drop of estrogen after menopause determines histological involution both in

the vulva and in the vagina^{11,12}, such as thinning, reduced vascularization and elasticity, decreased engorgement and lubrication. All these changes are likely to produce an altered response to sexual stimuli and to dyspareunia¹³. VVA is therefore generally associated with female sexual dysfunction (FSD)¹⁴; pain during sexual intercourse, in fact, often co-exists with a decline in women's desire, arousal, orgasm and frequency of sexual activity throughout the menopausal transition and beyond^{15–17}.

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The management of urogynecological and sexual health should be individualized according to the VVA-associated conditions¹⁸; many hormonal and non-hormonal strategies have been proposed to alleviate VVA symptoms and to restore urogenital physiology^{12,19–21}. A variety of treatment strategies for FSD are available²²; non-pharmacological approaches would be welcome especially in those postmenopausal women with contraindications to hormones²³.

Fractional microablative CO₂ laser is safe in many body regions, such as the skin of the face, neck and chest, and has the ability to produce new collagen and elastic fibers with remodelling tissue properties^{24–26}. Recently, a pilot study demonstrated that the use of fractional microablative CO₂ laser in the treatment of VVA was feasible, efficacious and safe at 12-week follow-up²⁷. Its positive effects on VVA symptoms and quality of life²⁷ could improve not only the aspect related to sexual pain (dyspareunia, secondary vaginismus, and non-coital pain) but also other dimensions of women's sexual response, such as desire, initiative and receptivity to their sexual partner.

On this basis, we have carried out the present study aiming to investigate sexual function and overall satisfaction with sexual life in postmenopausal women treated for VVA symptoms by using the fractional microablative CO₂ laser.

METHODS

Study design

This prospective study was conducted between January 2013 and March 2014 at the Department of Obstetrics and Gynecology of the IRCCS San Raffaele Hospital and Vita-Salute San Raffaele University of Milan (a University teaching hospital and tertiary referral center in Northern Italy). It included postmenopausal women referred to our menopause clinic because of symptoms related to VVA. The study protocol was approved by the Hospital Research Review Committee and it represented an extension of an already published pilot study demonstrating the efficacy and feasibility of fractional CO₂ laser in the treatment of VVA²⁷. Women entered the study after an informed written consent was obtained.

Study population

Out of 84 patients selected to participate in the present study, 77 women (91.6%) were recruited. Each woman completed the 12-week follow-up and was included in the final analyses. For an intention-to-treat analysis, women unable to tolerate the insertion of the probe due to the severity of VVA and/or vaginal stenosis were considered to have the worst possible results. Inclusion criteria for referral were: symptoms of VVA (vaginal dryness and/or dyspareunia rated as moderate/severe most bothersome symptoms²⁸); age > 50 years; absence of menstruation for ≥ 12 months; not responding/being unsatisfied with previous local estrogen therapies; wishing to

maintain an active sexual life. Exclusion criteria 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 infections; active genital infections (e.g. herpes genitalis, candida); prolapse staged ≥ II according to the pelvic organ prolapse quantification system²⁹; previous reconstructive pelvic surgery; any serious disease or chronic condition that could interfere with study compliance; psychiatric disorders precluding informed consent.

Study protocol

Postmenopausal women were treated intravaginally with the fractional microablative CO₂ laser system (SmartXide² V²LR, Monalisa Touch, DEKA, Florence, Italy), using the following setting: dot power 30 watt, dwell time 1000 μs, dot spacing 1000 μm and the smart stack parameter from 1 to 3. The laser beam was provided using a vaginal probe gently inserted up to the top of the vaginal canal and subsequently withdrawn and rotated in order to provide a complete treatment of the vaginal wall. At the level of the vaginal introitus, we decreased the dot power to 20 watt²⁷. A treatment cycle included three laser applications (every 4 weeks). The procedure was performed in the outpatient clinic and did not require any specific preparation (e.g. analgesia/anesthesia). Patients were recommended to avoid coital sexual activity for at least 3 days after each laser application because a mild inflammatory reaction may last up to 48 h.

The primary outcome of the study was to investigate the changes in sexual function of women treated for symptoms related to VVA with fractional CO₂ laser. Secondary outcomes were: (1) changes in overall satisfaction with sexual life; (2) effects of the laser treatment on VVA symptoms and quality of life.

