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Vaginal CO2 Fractional Laser in Women With Vaginal Atrophy: Medical Insights on Short- and Long-term Effects on Genitourinary Symptoms

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Abstract

Introduction: Genitourinary syndrome of menopause (GSM) is a common complication secondary to estrogen depletion which leads to tissue changes in the female genitourinary tract. Here, we sought to investigate the short- and long-term effects of CO_2 laser therapy on symptoms of GSM in postmenopausal women.

Methods: In this clinical trial, 47 postmenopausal women with symptoms of GSM were included. Participants underwent vaginal and extra-vaginal CO_2 fractional laser treatment in three sessions, with intervals of one month between each session. Symptom severity, including itching, dyspareunia, vaginal discharge, and dryness, was assessed at each session using a modified Vaginal Health Index (VHI), where the intensity was rated on a Visual Analog Scale (VAS) from 1 to 10 (1 indicating minimal symptoms and 10 representing maximum severity). Additionally, the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF) was administered. Patients were followed for one to three years after the final laser treatment session.

Results: The scores of all subscales, including itching, dyspareunia, urinary incontinence, vaginal discharge, and dryness, improved significantly following three sessions of CO_2 fractional laser (P values < 0.001). However, except for the urinary incontinence domain ($P = 0.058$), none of the symptoms maintained improved after one to three years from the last intervention.

Conclusion: CO_2 fractional laser treatment is appropriate for treating symptoms related to GSM. But it seems that it needs to be used continuously for the maintenance effect on itching, dyspareunia, urinary incontinence, vaginal discharge, and dryness. The exact timing of laser sessions should be identified in further studies since the beneficial outcomes of the intervention seem temporary.

Keywords: CO_2 fractional laser; Genitourinary syndrome of menopause; Vaginal atrophy; Postmenopausal women.

Introduction

Genitourinary syndrome of menopause (GSM) is a chronic disorder among postmenopausal women that occurs following the reduction of estrogen levels.[1] The most evident symptoms include dryness, itching, dyspareunia, as well as urinary symptoms[2] which may negatively affect patients' quality of life, daily functioning, and sexual function.[3] The prevalence of GSM ranges from 27% to 84%, highlighting its widespread impact.[4] In this regard, local estrogen creams, lubricants, ospemifene, and systemic hormonal replacement therapy (HRT)[5-7] may be the appropriate therapies for the management of symptoms related to GSM.

However, there are remarkable limitations as their long-term administration could give rise to side effects, including thromboembolism and various malignancies.[8,9] Therefore, further effective and safe therapeutic approaches such as laser therapy seem mandatory. The vaginal CO_2 laser is effective in tissue remodeling settings.[10,11] Laser energy is absorbed by the moist layer of connective tissue of the vagina underlying the epithelium. The fractional pattern of energy delivery produces some thermal micromillimeter tissue damage that is surrounded with healthy tissue and provides an opportunity for the production of new collagen over time.[12]

Some studies have addressed the therapeutic effects of fractional laser therapy on GSM symptoms.[13,14] Histopathological studies have confirmed these beneficial

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effects as they have exhibited the improved state of the vaginal wall in a postmenopausal female with GSM following the fractional laser intervention.[15] However, there are limited data on the long-term effects of fractional lasers on GSM. Given the evidence, we aimed to explore whether multiple sessions of CO_2 fractional laser administration could alleviate the symptoms related to GSM via modifying the wall structure in both the short term and the long term.

Methods

Study Setting

This uncontrolled clinical trial was carried out between May 2018 and May 2019 on outpatients of a pelvic clinic of an academic center affiliated with Tehran University of Medical Sciences. Additionally, a follow-up evaluation was conducted three months post-intervention and then periodically between one to three years.

Participants

The inclusion criteria of the study encompassed married postmenopausal women aged 45 to 65 who had been in menopause for a minimum of 24 months. These participants exhibited symptoms indicative of vaginal atrophy, such as vaginal dryness, inflammation, dyspareunia, dysuria, and urinary incontinence.

Exclusion criteria included women who had received any form of HRT and those with undiagnosed vaginal bleeding, a history of gynecological malignancy, an abnormal Pap smear within the last two years, a history of pelvic physiotherapy, or menopause resulting from an underlying disease or medical interventions such as surgery, radiation, or chemotherapy.

Intervention

Both intra- and extra-vaginal sites (labia and vestibule) were treated by using a CO_2 fractional laser system (Monalisa, Italy) over three sessions, with each session spaced one month apart.[12] For the intravaginal treatment, a specific vaginal probe was used, while for the extra-vaginal areas a perineal probe was employed. The laser settings were optimized to a square pattern and deep mode, with fractional density ranging from 4%-5% and energy levels set between 40-55 millijoules.

