The Effect of Fractional CO_2 Laser Treatment on the Symptoms of Pelvic Floor Dysfunctions: Pelvic Floor Distress Inventory-20 Questionnaire

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Background and Objectives: To assess the improvement on pelvic floor distress (PFD)-related urogenital symptoms using validated questionnaires after intravaginal CO_2 laser treatment.

Study Design/Materials and Methods: Forty postmenopausal women with genitourinary symptoms of menopause (GSM) were enrolled into this prospective cohort study and underwent vaginal laser treatment using MonaLisa Touch® fractional CO_2 laser system. Patients received three vaginal laser treatments with 360° probe 4 weeks apart. A three-component Pelvic Floor Distress Inventory (PFDI-20) validated questionnaire was filled out by each patient before each session and 4 weeks after the final treatment. Wilcoxon rank sum test was used to compare the before and after treatment scores.

Results: Pelvic Organ Prolapse Distress Inventory (POPDI-6) scores were not significantly different after the first treatment compared with baseline (mean ± standard deviation [SD], 21 ± 18 vs. 17 ± 15, $P = 0.44$). However, each subsequent treatment resulted in further, statistically significant improvement in symptom scores (14 ± 15, $P = 0.03$ and 13 ± 13, $P = 0.01$, after the second and third treatments, respectively). Similarly, Urinary Distress Inventory (UDI-6) scores were not significantly different after the first laser treatment (mean ± SD, 36 ± 25 vs. 29 ± 23, $P = 0.36$). After the second and third treatments there were significant improvement in the standardized scores (24 ± 20, $P = 0.03$ and 22 ± 21, $P = 0.01$). Colorectal-Anal Distress Inventory (CRADI-8) scores did not change significantly after three laser treatments.

Conclusions: Three sessions of microablative fractional CO_2 vaginal laser treatment significantly improves patient reported urinary and pelvic organ prolapse symptoms. © 2019 The Authors. *Lasers in Surgery and Medicine* Published by Wiley Periodicals, Inc.

Key words: CO_2 laser; vagina; pelvic floor dysfunctions; fractional laser

INTRODUCTION

Genitourinary syndrome of menopause (GSM) is the new term for vulvovaginal atrophy (VVA) according to the International Society for the Study of Women's Sexual Health and the North American Menopause Society [1]. These genitourinary changes are a response to the decreased level of circulating estrogen caused by ageing. The hypoestrogenic environment leads to significant tissue changes such as loss of collagen, elastin, and smooth muscle in the genital/vaginal tissues resulting in thinning of the vaginal epithelium, diminished blood flow, elasticity, and rugation [2]. Morphological changes lead to atrophic genitalias causing irritation, itching, burning, dyspareunia, and contact bleeding [3]. The syndrome altogether with its bothersome symptoms affects 40–54% of postmenopausal women and negatively influences their everyday lives [4].

There are several treatment options for GSM, which depend upon symptom severity. In cases of mild symptoms or when hormone therapy is contraindicated, nonhormonal over-the-counter (OTC) products like lubricants and moisturizers are useful. If nonhormonal therapy does not provide satisfactory symptom relief and the women have no contraindications, locally applied estrogen in cream, tablet, or a ring delivery system may be offered [5].

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Systemic hormone replacement therapy (HRT) is only offered to patients who need treatment for other perimenopausal symptoms besides GSM [6].

Many women are reluctant to use hormonal products and desire a more durable treatment than OTC products. Most recently vaginal laser treatment was introduced as a novel option for women with GSM. Many clinical trials have investigated its efficacy and described the beneficial effects of vaginal laser treatment, which include improvement in subjective symptoms of GSM, vaginal health and flora, sexual function and dyspareunia, and urinary incontinence [7–13]. Zerbinati et al. described microscopic ultrastructural changes of vaginal mucosa connective tissue after fractional CO_2 laser treatment. They were able to confirm the production of new extracellular matrix elements such as collagen, glycosaminoglycans, proteoglycans, and multi-adhesive glycoproteins [14]. Cruz et al. [15] investigated the effect of vaginal CO_2 laser treatment alone and also compared it in combination with topical estriol cream and placebo cream versus sham laser treatment and found that laser treatment is beneficial. Other studies suggest that laser therapy may be valuable as nonhormonal therapeutic modality when HRT is not recommended [16,17]. Although the Food and Drug Administration approved the CO_2 laser and YAG laser therapy for several dermatologic and plastic surgery indications, it has not been approved for GSM, but several previous studies have revealed a beneficial effect of vaginal microablative fractional laser on GSM.