Data collection

Sociodemographic characteristics of the study sample were collected at baseline and inclusion/exclusion criteria were verified before starting the first laser application. The intensity of VVA symptoms (vaginal dryness, vaginal burning, vaginal itching, dyspareunia and dysuria) was measured using a 10-cm visual analog scale (VAS), where the left extreme of the scale indicated 'absence of symptom' and the right indicated 'symptom as bad as it could be', as previously reported in VVA^{30,31}. The intensity of VVA symptoms was evaluated at baseline, before starting the first laser application, and at 12-week follow-up, after 4 weeks from the last laser application. At the same time points, postmenopausal women filled in:

- (1) The Italian version of the Female Sexual Function Index (FSFI), a 19-item questionnaire developed as a brief, multidimensional, self-reported instrument for assessing the key dimensions of sexual function in women³². The questionnaire has been already used in the Italian gynecological

population^{33,34} and in randomized clinical trials to investigate sexual function³⁵. Indeed, it allows to obtain individual domain scores on a five-point scale (desire, arousal, lubrication, orgasm, satisfaction and pain) and total scale score (ranging from 2 to 36);

- (2) A 10-cm VAS to measure the overall satisfaction with sexual life³⁶, where the left extreme of the scale indicated 'the worst level of satisfaction' and the right indicated 'the best level of satisfaction';
- (3) The Italian version of the Short Form 12 (SF-12) to assess physical (PCS12) and mental (MCS12) component summary scores of quality of life³⁷, as previously reported³⁸.

Questionnaires were anonymous and a dedicated specialist nurse, who was not involved in the clinical evaluation and was unaware of the clinical data, collected each questionnaire after completion and labelled it by using a random computer-generated enrolment number. An Excel database was created containing the name of the patient, the enrolment number attributed to that particular case and the results of the questionnaires. The principal investigator created another Excel database (clinical database) containing the name of the patient and the clinical information but not the enrolment number. At the end of the study, the clinical database was given to the nurse and she created a third Excel database (final database) containing the enrolment number, the clinical information and the results of the questionnaires for each patient but not their names. All the analyses were performed by the principal investigator using the final database.

Statistical analysis

The sample size was defined in an arbitrary fashion on the basis of the novelty of the study and the lack of available literature on the role of the fractional microablative CO₂ laser in the treatment of VVA on sexual function.

The normal distribution of continuous variable data was evaluated with the Kolmogorov–Smirnov test. Categorical variables were analyzed using the McNemar test. Continuous variables, before and after treatment, were analyzed by using the paired *t*-test and the Wilcoxon Rank Sum Test accordingly to data distribution. The Spearman's rank correlation coefficient was used to assess whether PCS12 and MCS12 scores were correlated with FSFI total score and overall satisfaction with sexual life, either at baseline or at 12-week follow-up. Data were presented as mean \pm standard deviation. Data were analyzed using the SPSS software version 21.0 (SPSS Science, Chicago, IL, USA). A value of $p < 0.05$ was considered statistically significant.

RESULTS

The main characteristics of our study population are described in Table 1. Seventy-five patients (97.4%) enrolled in the study and completed the treatment with fractional CO₂ laser and

Table 1 Baseline characteristics of the study population ($n = 77$). Data are given as mean \pm standard deviation, n (%) or median (range)

Age (years)	60.6 \pm 6.2
Body mass index (kg/m ²)	23.5 \pm 2.0
Smokers	24 (31.2%)
Level of education	
primary	5 (6.5%)
secondary	45 (58.4%)
university	27 (35.1%)
Patients with previous live births	69 (89.6%)
Parity	2 (1–5)
Sexually active women	57 (74.0%)
Previous systemic HRT	29 (37.6%)
Duration of previous HRT (months)	28 (2–60)

HRT, hormone replacement therapy

returned at the 12-week follow-up. Two patients (2.6%; 95% confidence interval (CI) 0–6.2%) could not be treated because their vagina was too narrow and not compliant with the vaginal probe.

Changes in sexual function and overall satisfaction with sexual life

At baseline, 57 women (74.0%; 95% CI 64.2–83.8%) were sexually active, while 20 (26.0%; 95% CI 16.2–35.8%) reported not having coital sexual activity because of the severity of symptoms related to VVA. Already after one cycle of laser treatment, 17 of these patients (85.0%; 95% CI 69.4–100%) resumed coital sexual activity, whereas three women (15.0%; 95% CI 0–30.7%) remained inactive at the 12-week follow-up due to the persistence of VVA symptoms. Therefore, at the end of the study period, a total of 74 women (96.1%; 95% CI 91.8–100.0%; $p < 0.001$) were sexually active. Figure 1 reports the FSFI total and domain scores at baseline and after the study period. A significant improvement ($p < 0.001$) of FSFI total score was observed among sexually active women at the 12-week follow-up (27.2 ± 5.6 ; 95% CI 25.8–28.7) in respect to baseline (14.8 ± 7.7 ; 95% CI 12.8–16.8). Similarly, each individual FSFI domain score was ameliorated after fractional CO₂ laser application ($p < 0.001$, all) (Figure 1). When compared with baseline (4.3 ± 1.3), the overall satisfaction with sexual life was significantly higher at the 12-week follow-up (7.7 ± 1.6 ; $p < 0.001$) in sexually active women (Figure 2).