During the procedure, a speculum cage was carefully inserted into the vaginal vestibule. The handpiece was positioned at the anterior edge of the treatment area, reaching depths of up to 11 cm into the vaginal canal. To ensure patient comfort, a lubricant was applied during the insertion of the speculum. The laser was delivered in pulses, targeting each centimeter of the vaginal canal. For comprehensive coverage, the handpiece was rotated 45 to 90 degrees after each pulse, achieving a total of 4-8 laser pulses per centimeter.

This outpatient procedure required no anesthesia or analgesics. Post-procedurally, participants were advised to avoid using tampons and refrain from sexual intercourse for seven days to allow proper healing and minimize discomfort. A follow-up evaluation was conducted three months post-intervention and then periodically between one and three years.

Outcome

Demographic information was collected from participants' medical records and a custom-designed questionnaire. Each participant underwent a thorough gynecological examination conducted by an expert gynecologist to assess vaginal health, including observations of vaginal color, discharge, the presence of vaginal rugae, elasticity, and pain. These examinations were performed at baseline, as well as at months 1, 2, and 3 following the initiation of the study.

During each session, the gynecologist interviewed the patients and completed the modified Vaginal Health Index (VHI) assessment, which assessed symptoms such as itching, dyspareunia, urinary incontinence, vaginal discharge, dryness, and the overall presence of urinary incontinence. The gynecologist administered the questionnaire, personally asking each question and recording the responses. Each symptom was scored by using a Visual Analog Scale (VAS) ranging from 1 to 10, where 1 represented minimal intensity and 10 indicated maximum severity. The total score was used to determine the degree of vaginal atrophy in the genital tract.

A follow-up assessment using the same questionnaire was conducted via phone calls between one and three years after the third session to evaluate the long-term maintenance of the beneficial effects of fractional laser therapy. Additionally, urinary incontinence was assessed by using the International Consultation on Incontinence Questionnaire-Urinary Incontinence Short Form (ICIQ-UI SF), which evaluates the frequency and severity of urinary leakage and its overall impact, and includes a self-diagnostic item. The ICIQ-UI SF scores range from 0 to 21 and have been validated in Persian.[16]

Statistical analysis

Statistical analyses were carried out by using SPSS software (version 24; IBM Company). P values ≤ 0.05 or below were regarded as significant. The Shapiro-Wilk test and probability Q-Q plots were used to assess the normal distribution of the baseline data. Since the data pattern did not follow the normal distribution, non-parametric tests were applied. The Friedman test was used to detect intervention-related improvements in the VAS score across time. Moreover, the Wilcoxon signed-rank t-test was used to evaluate the change in the scores of VAS subdomains over one to three years of follow-up. The quantitative variables were reported as mean ± standard deviation (SD) while the qualitative variables were

presented as percentage (%).

Results

Demographic characteristics of the subjects

The demographic characteristics of the study participants are presented in Table 1. The mean age of the participants was 57.2 years (±6.8), with the majority of women (85.1%) having between 1 and 5 previous pregnancies, while only 2.2% were nulligravid. The average duration of menopause among participants was 7.7 years (±7.3). In terms of medical history, 6.6% had diabetes, 2.2% had hypertension, and 4.4% had hypothyroidism. Additionally, the past surgical history indicated that 6.6% of the women had undergone bilateral mastectomy, while 2.2% had undergone pelvic prolapse surgery. Of the 46 women with a pregnancy history, 86.9% had experienced normal vaginal delivery, and 10.8% had undergone cesarean section.

VAS Subscales

According to Table 2, the scores on all five domains of VHI, including itching, showed a significant reduction over the three months following fractional laser therapy ($P<0.001$).

Long-term Effects

Itching ($P=0.014$), dryness ($P=0.001$), vaginal discharge ($P=0.022$), and dyspareunia ($P=0.008$) all showed significantly higher scores at the period of one to three follow-ups compared to month three. In contrast, urine incontinency remained statistically similar throughout the follow-up period ($P=0.058$).

Table 1. Demographic and Clinical Characteristics of Postmenopausal Women Undergoing Fractional CO_2 Laser Therapy

Characteristics (N=47)	
Age (y)	57.2±6.8
Parity	
Nulligravid	1 (2.2%)
1-5	40 (85.1%)
>5	6 (12.8%)
Menopause duration (year)	7.7±7.3
Past medical history	
Diabetes	3 (6.6%)
Hypertension	1 (2.2%)
Hypothyroidism	2 (4.4%)
Past surgical history	
Bilateral mastectomy	3(6.6%)
Pelvic prolapse surgery	1(2.2%)
Delivery Type	
Normal vaginal delivery	40 (86.9%)
Cesarean delivery	5 (10.8%)
Both	1 (2.2%)

The data are presented as number (percent) or mean±standard deviation.

