Use of a novel fractional CO₂ laser for the treatment of genitourinary syndrome of menopause: 1-year outcomes

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Abstract

Objectives: To assess safety and efficacy of a fractional CO₂ laser therapy for the treatment of genitourinary syndrome of menopause (GSM) with follow-up to 1 year posttreatment.

Methods: Women presenting with GSM and meeting inclusion criterion were enrolled. Visual Analog Scales were used to grade vaginal pain, burning, itching, dryness, dyspareunia, and dysuria. Dilators were used to rate vaginal elasticity at baseline and at each follow-up visit. Before each treatment and at follow-up, Vaginal Health Index scoring and Female Sexual Function Index questionnaires were completed. Women received three vaginal laser treatments spaced 6 weeks apart. Participant satisfaction was measured on 5-point Likert scales (1 = very dissatisfied, 5 = very satisfied).

Results: Of 30 women (mean age 58.6 ± 8.8 years), three were lost to follow-up at 3 months and six at 1 year. None were discontinued or withdrew due to an adverse event. Average improvement in Visual Analog Scale scores for all symptom categories was statistically significant at 3 months and remained so through 1 year, except dysuria. Differences between data at 3 months and 1 year were not statistically significant, indicating persistence of positive outcomes. Average overall improvement in pain was 1.9 (±3.4), burning 1.9 (±3.1), itching 1.4 (±1.9), dryness 5.9 (±2.8), dyspareunia 4.9 (±3.3), and dysuria 0.9 (±3.1). Improvement in average Vaginal Health Index and Female Sexual Function Index scores was also statistically significant (P < 0.0001). Of 19 women undergoing dilator examination at 1 year, 18 (94.8%) were comfortable with the same or larger dilator size. Twenty-two of 24 women (92%) were satisfied or extremely satisfied with the treatment at 1 year.

Conclusions: Based on study data up to 1 year, the fractional CO₂ laser may be an effective and safe treatment for women suffering from symptoms of GSM, although additional studies with larger populations and placebo control is needed to confirm these results.

Key Words: Dyspareunia – Fractional CO₂ laser – Genitourinary syndrome of menopause – Menopause – Vaginal dryness – Vulvovaginal atrophy.
introtitus. Treatment parameters are modulated downward to participant tolerance, if required.

Results of this pilot study suggested high levels of safety, tolerability, and participant satisfaction with demonstrated efficacy at 3 months after treatment. We currently report safety and efficacy outcomes for women treated with a fractional CO₂ laser for symptomatic GSM 1 year after treatment.

METHODS

As outlined in the original report, two-center study included 30 consecutive healthy, nonsmoking postmenopausal women, who presented with symptoms of GSM. Women had to exhibit bothersome symptoms of VVA, could not have menstruated for at least 12 months, had to have less than stage 2 prolapse according to the pelvic organ prolapse quantification (POP-Q) system, and could not have had any procedures in the anatomical area for the previous 6 months. The use of vaginal creams, moisturizers, lubricants, or homeopathic preparations was not permitted for at least 3 months before study commencement and throughout the entire study period. The investigation was conducted according to Good Practice Guidelines (GCP) and was IRB-approved. Informed consent was obtained from all participants.

Exclusion criteria included presence of pelvic organ prolapse greater than stage II by the POP-Q system; previous reconstructive pelvic surgery; history of acute infections, thrombophlebitis, keloid formation, or heart failure; use or anticipated use of anticoagulants or antiplatelet treatments, thrombolitics, vitamin E, or anti-inflammatory agents within 2 weeks before study treatment; concurrent use of medications that increase photosensitivity; and the presence of any disease, disease history, or chronic condition that could interfere with study compliance.

Six categories of VVA-associated symptoms (vaginal pain, burning, itching, dryness, dyspareunia, and dysuria) were tracked using an 11-point Visual Analog Scale (VAS) where 0 was the lowest level (none) and 10 was the highest level (extreme). Secondary outcome measures included Bachmann Vaginal Health Index (VHI)22 scoring, dilator-based testing of vaginal wall elasticity (using XS/extra small, S/small, M/medium, and/or L/large dilators), Female Sexual Function Index (FSFI) questionnaire, general QoL via Short Form 12 (SF-12) specific questionnaire, and a 5-point Likert scale (1 = very dissatisfied, 5 = very satisfied). As in the original study, statistical analysis included appropriate measures for statistical significance (Student’s paired two-sample t test, standard cut-off for significance \(P < 0.05\) via Microsoft Excel.

