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SHORT REPORT

Sexual function after vaginal erbium laser: the results of a large, multicentric, prospective study

M. Gambacciani[a], E. Albertin[b], M. G. Torelli[c], G. L. Bracco[d], A. C. Casagrande[e], L. Martella[f], G. Baiocchi[g], S. Alfieri[h], N. Russo[i] and M. Cervigni[j]; for the Italian Vaginal Erbium Laser Academy

[a]Department of Obstetrics and Gynecology, University Hospital, Pisa, Italy; [b]Gynecological Clinic Elysium, Albignasego (Padova), Italy; [c]Centro Palmer, Reggio Emilia, Italy; [d]Ospedale Campo di Marte, Lucca, Italy; [e]Studio Medico, Novara, Italy; [f]Centro Medico Radiologico 3P, Noventa di Piave, Italy; [g]Department of Obstetrics and Gynecology, University of Perugia, Italy; [h]Centro Mediprò Bologna, Italy; [i]Centro Medico Demetra, Grottaferrata, Italy; [j]Clinica Paideia, Rome, Italy

ABSTRACT

The aim of this multicentric, prospective study was to evaluate the effects of vaginal erbium laser (VEL-SMOOTH®) on sexual function in postmenopausal women suffering from the genitourinary syndrome of menopause (GSM). This study was performed on an outpatient basis without anesthesia or drug use before or after the intervention, using an erbium laser (XS Fotona Smooth®, Fotona, Ljubljana, Slovenia) in 1081 postmenopausal women (age 54.3 ± 3.9 years) treated with up to three laser applications every 30 days. Patients were assessed using the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale-Revised (FSDS-R). No adverse events were recorded during the study. The FSDS-R scores ($n = 554$), from basal values of 25.5 ± 3.5, were 11.5 ± 3.0, 10.5 ± 3.5 and 11.5 ± 3.5 at the 4-, 12- and 24-week follow-ups, respectively ($p < 0.01$ vs. corresponding basal values). Individual FSFI domain scores ($n = 569$) significantly ($p < 0.001$) increased after VEL-SMOOTH® treatment and remained significantly higher up to the 24th week after the end of treatment. The total scores, from basal values of 15.5 ± 1.5, were 27.5 ± 2.5, 27.6 ± 2.7and 27.0 ± 3.5 at the 4-, 12- and 24-week follow-ups, respectively ($p < 0.01$ vs. corresponding basal values). Albeit not randomized, this large, prospective study shows that VEL-SMOOTH® treatment may improve sexual function in postmenopausal women suffering from GSM.

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Introduction

The genitourinary syndrome of menopause (GSM) includes a variety of menopausal signs and symptoms related to estrogen deficiency, including also sexual symptoms, jeopardizing the quality of life and sexual relationships of postmenopausal women[1]. GSM is chronic and is likely to worsen over time, affecting up to 50% of postmenopausal women[1,2]. The symptoms related to GSM include genital symptoms of dryness, burning, irritation, but also sexual symptoms of lack of lubrication, discomfort or pain, and impaired function, as well as urinary symptoms of urgency, dysuria and recurrent urinary tract infections[1]. Female sexual dysfunction (FSD) afflicts approximately 40% of women and is characterized by diminished vaginal lubrication, pain and discomfort upon intercourse, decreased sense of arousal and difficulty in achieving orgasm[2]. FSD is far more common in postmenopausal women suffering from GSM than in the normal population[2]. The management of GSM can be individualized according to the woman's conditions and preferences, including hormonal and non-hormonal products, either for local or systemic administration[2–5]. Recently, several papers have reported that the new, non-invasive vaginal erbium laser (VEL-SMOOTH®) therapy is effective in the treatment of GSM[6–13]. The aim of the present study was to evaluate the effectiveness and acceptability of VEL-SMOOTH® in postmenopausal women with GSM suffering from FSD.