Discussion

This study demonstrated that while fractional CO_2 laser therapy offered short-term benefits for vulvovaginal atrophy and urinary symptoms, the long-term effects were not sustained for some patients. However, no serious adverse events were detected throughout the follow-up period, which is consistent with other studies confirming the safety of CO_2 laser therapy.[17,18]

There are several treatment options available for symptomatic GSM, which vary based on the underlying etiology, symptom severity, and individual health conditions. Nonhormonal treatments such as lubricants and moisturizers are often recommended as first-line options. For more severe cases, low-dose vaginal estrogen therapy, vaginal dehydroepiandrosterone, and oral ospemifene have proven effective.[19,20] In women who do not respond to nonhormonal therapies, low-dose vaginal estrogen is typically the preferred pharmacological option.[21] However, caution is necessary for survivors of hormone-sensitive cancers, as estrogen treatments may pose risks. Newer therapeutic approaches include selective estrogen receptor modulators and laser therapy, which provide alternative, nonhormonal solutions for those unable to use estrogen-based treatments.[22]

Table 2. Summary of Alterations of VHI, Scores Related to Vulvovaginal Atrophy Following CO2 Fractional Laser Therapy

Symptoms	Follow-up Visits	Mean Score	*P* Value
Dryness	Baseline	3.99±0.50	<0.001
	Post session 1	3.01±0.35	
	Post session 2	1.99±0.25	
	Post session 3	1.01±0.10	
Dyspareunia	Baseline	4.00±0.55	<0.001
	Post session 1	2.97±0.40	
	Post session 2	2.03±0.30	
	Post session 3	1.00±0.12	
Itching	Baseline	3.20±0.45	<0.001
	Post session 1	2.73±0.35	
	Post session 2	2.27±0.28	
	Post session 3	1.80±0.15	
Vaginal discharge	Baseline	3.22±0.50	<0.001
	Post session 1	2.72±0.38	
	Post session 2	2.23±0.30	
	Post session 3	1.82±0.18	
Urine incontinency	Baseline	3.51±0.55	<0.001
	Post session 1	2.84±0.40	
	Post session 2	2.11±0.35	
	Post session 3	1.54±0.20	

Data are presented as mean±standard deviation. One-way ANOVA was used to assess differences, with a p-value of less than 0.05 considered statistically significant.

CO_2 lasers are recognized for their ablative effects on abnormal tissue, leading to collagen regeneration and remodeling, which has been well documented in the treatment of photoaged skin.[18,23] The laser delivers controlled thermal energy into the vaginal tissue, targeting the submucosal layers without damaging the epithelium. This process stimulates fibroblasts, leading to the production of new collagen and elastin fibers. Over time, this results in the restoration of tissue integrity, increased moisture content, and improved elasticity in the vaginal mucosa, mimicking the effects of estrogen in premenopausal tissue.[24-26]

Histopathological studies support the notion that CO_2 laser therapy induces collagen contraction, an effect that can persist for at least six months.[27] Extending these findings to vaginal tissue, a number of studies have evaluated the efficacy of 2-3 sessions of fractional CO_2 laser administered once a month in postmenopausal women, showing results consistent with this study.[14,15,28-31] The clinical utility of these findings is reflected in the possibility of reducing reliance on hormonal therapies, which carry risks, particularly in women for whom estrogen replacement is contraindicated.[32]

Although fractional CO_2 laser therapy provides significant short-term improvements, the current study highlights the need for periodic maintenance sessions to sustain symptom relief, particularly in cases of urinary incontinence. Some evidence suggests that laser therapy may not be suitable for long-term treatment unless followed by repeat sessions.[18] However, this remains a topic of debate, as other studies, such as that by Siliquini et al, have reported long-lasting improvements of up to 15 months post-treatment.[33] These discrepancies may stem from differences in follow-up duration, as our study included a longer observation period.

This study had certain limitations. A larger sample size and longer follow-up period would increase the reliability of the findings. Furthermore, histopathological changes in the vaginal wall were not assessed throughout the study. Future randomized, double-blinded clinical trials comparing the efficacy and safety of fractional CO_2 laser therapy with hormone replacement therapy are necessary to clarify the role of laser treatment in managing postmenopausal symptoms.

Conclusion

The results of this study should be considered preliminary. In this clinical-based investigation, fractional CO_2 laser treatment provided a short-term improvement in GSM-related symptoms, particularly in postmenopausal women. While urinary incontinence showed some sustained improvement up to one to three years after treatment, other symptoms did not. Future studies are needed to determine the optimal timing and number of sessions for managing GSM symptoms with fractional CO_2 laser therapy and to explore the long-term effects and safety of this treatment option.

Authors' Contribution

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Competing Interests

The authors have no conflict of interest to disclose.

Ethical Approval

The trial adhered to successive revisions of the Declaration of Helsinki, and the protocol was approved by the Institutional Review Board (IRB) of TUMS (Reference code: IT.TUMS.REC.1397.5008). The study was also registered in the Iranian Registry of Clinical Trials under the trial number (identifier: IRCT20180409039247N2). After a complete description of the procedures and purposes of the trial, written informed consent was obtained from each patient. Patients were informed of their right to withdraw from the trial at any moment without any negative effect on their treatment plan.

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