Pelvic floor dysfunction is a global term used to describe conditions such as irritative lower urinary tract symptoms (LUTS) or dry form of overactive bladder (OAB), pelvic organ prolapse (POP), anal/fecal (AI/FI) or urinary incontinence (UI), and chronic pelvic pain. The pathogenesis and symptoms of these conditions are partially overlapped with GSM [18]. The prevalence of PFD increases by age especially after menopause as a consequence of reduced circulating esrogen. On the basis of epidemiological studies POP, UI, FI, and other PFD symptoms affect approximately 32–35% of perimenopausal and postmenopausal women [19,20], the same population which frequently complains about GSM. Prior studies have not evaluated the effects of laser treatment on pelvic floor dysfunctions. Our hypothesis was that women undergoing vaginal laser treatment will report improvement not just in GSM but also in pelvic floor dysfunctions. Our goal in this pilot study was to assess the effects of vaginal laser treatment on pelvic floor dysfunctions using validated and commonly used questionnaires.

MATERIAL AND METHODS

In this prospective cohort study, patients were enrolled at the outpatient urogynecology clinic of the Department of Obstetrics and Gynecology, University of Debrecen, Hungary between March 2017 and March 2018. Enrollment criteria included the presence of any of the following symptoms in a postmenopausal woman: GSM/VVA, mild stress, or urgency urinary incontinence (UI), feeling of looseness of the vagina due to the lack of pelvic muscle tone, or symptoms of low grade pelvic organ prolapse (POP), defined as ≤Stage II prolapse according to the pelvic organ prolapse quantification system (POP-Q) [21]. To be considered postmenopausal, individuals had to have at least 12 consecutive months of amenorrhea without any other obvious reason or consistently elevated follicle-stimulating hormone (FSH) blood levels of 30 mIU/ml or higher. Exclusion criteria included pregnancy, hormone therapy in the previous 2 years (local or systemic), vaginal infection at presentation, cytological atypia, dysmenorrhea, POP > Stage II, severe UI, severe fecal incontinence (FI) or any disease, which would interfere with the study protocol. Patients were also asked to suspend the vaginal use of any nonhormonal or other products at least six weeks prior to intravaginal laser treatment.

At the first visit general gynecological visit, a medical history was taken (age, body mass index, previous deliveries or operations, menstruation cycle, onset of menopause, hormonal therapy). Patients were asked to complete the Pelvic Floor Distress Inventory (PFDI-20) questionnaire, which has three components: Pelvic Organ Prolapse Distress Inventory 6 (POPDI-6), Colorectal-Anal Distress Inventory 8 (CRADI-8), and Urinary Distress Inventory (UDI-6). POPDI-6 assesses bother from prolapse, the CRADI-8 inquires about defecatory distress, and the UDI-6 assesses urinary bother. Women underwent three sessions of intravaginal microablative CO_2 laser therapy 4–6 weeks apart and filled out the PFDI-20 questionnaire at the following timepoints: "baseline" before the first treatment; after the first treatment (right before the second treatment); after the second treatment (right before the third treatment); and 6 weeks after the final, third treatment of CO_2-Laser system (SmartXide2V2LR, MonaLisa Touch®; DEKA, Florence, Italy). Demographic and pertinent clinical information was recorded prospectively and stored in a dedicated database.

Our study was approved by the Hungarian National Institutional Review Medical Research Council. All women signed a written informed consent prior to participating in our research. There were no withdrawals or discontinuation of treatment due to adverse events.

Questionnaires

Internationally standardized questionnaires intended to demonstrate subjective pelvic floor symptoms were examined. Out of the several questionnaires available, we have selected the short-form version of the PFDI-20. Previously this questionnaire was found valid, reliable, and responsive to clinically important changes [22,23].

The PFDI-20 has three scales: POPDI-6, CRADI-8, and UDI-6. To specify the severity of pelvic floor distress symptoms the patients find response options ranged from 0 ("no" references "no symptoms"), 1 ("not at all" references "symptoms are present but not bothered at all") to 4 ("quite a bit" as in symptoms are present and quite bothersome). To calculate the score, the mean score of answered items within each component is multiplied by 25 to obtain the scale score (range 0–100). Summary

scores are calculated by summing the scale scores (range 0–300). Higher scores indicate more symptom distress [22,24].

Laser Therapy

For laser treatment microablative, fractional CO_2 laser system (SmartXide2V_2LR; Deka) was applied, with a specific 360° probe designed for intravaginal procedures. Laser beams were fractionally emitted in small points (DOT's) around the vaginal mucosa during treatment. To achieve the required effect, the laser was used in D-Pulse mode. Depth was set, laser power, dwell time and spacing were adjusted: SmartStak 1, 30 W power, 1,000 μs dwell time and 1,000 μm spacing [25].

