Energy Based Therapies in Gynecology and Vaginal Health: Update on CO$_2$

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Disclosures

• Grant funding to Stanford University from DEKA

• Unrelated disclosures:
  – Grant funding to Stanford University
    • Cook MyoSite
    • ACell
    • Coloplast
  – Advisor
    • Pelvalon
Causes of vaginal atrophy

- Menopause
- Oophorectomy (surgical removal of the ovaries)
- Pelvic radiation for cancer
- Medications (anti-estrogens)
- Breastfeeding
Symptoms of vaginal atrophy

- Dryness
- Burning
- Itching
- Pain
- Dyspareunia

- Bleeding with intercourse
- UTIs
- Burning with urination
- Tightening of the vagina
- Urinary urgency/frequency
Therapies for vaginal atrophy

- Vaginal estrogens
  - Vagifem
  - Premarin cream
  - Estrace
  - Estring
- Vaginal moisturizers (e.g. Replens)
- Vaginal lubricants (e.g. Astroglide)
- Ospemifine (Osphena)
  - Selective estrogen receptor modulator
BACKGROUND

- Genitourinary syndrome of menopause (GSM) is a suite of conditions resulting from atrophy of vulvovaginal tissue due to decreased circulating estrogen levels during menopause.

- Histological evaluation of vaginal tissue after fractional CO$_2$ laser treatment has demonstrated regeneration of connective tissue in the vaginal lamina propria without leading to tissue damage or side effects.

- The fractional CO$_2$ laser system we studied has a maximum power of 60 W, emitting laser energy at a 10,600 nm wavelength.
CO$_2$ Lasers

- DEKA – SmartXide$^2$ V$^2$LR, Monalisa Touch
- Alma Lasers – FemiLift Pixel
- Syneron – CO$_2$RE Intima
- Lumenis – UltraPulse & AcuPulse (FemTouch handpiece)
Available CO$_2$ Lasers

• Mona Lisa Touch (SmartXide$^2$ CO$_2$ laser by DEKA) is a fractional CO$_2$ laser system with a maximum power of 60 W, emitting laser energy at a 10,600 nm wavelength, which was developed for gynecologic uses.

• FemiLift Pixel (Alma Lasers) is a “fractionated beam” laser (rather than a true fractional laser) - the laser beam is fractionated into several micro-beams by a micro-lens array located at the distal end of the articulated arm, before the probe.

• CO$_2$RE Intima (Syneron-Candela) is an aesthetic CO$_2$ laser converted to gynecologic use.

• FemTouch (Lumenis) is a handpiece similar to DEKA’s probe which can be used with UltraPulse and AcuPulse lasers.
New therapy for atrophy: CO\textsubscript{2} laser

- Treatment performed with a thin vaginal probe
- 3 treatments spaced 6 weeks apart
- Laser treatments are painless
- No anesthesia
- Performed in the office
- Treatments take less than 2 minutes
- Only restriction – no sex for 3 days after treatment
How does it work?
Fun with laser physics!!!

- Two mirrors, one is super reflective, one is kind of leaky
- Place CO$_2$ gas mixture between the mirrors
- Run current through the gas mixture, exciting CO$_2$ molecules
- Some CO$_2$ molecules relax spontaneously, emitting 9.4 micron and 10.6 micron photons
- These photons collide with excited CO$_2$ molecules, stimulating those CO$_2$ molecules to relax as well, creating more 9.4 and 10.6 micron photons
- The mirrors redirect escaping photons back into the CO$_2$ gas mixture, keeping the chain reaction going
- The photons that escape through the leaky mirror comprise the laser beam
Growth factors / cytokines increase following fractional CO₂ laser treatment

- **Transforming Growth Factor-β**
  (TGF-β: stimulating matrix proteins synthesis, such as collagen)

- **Basic Fibroblast Growth Factor**
  (bFGF: stimulating angiogenic activity with endothelial cell migration and proliferation)

- **Epidermal Growth Factor**
  (EGF: stimulating re-epithelization)

- **Platelet-Derived Growth Factor**
  (PDGF: stimulating fibroblasts to produce extracellular matrix components)

- **Vascular Endothelial Growth Factor**
  (VEGF: regulating angiogenesis)
Molecular organization of the ground substance
EFFECTS OF CO2 LASER TREATMENT ON ATROPHIC POSTMENOPAUSAL VAGINAL MUCOSA

- Increase of collagen
- Increase of acidic mucopolysaccarides in the ground matrix
- Increase of glycogen content and delivery

better mechanical support
better mucosal hydration and permeability to nutrients and hormones
increase of lactobacilli activity (< pH)

VAGINAL HEALTH RESTORATION
CO2 Laser

- Tissue
  - Coagulation (Lateral Thermal Damage)
  - Ablation

- (Body Natural Response)
  - Heat Shock Protein 47 (HSP 47)
  - Cytokines

- Re-epithelialization
  - Thicker Epithelium

- Angiogenesis (New Blood Vessels)