Changes in VVA symptoms and SF-12

Table 2 reports the presence and severity of VVA symptoms at baseline and after the study period. Before starting the laser treatment, vaginal dryness was reported by 69 women (89.6%; 95% CI 82.8–96.4%), vaginal burning by 66 (85.7%; 95%

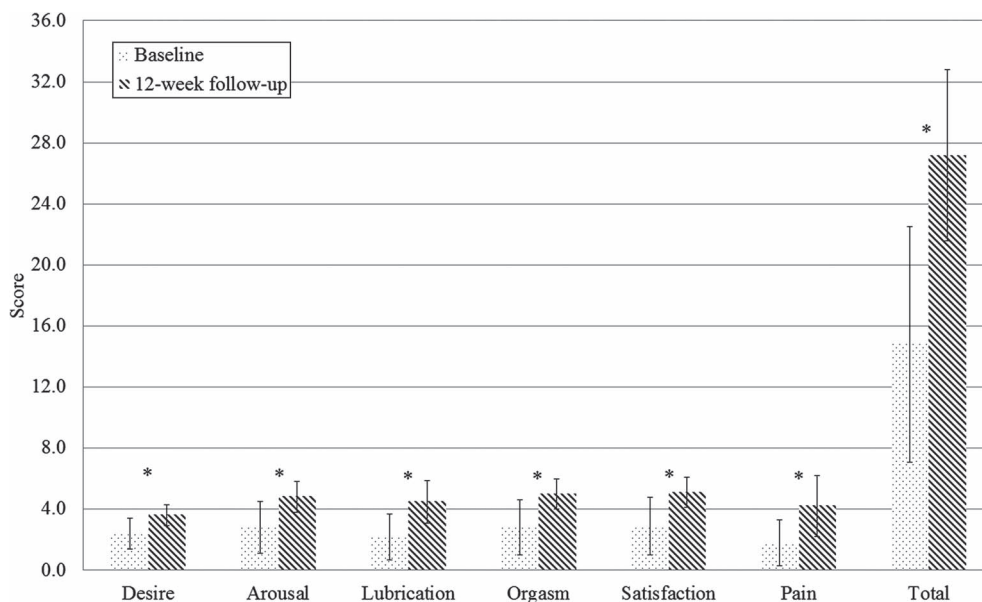


Figure 1 Female Sexual Function Index scores at baseline and at 12-week follow-up

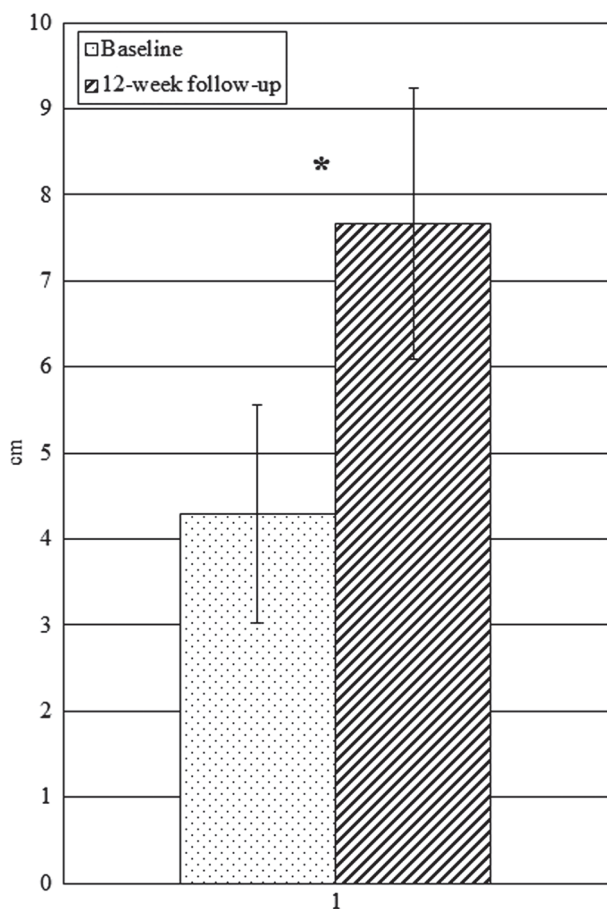


Figure 2 Overall satisfaction with sexual life (expressed as cm) at baseline and at 12-week follow-up