Statistical Analysis

The statistical analysis was performed with SigmaStat/SPSS (SPSS Inc., Chicago, IL) software. To describe the clinical and demographic characteristics means and standard deviations were used for continuous variables. Wilcoxon rank sum test (also called Mann–Whitney U test) was used to compare the differences between the baseline scores and scores after subsequent treatments. Differences were considered significant when the $P < 0.05$. Data are presented as mean values (± standard deviation [SD]) if not otherwise specified.

RESULTS

Forty menopausal women with typical GSM symptoms were enrolled into the study. The mean age was 58 ± 10 years. Clinical and demographical characteristics are described in Table 1.

The summary scores of PFDI-20 displayed no significant improvement after the first treatment compared to baseline scores (mean ± SD score, 74 ± 47 at baseline vs. 57 ± 38 after the first treatment, $P = 0.1$). After the second and third treatment we detected significantly lower summary scores of 46 ± 38 ($P < 0.01$) and 44 ± 39 ($P < 0.01$) as it was at baseline (Table 2).

Evaluating each individual domain of this questionnaire the mean scores developed as follows:

(1) POPDI-6 standardized scores showed no significant difference in prolapse symptoms after the first treatment (mean ± SD score, 21 ± 18 at baseline vs. 17 ± 15 after the first treatment, $P = 0.44$). But, after the second treatment there was a significant improvement in the standardized score to 14 ± 15 ($P = 0.03$). Similarly, further improvement was seen after the third treatment with a mean score of 13 ± 13 ($P = 0.01$) (Table 2).

(2) UDI-6 standardized scores describe severity of the urinary distress symptoms. These were not significantly different after the first laser treatment (mean ± SD score, 36 ± 25 vs. 29 ± 23 after the first treatment, $P = 0.36$). However, after the second and third treatments study participants had significant improvement with scores of 24 ± 20 ($P = 0.03$) and 22 ± 21 ($P = 0.01$) (Table 2), respectively.

(3) CRADI-8 standardized scores characterize the colorectal-anal complaints of the participants. These values did not change significantly after three laser treatments (mean ± SD score, 16 ± 16 vs. 12 ± 13 after the first treatment/11 ± 12 after the second treatment/10 ± 14 after the third treatment) (Table 2).

DISCUSSION

In our pilot study, we have demonstrated that vaginal CO_2 laser therapy improves urinary and prolapse symptoms in postmenopausal women with GSM, as measured by their responses on the PFDI-20.

GSM has a significant adverse impact on the integrity and function of the pelvic floor. The decreased level of circulating estrogen causes microstructural changes in the vaginal and pelvic floor tissues. These changes lead to the development of bothersome GSM symptoms such as itching, burning, dyspareunia, or urinary distress that negatively affect quality of life (QoL) [3]. In the last few years, intravaginal CO_2 laser was introduced as a new nonhormonal therapeutic modality for GSM.

We focused on the symptoms of pelvic floor dysfunction in postmenopausal women and attempted to find the best possible combination of questionnaires available to evaluate the results before, during, and after three sessions of intravaginal microablative, fractional CO_2 laser treatment. In our opinion the validated PFDI-20 questionnaire with its subquestionnaires covers broad symptoms of PFD by including lower urinary tract and urinary incontinence symptoms, symptoms related to prolapse, and colorectal-anal dysfunction or fecal incontinence.

Standardized questionnaires have been used in several prior studies. Our study both confirms and adds to the existing literature. Salvatore et al. treated 50 women with intravaginal CO_2 laser and utilized the Sort Form Health Survey (SF-12) to assess response. SF-12 is a general QoL questionnaire and it is not specific for pelvic floor complaints. Another study assessed sexual function with the FSFI questionnaire, which reflects sexual complaints related to PFD more accurately [7,8]. In a study from 2016, Sokol et al. [26] analyzed PFD symptoms based on Female Sexual Function Index (FSFI) and SF-12 questionnaires in 30 women after intravaginal CO_2 laser therapy and reported significant improvement on sexual function. Pitsouni et al. applied also the FSFI questionnaire to evaluate sexual function related to this treatment. Overall 20–60% of the patients experienced improvement in their sexual life, and specifically reported an increased number

TABLE 1. Clinical and Demographic Characteristics

Variables	Mean ± standard deviation
Number of women, N	40
Age (years)	58 ± 10
Gravida	2 ± 1
Para	2 ± 1
Body mass index (kg/m^2)	26 ± 5

TABLE 2. The Standardized Scores of PFDI-20, POPDI-6, CRADI-8, and UDI-6 Questionnaire Before and After First Treatment, After Second Treatment, and 6 Weeks After the Third Treatment of CO_2 Vaginal Rejuvenation Laser