A. Increase of Nourishment (N)
   - Mucosa
     - Glycogen Cris to Surface of Epithelium
   - Increase of Lymphatics

B. Increase of Circulation
   - Blood Eversion
   - Blood Overflow from Capillaries during Interchange
   - Glycogen Shedding from Epithelium

- Decrease of Dyspareunia
- Increase of Lactobacilli

- Decrease of pH
- Decrease of UTI

(*)& Nourishment:
- Nutrients
- Metabolites
- Hormones (from muscle, fat, endocrine glands)

[Stills present, even if in small quantity and hormone receptors are still there]
Effects of vaginal laser treatment
Vaginal mucosa
(premenopausal)
Atrophic vaginal mucosa
(post-menopausal)
Baseline
Just before Tx #1

One month after Tx #1
Just before Tx #2

Two months after Tx #1
One month after Tx #2
Just before Tx #3
Atrophic mucosa – Baseline

Same patient’s mucosa
Two months after Tx #2
The increased permeability of the rehydrated ECM facilitates the diffusion of nutrients, mineral salts and ions, vitamins, antibodies and hormones from the blood vessels to the tissues of the vaginal wall (epithelium, connective tissue of the mucosa and muscle).
Clinical outcomes
An assessment of the safety and efficacy of a fractional CO2 laser system for the treatment of vulvovaginal atrophy.

Sokol ER¹, Karram MM.

Author information

Abstract

OBJECTIVES: The aim of the study was to assess the safety and efficacy of a novel fractional CO2 laser for the treatment of genitourinary syndrome of menopause (GSM).

METHODS: Women presenting with GSM and meeting study criteria were enrolled. Examinations at baseline and follow-up (3 mo after final treatment) evaluated dilator tolerance and vaginal pH. Visual analog scales were used to assess pain, vaginal burning, vaginal itching, vaginal dryness, dyspareunia, and dysuria; Vaginal Health Index scores were completed before each treatment and at follow-up; Female Sexual Function Index and Short Form 12 questionnaires were also completed. Participant satisfaction was measured on a 5-point Likert scale (1=very dissatisfied, 5=very satisfied). Women received three laser treatments, 6 weeks apart.

RESULTS: Thirty women participated (mean age 58.6±8.8 y). None withdrew or were discontinued due to an adverse event; three were lost to follow-up. Average improvement in visual analog scale scoring was 1.7±3.2 for pain, 1.4±2.9 for burning, 1.4±1.9 for itching, 6.1±2.7 for dryness, 5.1±3.0 for dyspareunia, and 1.0±2.4 for dysuria; improvement in average Vaginal Health Index and Female Sexual Function Index scores were statistically significant (P<0.001). Twenty-five of 30 participants (83%) showed increase in comfortable dilator size at 3-month follow up. Before the second and third treatments, 86.6% (26 of 30) of women reported they were better or much better than at the previous treatment; 26 of 27 women (96%) were reportedly satisfied or extremely satisfied at follow-up.

CONCLUSIONS: In this sample, the data suggest that the fractional CO2 laser is effective and safe for treatment of the symptoms associated with GSM.

Sokol ER¹, Karram MM.

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.
Use of a Novel Fractional CO$_2$ Laser for the Treatment of Genitourinary Syndrome of Menopause: 1-Year Outcomes

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PRIMARY OBJECTIVE

To assess the safety and efficacy of the SmartXide² – V²LR fractional CO₂ laser for the treatment of genitourinary syndrome of menopause (GSM) 1 year after treatment.
SECONDARY OBJECTIVES

1. Assess urogenital health using Vaginal Health Index (VHI)
2. Assess vaginal elasticity using dilator size
3. Assess sexual function using Female Sexual Function Index (FSFI)
4. Assess QoL using Short Form 12 (SF-12)
5. Assess treatment ease using 5-point Likert scale
6. Assess patient satisfaction using Patient Global Impression of Improvement (PGI)
METHODS

• 30 consecutive women with GSM
  – No lubricants or estrogens could be used
• 3 laser treatments 6 weeks apart
• VAS used to grade vaginal pain, burning, itching, dryness, dyspareunia and dysuria
• Dilators used to rate elasticity at baseline and f/u
• VHI done prior to each treatment and at f/u
• FSFI done prior to each treatment and at f/u
• Satisfaction measured on 5-point Likert scales
RESULTS
All GSM symptoms significantly improved at 12 months
79% tolerated medium/large dilator at 12 months (vs. 20% at baseline)
12 month FSFI scores significantly improved