CI 77.9–93.5%), vaginal itching by 64 (83.1%; 95% CI 74.7–91.5%) and dysuria by 60 (77.9%; 95% CI 68.6–87.2%). Dyspareunia was experienced by 52 (91.2%; 95% CI 84.9–97.5%) women who were sexually active. At the 12-week follow-up, fractional CO₂ laser treatment was confirmed to be associated with a significant improvement in each VVA symptom ($p < 0.001$, all) (Table 2).

As far as quality of life measured by SF-12 was concerned, the PCS12 significantly improved ($p = 0.013$) at the 12-week follow-up (50.7 ± 6.5 ; 95% CI 49.3–52.2) in comparison with baseline (48.8 ± 6.4 ; 95% CI 47.4–50.2). The same significant improvement was observed for the MCS12 (43.2 ± 8.3 , 95% CI 41.4–45.1 at baseline vs. 46.1 ± 7.6 , 95% CI 44.4–47.8 at 12-week follow-up; $p = 0.002$). However, no significant correlation was evident between physical and mental components of quality of life and sexual function and overall satisfaction with sexual life, either at baseline or at the 12-week follow-up ($p > 0.05$, all).

DISCUSSION

This prospective study demonstrated that fractional microablative CO₂ laser is associated with a significant improvement in sexual function and overall satisfaction with sexual life in postmenopausal women complaining of VVA symptoms. After one cycle of laser treatment, 85% of sexually inactive women, presumably as a consequence of VVA, resumed an active sexual life. Such a positive effect was likely related to both restoration of genital tissues and alleviation of urogenital symptoms. Indeed, our current data confirmed the efficacy of fractional microablative CO₂ laser treatment in improving

Table 2 Presence and severity of vulvovaginal atrophy symptoms in our study sample. Data are given as mean \pm standard deviation (95% confidence interval)

	Number of women (%)	Baseline	12-week follow-up
Vaginal dryness [†] (cm)	69 (89.6%)	8.4 \pm 2.0 (7.9–8.9)	2.8 \pm 1.8* (2.4–3.2)
Vaginal burning [†] (cm)	66 (85.7%)	6.2 \pm 2.7 (5.6–6.9)	2.2 \pm 2.8* (1.5–2.9)
Vaginal itching [†] (cm)	64 (83.1%)	6.4 \pm 2.7 (5.7–7.1)	2.1 \pm 2.0* (1.6–2.6)
Dyspareunia [†] (cm)	52 (91.2%) [‡]	8.4 \pm 2.4 (7.8–9.1)	2.8 \pm 2.1* (2.2–3.4)
Dysuria [†] (cm)	60 (77.9%)	5.7 \pm 2.8 (5.0–6.4)	2.6 \pm 1.9* (2.1–3.1)

*, Statistically significant difference in comparison with baseline ($p < 0.001$ for each); [†], measured on a 10-cm VAS scale (range: 0–10); [‡], calculated out of the 57 women who were sexually active at baseline

VVA symptoms and quality of life at the 12-week follow-up; these results are consistent with the ones of our previous pilot study showing also a significant improvement in the vaginal health index²⁷.

A strength of our study was the evaluation of women's sexual function by using a standardized specific questionnaire^{32–34} to measure, in a statistically significant manner, multiple dimensions of their sexual response; we also added a subjective evaluation based on patients' perception of satisfaction with sexual experience and of VVA symptoms^{27,36}. Moreover, the high rate of women becoming sexually active and the significant reduction in dyspareunia were further elements supporting fractional microablative CO₂ laser as an effective treatment for postmenopausal women complaining of VVA symptoms and concomitant FSD. The most important limitation of our study is the absence of a control arm with a sham procedure (given the high placebo response reported in interventional trials on FSD³⁹) or with hormonal treatment. Furthermore, the lack of randomization did not allow an effective control of confounding factors (i.e. higher motivation for sexual activity because of participation in the study, partners' higher interest for sexual intercourse as they know their partners underwent the treatment, selection bias toward higher inclusion rate among women more motivated for the change in their sexual life) which may affect the findings of the current study. In addition, at the present time, the short-term follow-up limits our ability to document the duration of such a treatment in term of sexual well-being; however, in dermatology the persistence of skin collagen remodeling has been reported after 3 months since the last laser session⁴⁰. Another potential limitation of our study is that we cannot be completely sure that women did not use any vaginal products throughout the study period, despite our clear instruction to avoid any kind of product. Indeed, it is well known that postmenopausal women with symptoms related to VVA widely use non-prescription lubricants when needed, as a personal strategy to counteract sexual pain at intercourse, because they do not easily recognize the chronic nature of the VVA condition^{7,41}.