		CO_2 laser treatment			*P* value		
	Baseline	After first	After second	After third	Baseline vs. first	Baseline vs. second	Baseline vs. third
PFDI-20 (mean±SD)	74 ± 47	57 ± 38	46 ± 38	44 ± 39	0.10	<0.01*	<0.01*
POPDI-6 (mean ± SD)	21 ± 18	17 ± 15	14 ± 15	13 ± 13	0.44	0.03*	0.01*
CRADI-8 (mean ± SD)	16 ± 16	12 ± 13	11 ± 12	10 ± 14	0.17	0.22	0.06
UDI-6 (mean ± SD)	36 ± 25	29 ± 23	24 ± 20	22 ± 21	0.36	0.03*	0.01*

CRADI-8, Colorectal-Anal Distress Inventory; PFDI-20, Pelvic Floor Distress Inventory; POPDI-6, Pelvic Organ Prolapse Distress Inventory; UDI-6, Urinary Distress Inventory.
*Indicate statistically significant data ($P < 0.05$).

of sexual encounters. LUTS were also measured using International Consultation On Incontinence Questionnaire-Female Lower Urinary Tract Symptoms and Urinary Incontinence (ICIQ-FLUTS and ICIQ-UI), UDI-6 and King's Health Questionnaire (KHQ). The authors found significant reduction of questionnaire scores in almost every domain, reflecting the improvement of urinary symptoms. This study confirms existing findings that UDI-6 is a reliable tool to evaluate LUTS and their impact on quality of life after CO_2 laser treatment [27]. Behnia-Willison et al. investigated the efficacy of vaginal CO_2 laser in Australian postmenopausal women. To evaluate favorable effect of the treatment a validated interviewer-administered pelvic floor questionnaire, the Australian Pelvic Floor Questionnaire was completed by patients. This questionnaire assesses the severity of bladder, bowel, and sexual function bothersomeness and also condition-specific quality of life. However, it measures sexual function directly and self-administration seems to even be more useful during everyday practice [28]. Gambacciani and Gonzalez et al. chose ICIQ-SF questionnaire for urinary symptoms after laser treatment. Both studies described improved quality of life as a result of treatment, although Gambacciani et al. used a different, erbium laser for the treatment [13,29].

Using the PFDI-20, we confirmed and expanded existing findings on the impact of laser therapy on pelvic floor dysfunction. Consistent with other studies, we found improvement in urinary symptoms. After two laser sessions, the urinary distress (UDI-6) domain of the questionnaire improved significantly. We also found a significant improvement in the prolapse related answers (POPDI-6) after more than one laser treatment. CRADI-8 colorectal scores improved after every laser session, even though the results were not statistically significant.

Jaeschke et al. [30] published the concept of the minimal important change (MIC), which helps to determine if statistically significant changes are also clinically important. According to this a change should be greater than MIC to consider clinically relevant.

Barber et al. and Wiegersma et al. both investigated the reliability of PFDI-20 questionnaire and also defined the MIC of the questionnaire answers in their study population. The study of Barber et al. investigated the summary score of PFDI-20 after surgery due to PDF complaints. They found that a reduction of 15% or more in the summary score would be considered as "clinically important" [22]. Wiegersma et al. investigated the same changes in a study population of 214 women who chose conservative prolapse treatment and filled out the PFDI-20 questionnaire. According to their results, the summary score of the PFDI-20 should decrease by 23% or more to be clinically relevant [31]. In our study the mean total PFD score decreased by 23% after the first, by 38% after the second, and by 41% after the third laser treatment compared with the baseline scores. Taking into consideration the more conservative MIC requirement of ≥23% score decrease, after the second treatment the observed PFD score decrease surpassed the minimum MIC and the total score decreased even more after the third laser treatment. Overall these results confirm that CO_2 laser treatment is useful to diminish bothersome symptoms caused by Pelvic Floor Dysfunction.

There is very limited information in literature regarding prospective cohort studies evaluating PFD symptoms with PFDI-20 questionnaire after vaginal microablative CO_2 laser treatment. We believe this study brings added value to the existing literature.

The primary limitations of this study are the lack of control group, the relatively small sample size and short follow-up period. Also, our study design is unable to distinguish whether the observed improvement in PFD bother is a direct result or simply secondary to the improvement of GSM. To properly assess treatment efficacy of vaginal laser treatment on PFD-related symptoms a randomized, sham-controlled (laser vs. sham laser) trial would be necessary.

CONCLUSION

In conclusion, our findings suggest that at least two sessions of vaginal microablative CO_2 laser treatment significantly improved postmenopausal pelvic floor dysfunction-related urinary and prolapse symptoms.

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