Methods

Study design

The Vaginal Erbium Laser Academy (VELA) designed this spontaneous, multicenter, prospective study[7]. Inclusion criteria were: the presence of GSM diagnosed on the basis of subjective symptoms and signs, the presence of a concomitant jeopardized sexual life in otherwise healthy, sexually active postmenopausal women; all patients included in the study were referred to the VELA center for the laser treatment. All patients were at least 12 months since their last menstrual period or bilateral oophorectomy, presenting a negative Papanicolaou smear. Exclusion criteria were: vaginal lesions, scars, active or recent (30 days) infections of the genitourinary tract; abnormal uterine bleeding; use of vaginal preparations within the 30 days prior to the study; history of photosensitivity disorder or use of photosensitizing drugs; genital prolapse; serious or chronic condition that could interfere with study compliance; treatment with hormones to

CONTACT M. Gambacciani margamba54@gmail.com Department of Obstetrics and Gynecology, Pisa University Hospital, Via Roma 67, 56100 Pisa, Italy

relieve menopausal symptoms in the 6 months before the study. This prospective study was performed on an outpatient basis using erbium laser (XS Fotona Smooth®, Fotona, Ljubljana, Slovenia) in postmenopausal women treated with VEL-SMOOTH® every 30 days[13]. Laser parameters (Renovalase™ mode) were set as previously reported[13].

At the first visit, the eligibility of the patient was verified, the written informed consent was obtained, and the sociodemographic and clinical characteristics were collected. Symptoms were assessed before and after 24 weeks from the last VEL-SMOOTH® treatment, using the Female Sexual Function Index (FSFI)[14] and the Female Sexual Distress Scale-Revised (FSDS-R). The Italian version of FSFI, a 19-item questionnaire developed as a brief, multidimensional, self-reported instrument for assessing the key dimensions of sexual function in women (desire, arousal, lubrication, orgasm, satisfaction, and pain) has been validated and used in the Italian population[15–17]. Questionnaires were anonymous, labelled by an enrolment number and collected at baseline, and at the follow-up visits at 4 and 12 weeks after the last VEL-SMOOTH® treatment. Patients were enrolled in the study presenting a FSDS score over 11 and a total FSFI score under 26, the cut-off values of both questionnaires for the diagnosis of FSD. Only subjects in the safety population who had filled in the questionnaire at both baseline and post-treatment time points were included in analyses. If one question (or more) had not been answered, the answer(s) given at baseline was included. If there were missing data, this subject had the last observation carried forward for analysis. The laser treatment was performed every 4 weeks (two laser procedures in 651 patients and three laser procedures in 221 patients). Since no differences in the study outcomes were evidenced, the two groups of patients were examined together. The procedure was performed in the outpatient clinic and did not require any specific preparation (e.g. analgesia/anesthesia). No additional hormonal or non-hormonal treatment was allowed during the study.

All the results are reported as the mean ± standard error of absolute values. Analysis of variance for repeated measures was used to test the differences in different time points. The *post-hoc* comparison was made by Scheffe *F*-test, using the Sigma Stat View software (SPSS Science, Chicago, IL, USA).

Results

A total of 1081 sexually active postmenopausal women (age 54.3 ± 3.9 years) reporting GSM were recruited in 47 Italian centers. The study recruitment[7] was stopped when the interim evaluation of the data, performed bi-annually, was consistently showing the effects of VEL-SMOOTH® on the selected parameters. More than 50% of the patients completed and returned the study protocol questionnaires at all time points (554 FSDS tests and 569 FSFI tests). The remaining questionnaires were not completed at all given time points and therefore were not included in the statistical analysis.

The FSDS-R scores, from basal values of 25.5 ± 3.5, were 11.5 ± 3.0, 10.5 ± 3.5 and 11.5 ± 3.5 at the 4-, 12- and 24-week follow-ups, respectively ($p < 0.01$ vs. corresponding basal values, Figure 1).

Individual FSFI domain scores significantly ($p < 0.01$) increased after VEL-SMOOTH® treatment, and remained significantly higher, up to the 24th week after the end of treatment (Table 1). The total scores, from basal values of 15.5 ± 1.5, were 27.5 ± 2.5, 27.6 ± 2.7 and 27.0 ± 3.5 at the 4-, 12- and 24-week follow-ups, respectively ($p < 0.01$ vs. corresponding basal values, Table 1).