RESULTS

Participants were primarily white women with a mean age of 58.6 ± 8.8 years, average onset of menopause at 48.9 ± 7.6 years, and average age of onset of vulvar and vaginal atrophy symptoms at 51.2 ± 8.3 years. Of the 30 women who initially enrolled, 3 women did not attend the 3-month posttreatment time point; 6 were considered lost to follow-up at the 1-year time point (missed scheduled visit). The original study previously reports all data through the 3-month posttreatment time point.21 No women withdrew due to an adverse event.

Mild adverse events included mild to moderate pain posttreatment, resolving within 2 or 3 days (n = 2), and slight bleeding for less than 1 day (n = 2). Overall, the most improvement in symptoms as assessed by VAS was seen after the initial treatment session, with additional incremental improvement noted after treatments 2 and 3. Improvement was statistically significant at 3 months for all VVA categories. Of all categories, dryness and dyspareunia had the most improvement.21 At 12 months, improvement continued to be statistically significant for all categories except dysuria. Average overall improvement in pain was 1.9 (±3.4), burning 1.9 (±3.1), itching 1.4 (±1.9), dryness 5.9 (±2.8), dyspareunia 4.9 (±3.3), and dysuria 0.9 (±3.1). Table 1 places these numbers alongside those from baseline and follow-up at 3 months. Differences between 3-month and 1-year results were not statistically significant, indicating that a long-term benefit was seen.

For secondary outcome measures, VHI baseline average was 14.4 ± 2.9, with overall average improvement of 7.0 ± 3.1 at 3 months, which was statistically significant (\(P < 0.0001\)); at 1 year, overall average improvement was 7.0 ± 3.7 from baseline, which was also statistically significant (\(P < 0.0001\)). FSFI baseline average was 11.5 ± 7.8, with
**FRACTIONAL CO2 LASER FOR GSM AT 1 YEAR**

**TABLE 1. Assessment of average change in symptoms of vulvovaginal atrophy at follow-up**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Baseline Mean score</th>
<th>Three-mo follow-up Mean score</th>
<th>Improvement</th>
<th>P</th>
<th>One-y follow-up Mean score</th>
<th>Improvement</th>
<th>P</th>
<th>Three mo versus 1-y, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>2.3 ± 0.1</td>
<td>0.6 ± 1.4</td>
<td>1.7 ± 3.2</td>
<td>0.009</td>
<td>0.5 ± 1.5</td>
<td>1.9 ± 3.4</td>
<td>0.01</td>
<td>0.4</td>
</tr>
<tr>
<td>Burning</td>
<td>2.3 ± 0.3</td>
<td>0.9 ± 1.9</td>
<td>1.4 ± 2.9</td>
<td>0.02</td>
<td>0.5 ± 1.9</td>
<td>1.9 ± 3.1</td>
<td>0.007</td>
<td>0.1</td>
</tr>
<tr>
<td>Itching</td>
<td>1.9 ± 0.1</td>
<td>0.5 ± 1.2</td>
<td>1.4 ± 1.9</td>
<td>0.001</td>
<td>0.5 ± 1.1</td>
<td>1.4 ± 1.9</td>
<td>0.002</td>
<td>0.7</td>
</tr>
<tr>
<td>Dryness</td>
<td>7.5 ± 2.5</td>
<td>1.4 ± 2.5</td>
<td>6.1 ± 2.7</td>
<td>&lt;0.0001</td>
<td>1.5 ± 2.0</td>
<td>5.9 ± 2.8</td>
<td>&lt;0.0001</td>
<td>0.3</td>
</tr>
<tr>
<td>Dyspareunia</td>
<td>8.2 ± 1.7</td>
<td>3.0 ± 2.9</td>
<td>5.2 ± 3.0</td>
<td>&lt;0.0001</td>
<td>3.1 ± 3.1</td>
<td>4.9 ± 3.3</td>
<td>&lt;0.0001</td>
<td>0.5</td>
</tr>
<tr>
<td>Dysuria</td>
<td>1.1 ± 2.5</td>
<td>0.0 ± 0.2</td>
<td>1.1 ± 2.4</td>
<td>0.04</td>
<td>0.4 ± 1.3</td>
<td>0.9 ± 3.1</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Improvement measured on a Visual Analog Scale (0-10, where 0 = none and 10 = extreme), listed as mean ± standard deviation. Cut-off for statistical significance was P > 0.05.