The strong association between fractional microablative CO₂ laser treatment and significant improvement in sexual function, perception of sexual health and VVA symptoms

encourages us to continue with further research in different clinical populations and with a long-term follow-up. Moreover, whether such a technique may exert a synergic effect with systemic and/or local hormonal treatments and other non-hormonal substances/devices to treat VVA remains to be fully investigated.

It is well established that the clinical expression of sexual symptoms in menopause is influenced by several factors, ranging from significant decline of estrogen and androgen production to intrapersonal and interpersonal factors⁴². Hormonal changes may impair the normal structure and function of genital tissues by influencing sensation, vasocongestion, lubrication, smooth muscle relaxation and vaginal microbiota. Indeed, especially the absence of estrogen stimulation contributes to the loss of mucosal elasticity by inducing fusion and hyalinization of collagen fibers and fragmentation of elastin fibers. Even mucosal hydration is reduced in the dermal layer with a reduction of intercellular mucopolysaccharide and hyaluronic acid^{1,2,11,12,43}. The hemodynamic process of sexual arousal, involving the peripheral neurovascular complex and the pelvic floor muscles, is tightly linked to the biomechanical and viscoelastic properties of the vaginal wall. Women with VVA have difficulties in opening and distending the introitus, are less capable of lubricating in response to sexual stimuli and, as a consequence of the shortening and narrowing of the vaginal vault, experience painful and/or unpleasant intercourse^{2,10,12,44}. Over time, postmenopausal women who are sexually active may develop hypertonic pelvic floor with secondary vaginism triggered by avoidance, anxiety and loss of sexual desire because of the anticipation of coital pain⁴⁵.

We have previously shown that vaginal laser technology was able to ameliorate elasticity, fluid volume, pH, epithelial integrity and moisture in postmenopausal women with symptoms related to VVA not responding/being unsatisfied with previous local estrogen therapies²⁷. The precise mechanisms underlining the normalization of some vaginal properties is not yet completely clear but collagen remodelling and increased vascularization have been documented in *ex vivo* vaginal specimens following laser application⁴⁶. Such an improvement of vaginal receptivity seems to be crucial for resuming sexual activity in women with FSD associated with VVA, as confirmed by the present data. On the other hand,

maintaining an active sexual life is a well-known protective element to counteract the loss of mucosal elasticity and hydration consequent to estrogen deprivation⁴⁷.

It is of paramount importance that health-care professionals display a positive attitude in discussing sexual health with postmenopausal women, to recognize signs and symptoms of VVA and, eventually, to look for potential treatment strategies^{6,7,10}. Therapeutic options should be tailored for each individual woman in the context of her personal biopsychosocial profile to optimize healthy aging and partnership. Indeed, the interest in continuing sexual activity is a component of life satisfaction and successful aging⁴⁸. Even though a significant proportion of middle-aged and older women still engages in satisfying sexual activity⁴⁹, more than one-third reports some problems with sexual function⁵⁰ and deserves specialized attention and care.

In conclusion, the present study demonstrated that the fractional microablative CO₂ laser is associated with an

improvement of sexual function and satisfaction with sexual life in postmenopausal women by treating symptoms related to VVA. Whether or not such an effect is long lasting and meaningful for sexual intimacy over time remains to be investigated in further studies with a longer follow-up and in comparison with other effective therapies.

Conflict of interest During the past 2 years, Dr Nappi had financial relationships (lecturer, member of advisory boards and/or consultant) with Bayer-Schering Pharma, Eli Lilly, Gedeon-Richter, HRA Pharma, Merck Sharpe & Dohme, Novo Nordisk, Pfizer Inc, Shionogi Limited, Teva/Theramex. Dr Salvatore had financial relationships (lectures, member of advisory boards and/or consultant) with DEKA. The other authors did not report any potential conflicts of interest.

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