Discussion

The results of this large, multicentric, prospective study show that VEL-SMOOTH® is effective in improving sexual function and overall satisfaction with sexual life in postmenopausal women suffering from severe GSM. Previous studies demonstrated that the effects of VEL-SMOOTH® on GSM signs and symptoms are rapid and long-lasting[6–13]. Present data confirm the positive effects of VEL-SMOOTH®, suggesting that

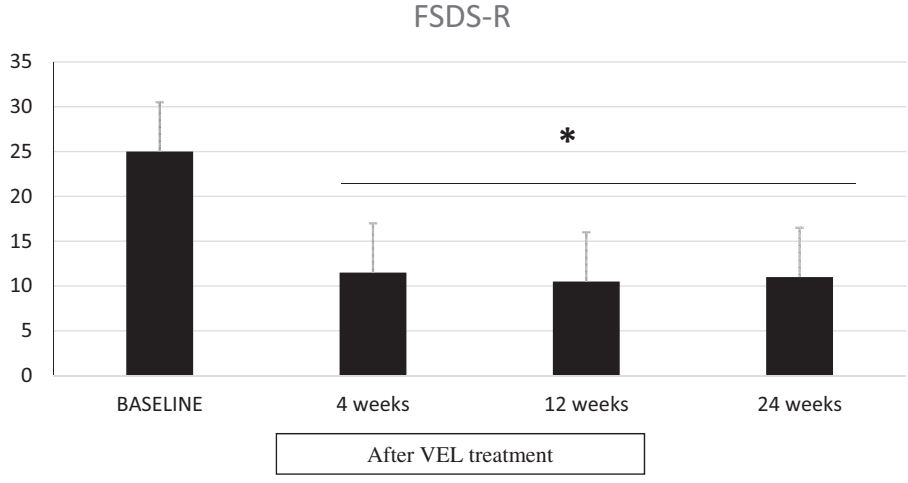

Figure 1. The values of 554 Female Sexual Distress Scale-Revised (FSDS-R) tests in baseline conditions and after treatment with vaginal erbium laser (VEL), irrespective of number of laser treatments (see text for details). Data are presented as mean ± standard error. *The values were significantly ($p < 0.01$) different vs. basal values.

Table 1. The values of 569 Female Sexual Function Index (FSFI) tests in baseline conditions and after treatment with vaginal erbium laser, irrespective of number of laser treatments (see text for details). Data are presented as mean ± standard error. The values of each specific domain and total score after the treatment and at the end of the observation period were significantly ($p < 0.01$) different vs. corresponding basal values.

		After treatment		
FSFI domain	*Before treatment*	*4 weeks*	*12 weeks*	*24 weeks*
Desire	3.0 ± 0.5	4.0 ± 1.5	4.5 ± 1.5	4.7 ± 1.5
Arousal	2.7 ± 1.5	4.0 ± 1.5	4.0 ± 1.5	4.0 ± 1.5
Lubrication	2.1 ± 0.5	4.8 ± 0.5	4.9 ± 0.5	4.8 ± 1.5
Orgasm	2.7 ± 0.7	4.0 ± 0.5	4.0 ± 0.5	4.0 ± 1.5
Satisfaction	2.5 ± 1.5	4.9 ± 1.5	4.9 ± 1.5	4.9 ± 1.5
Pain	2.5 ± 0.5	4.8 ± 0.5	4.9 ± 0.5	4.7 ± 1.5
Total score	15.5 ± 1.5	27.5 ± 2.5	27.6 ± 2.7	27.0 ± 3.5

this non-invasive treatment is appropriate for women suffering from GSM-related FSD[18]. The present study was not designed to evaluate the multicomponent aspects of sexuality in postmenopausal women. However, since vaginal atrophy is an essential component of dyspareunia and its reflexes on sexuality, the VEL-SMOOTH®-induced vasodilation and collagen remodeling could be considered essential for the improvement of sexual activity in women with FSD associated with GSM. The improvement of vaginal tissue conditions, thus, may lead to better sexual activity and satisfaction, explaining why distinctive items of the FSFI test, such as desire, arousal and orgasm, improve after VEL-SMOOTH® treatment.