Overall average improvement of 8.9 ± 7.3 at 3 months, which was statistically significant (P < 0.0001); at 1 year, overall average improvement from baseline was 10.6 ± 10.0, which was also statistically significant (P < 0.0001). SF-12 grading included scores weighted for physical and mental health. Baseline average (physical) was 51.6 ± 6.2, with overall average improvement from baseline of 1.6 ± 8.1 at 3 months, which was not statistically significant (P = 0.3); at 1 year, overall average improvement was 2.2 ± 7.5 from baseline, which was also not significant (P = 0.2). Baseline average (mental) was 49.9 ± 10.2, with overall average improvement of −2.6 ± 10.6 at 3 months, which was not significant (P = 0.2); at 1 year, overall average improvement was 4.8 ± 11.1 from baseline, which was also not statistically significant (P = 0.1). A more complete comparison of secondary outcomes is shown in Table 2.

Changes in vaginal elasticity were measured via gynecological examination with vaginal dilators. At baseline, 24 of 30 women (80%) could only accept the extra small or small dilator, and at 3 months, 23 of that subset could comfortably accept the medium or large dilator; 25 women (83%) saw an increase in comfortable dilator size from baseline to 3-month time point. At the 1-year time point, 19 women underwent dilator examination; 14 (73.7%) were comfortable with a larger dilator size, 4 (21.0%) were comfortable with the same dilator size, and 1 (5.3%) was comfortable with one size smaller.

Participant satisfaction at 3 months after the final treatment session was high, with 26 of 27 women (96.3%) reportedly satisfied (n = 10) or very satisfied (n = 16) with the laser treatment. Of the 24 women who followed up at 1 year, 22 (92%) said they were either satisfied (n = 10) or very satisfied (n = 12).

Overall, at 3 months, all women (100%) showed improvement in 4 of 6 VVA symptoms measured by VAS; 19 of 27 (70%) showed an improvement in 5 of 6 symptom categories. At the 1-year time point, 22 of 24 women (92%) showed improvement in 4 of 6 symptom categories, with 58% (14 of 24) showing improvement in 5 of 6 scales.

**DISCUSSION**

This study presents follow-up information on outcomes given in the original study, based on further data obtained from the same group of women in the original investigation, minus those lost to follow-up (which were not due to adverse events).

Our results suggest persistent improvement in the bothersome symptoms of VVA associated with GSM 1 year after vaginal treatment with a novel fractional CO2 laser. Overall improvements in vaginal pain, burning, and itching were noted at 1 year, with improvements in dyspareunia and vaginal dryness being most pronounced. Improvements in the VHI and sexual health functioning as measured by the FSFI showed similar resistance to change between 3 months and 1 year after final treatment, with minor degradation in vaginal elasticity as measured by vaginal dilators. Taken together, these results suggest a durable positive effect on the vaginal symptoms of GSM 1 year out from treatment with the fractional CO2 laser. Randomized controlled trials comparing this laser therapy with other therapies, including vaginal HT, are currently in progress.