<table>
<thead>
<tr>
<th>Female Sexual Function Index (FSFI)</th>
<th>Baseline</th>
<th>12 Month FU</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>2</td>
<td>3.3</td>
<td>-5.4</td>
</tr>
<tr>
<td>Maximum</td>
<td>25</td>
<td>33.8</td>
<td>31.5</td>
</tr>
<tr>
<td>Average</td>
<td>11.3</td>
<td>21.25</td>
<td>10.63</td>
</tr>
<tr>
<td>Std. Dev</td>
<td>7.3</td>
<td>11.47</td>
<td>10.01</td>
</tr>
</tbody>
</table>
92% satisfied/very satisfied at 12 months
CONCLUSION

The SmartXide² - V²LR fractional CO₂ laser is a safe and efficacious treatment for the symptoms of genitourinary syndrome of menopause with results that last up to 1 year.
Stanford $\text{CO}_2$ laser studies

- **VeLVET**
  - Randomized trial of vaginal $\text{CO}_2$ laser versus estrogen
  - Follow up for 6 months

- **Histology study to assess $\text{CO}_2$ laser therapy for GSM**
  - Pinch biopsies of vaginal wall evaluated before and after laser treatment
Uses for CO$_2$ laser under study

- External vulvar atrophy
- Lichen sclerosis
- Vestibulodynia
- Urinary incontinence
Long-term reliability of fractioned CO$_2$ laser as a treatment for vulvovaginal atrophy (VVA) symptoms

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Randomized, double-blind, placebo-controlled clinical trial for evaluating the efficacy of fractional CO₂ laser compared with topical estriol in the treatment of vaginal atrophy in postmenopausal women

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Abstract

Objective: The aim of the study was to evaluate efficacy of fractional CO₂ vaginal laser treatment (Laser, L) and compare it to local estrogen therapy (Estriol, E) and the combination of both treatments (Laser + Estriol, LE) in the treatment of vulvovaginal atrophy (VVA).

Methods: A total of 45 postmenopausal women meeting inclusion criteria were randomized in L, E, or LE groups. Assessments at baseline, 8 and 20 weeks, were conducted using Vaginal Health Index (VHI), Visual Analog Scale for VVA symptoms (dyspareunia, dryness, and burning), Female Sexual Function Index, and maturation value (MV) of Meisels.

Results: Forty-five women were included and 3 women were lost to follow-up. VHI average score was significantly higher at weeks 8 and 20 in all study arms. At week 20, the LE arm also showed incremental improvement of VHI score ($P = 0.01$). L and LE groups showed a significant improvement of dyspareunia, burning, and dryness, and the E arm only of dryness ($P < 0.001$). LE group presented significant improvement of total Female Sex Function Index (FSFI) score ($P = 0.02$) and individual domains of pain, desire, and lubrication. In contrast, the L group showed significant worsening of pain domain in FSFI ($P = 0.04$), but FSFI total scores were comparable in all treatment arms at week 20.

Conclusions: CO₂ vaginal laser alone or in combination with topical estriol is a good treatment option for VVA symptoms. Sexual-related pain with vaginal laser treatment might be of concern.
CO₂-laser for the genitourinary syndrome of menopause. How many laser sessions?

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Sexual dysfunction

ABSTRACT

Objectives: The aim of this prospective study was to assess the efficacy of 3, 4 or 5 CO₂-laser sessions for the management of the genitourinary syndrome of menopause (GSM).

Methods: Postmenopausal women with moderate to severe symptoms of dyspareunia, wanting to resume/retain sexual activity, were treated with 3–5 laser sessions depending on symptom severity/presence, sexual function, clinical findings and women's preference following the third laser application.

Main outcomes: Severity of dyspareunia, dryness, sexual function, sexual satisfaction and frequency of sexual intercourse defined the primary outcomes. Vaginal Maturation Value (VMV) and Vaginal Health Index Score (VHIS) defined the secondary ones.

Results: Fifty-five women received three sessions, 53 an extra fourth and 22 an extra fifth. Following the third, fourth and fifth laser sessions, respectively: dyspareunia completely regressed in 15/55 (27%), 32/55 (58%) and 38/47 (81%) of participants; dryness completely regressed in 20/55 (36%), 36/55 (66%) and 44/51 (86%); normal sexual function resumed in 23/55 (41%), 37/54 (69%) and 41/49 (84%); VMV regained non-atrophic values in 29/55 (53%), 38/55 (69%) and 42/50 (84%); and VHIS regained non-atrophic values in 44/55 (80%), 53/55 (96%) and 55/55 (100%) of participants.

Conclusion: Results of this study indicate that CO₂-laser therapy may contribute to complete regression of dyspareunia and dryness and reestablishment of normal sexual function in postmenopausal women, in a dose–response manner. An extra fourth or fifth session may further increase the GSM symptom-free rate.
Microablative fractional CO₂ laser for the genitourinary syndrome of menopause: power of 30 or 40 W?

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THANK YOU

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