Albeit not controlled and randomized, the strength of our longitudinal, prospective study resides in the large number of subjects included and the evaluation of sexual function by using standardized questionnaires in a large, homogeneous group of postmenopausal women suffering from GSM and concomitant FSD. All patients included in the study were suffering from FSD, as evidenced by the basal values of FSDS and FSFI tests. In fact, the mean basal FSDS-R score was 25.5 ± 3.5, more than double the cut-off limit of 11, while the basal FSFI was 15.5 ± 1.5, far from the cut-off value of 25 for the FSD diagnosis.

As mentioned earlier in the introduction, the women were not recruited on the basis of a defined level of sexual dysfunction but on the basis of the requirement for GSM treatment. The major flaw of our study is the absence of a control arm with a sham laser procedure. Placebo responses are substantial in many clinical trials of treatments for FSD[19]. However, VEL-SMOOTH® induces improvement of subjective symptoms and objective signs of vaginal atrophy[6–13], up to the 12th month of observation in a long-term, 24-month, follow-up study[13]. Thus, we can hypothesize that the results in the VEL-SMOOTH®-treated women may be attributed to the laser's efficacy and not to a speculative, hypothetical placebo effect. In addition, it would be quite unusual that a putative placebo effect could last 24 weeks after VEL-SMOOTH® treatments, when as, *per protocol*, the women were evaluated. Although a possible placebo effect cannot be ruled out, the consistency of positive results up to a 24-week follow-up period indicates that placebo is not the main mode of action of VEL-SMOOTH® therapy[8–13]. Moreover, the lack of randomization did not allow an effective control of confounding factors (i.e. selection bias, changes in partners, etc.). In addition, we cannot eliminate the doubt that women did not use any vaginal products during the follow-up period, even though we clearly suggested they avoid any kind of treatment. However, the women enrolled were recruited for their severe GSM-related FSD before the study, when they were free to use any kind of prescription or over-the-counter product. The VEL-SMOOTH® treatment was associated with a significant improvement in FSD. Therefore, it is odd that the improvement could be ascribed to the more recent use of non-prescription products just after the VEL-SMOOTH® treatment. In the present study, all women received laser therapies due to GSM symptoms. Consequently, our population is not representative of all women suffering from FSD, and the results can just reflect the effects of VEL-SMOOTH® on GSM. In addition, at the present time, the short-term follow-up limits our ability to document the lasting effect of laser technology in term of sexual well-being, as has been demonstrated for the subjective and objective signs of GSM[11–13]. As it was designed and conducted, this study cannot fully assess the rate of non-responders to the treatment. However, 465 women showed a significant improvement in the FSDS score (83.9%), and 484 women (87.4%) showed a significant increase in the FSFI total score out of 554 valid completers. On the other hand, in a previous prospective study[13], we reported a high response rate to VEL-SMOOTH® therapy, since 174 women out of a total of 205 patients (84.9%) decided to repeat the complete VEL-SMOOTH® procedure.

Several therapeutic options are available to alleviate GSM symptoms, including hormonal and non-hormonal products, and selective estrogen receptor modulators, either for local or systemic administration[3–5,20,21]. At variance with microablative CO_2 lasers[18,22,23], VEL-SMOOTH® produces non-ablative, controlled hyperthermia followed by vasodilatation and collagen remodelling, resulting in overall restoration of vaginal tissues[18]. There are no tissue damage, drilling, ablations, bruises, bleedings or burning, making this technique suitable for multiple repetitions, with no serious adverse events, as reported in more than 43,000 women treated worldwide[24]. Medical societies support vaginal estrogen use, even in women with a history of estrogen-dependent breast cancer in consultation with their oncologist[3–5,20,21]. However, in their Statements, these societies underline limitations, such as the duration of treatment which must be short, that conflict with the chronic and progressive nature of GSM and its consequences for sexuality. Therefore, alternative treatments are needed to offer safe and long-term therapeutic strategies. Present data suggest that VEL-SMOOTH® can be considered an option for the management of FSD associated with GSM in women that do not want or cannot be treated with estrogen or any other local therapy.

Further properly designed, randomized studies are required to explore the use of VEL-SMOOTH® in GSM patients suffering from FSD, in order to evaluate whether VEL-SMOOTH® may exert an integrated, synergic effect in association and/or in sequence with other non-hormonal or hormonal treatments.

Potential conflict of interest The authors declare no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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