**TABLE 2. Average change in secondary endpoints of VHI, FSFI, and SF-12 at follow-up versus baseline**

<table>
<thead>
<tr>
<th>Secondary endpoint</th>
<th>Baseline Mean score</th>
<th>Three-mo follow-up Mean score</th>
<th>Improvement</th>
<th>P</th>
<th>One-y follow-up Mean score</th>
<th>Improvement</th>
<th>P</th>
<th>Three mo versus 1-y, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VHI</td>
<td>14.4 ± 2.9</td>
<td>21.4 ± 2.9</td>
<td>7.0 ± 3.1</td>
<td>&lt;0.0001</td>
<td>21.7 ± 3.6</td>
<td>7.0 ± 3.7</td>
<td>&lt;0.0001</td>
<td>0.9</td>
</tr>
<tr>
<td>FFSI</td>
<td>11.5 ± 7.8</td>
<td>20.1 ± 11.0</td>
<td>8.9 ± 7.3</td>
<td>&lt;0.0001</td>
<td>21.3 ± 11.5</td>
<td>10.6 ± 10.0</td>
<td>&lt;0.0001</td>
<td>0.9</td>
</tr>
<tr>
<td>SF-12 (phys)</td>
<td>51.6 ± 6.2</td>
<td>53.0 ± 9.0</td>
<td>1.6 ± 8.1</td>
<td>0.3</td>
<td>53.6 ± 5.3</td>
<td>2.2 ± 7.5</td>
<td>0.2</td>
<td>1.0</td>
</tr>
<tr>
<td>SF-12 (mnt)</td>
<td>49.1 ± 10.2</td>
<td>47.0 ± 11.8</td>
<td>2.0 ± 10.6</td>
<td>0.2</td>
<td>54.3 ± 7.9</td>
<td>4.8 ± 11.1</td>
<td>0.1</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Items listed as mean ± standard deviation. Cut-off for statistical significance was P > 0.05.

FSFI, Female Sexual Function Index; SF-12, general Quality of Life Questionnaire Short Form 12; VHI, Vaginal Health Index.

*SF-12 broken into weighted physical (phys) and mental (mnt) health components.
As detailed in the original study, the application of fractional 10,600 nm CO2 laser therapy for vulvovaginal tissue is a natural progression from previous, well-documented use of the modality in aesthetic medicine for remodeling of skin of the face, neck, and other areas. CO2 and other lasers have been used to cause controlled thermal damage to skin, stimulating neocollagenesis and neoelastogenesis to fortify the extracellular matrix (ECM). Tissue of the vaginal wall is more vascular and more innervated than typical skin tissue, but is otherwise quite similar, and behaves similarly in response to thermal insult, suggesting a therapeutic vector. Recent studies using this and other wavelengths have demonstrated this concept.

Fractional delivery of energy creates micro-wound patterns rather than causing damage via complete surface irradiation, leaving nearby skin and tissue structures undamaged. This reduces recovery time and downtime by promoting rapid re-epithelialization and healing. Each individual micro-wound may be ablative or coagulative (or some combination of the two), depending on the wavelength and energy level chosen.

The device used for this trial has received US Food and Drug Administration (FDA) clearance for incision, excision, ablation, vaporization, and coagulation of soft tissue; its HiScan DOT scanner is indicated specifically to create highly controlled, uniform, layer-by-layer ablation without carbonization of tissue, with energy penetration as deep as 200 μm. The probe allows 360° emission of energy. The SmartStack feature allows modulation of the depth of penetration of the laser beam in tissue to guarantee that, regardless of the conditions of the vaginal wall, emitted laser energy is always delivered to the lamina propria, through the epithelium, since that tissue layer is the actual target of the treatment. A graphic representation of the effect of SmartStack technology is given in Figure 1.

As a pilot study and should be interpreted as such. Limitations include a small and racially uniform participant population, lack of a control arm to account for placebo effect, and lack of comparison therapy. In the case of this 1-year follow-up study, an additional limitation was the loss to follow-up of a few more women. Nonetheless, this pilot study...
suggests that vaginal treatment with a fractional CO2 laser might be a viable and durable treatment option for some women suffering from GSM.

CONCLUSIONS
The low risk of adverse events and durable positive effects out to 1 year suggest that fractional CO2 laser therapy may be safe and effective for the treatment of VVA, also known as GSM. Given the small participant population and lack of a sham control, additional study to confirm these results using controlled clinical trials with larger populations will be beneficial and are underway.

REFERENCES