



Fractional CO₂ Laser for Genitourinary Syndrome of Menopause: Evaluating the Evidence

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The fractionated CO₂ laser has been marketed to women for a variety of gynecologic symptoms and conditions, including the genitourinary syndrome of menopause (GSM). The evidence has been limited, precluding conclusions regarding the efficacy and safety of the therapy. However, data from randomized, controlled trials evaluating this technology for GSM are now available. This Practice Pearl addresses the latest data concerning the use of the fractionated CO₂ laser for the treatment of GSM.

Genitourinary syndrome of menopause (GSM) affects up to 84% of women.¹ Because GSM does not improve over time, many of those affected may have symptoms for decades if left untreated. Symptoms can be distressing and uncomfortable and can significantly affect quality of life.^{1,2}

Scope of the problem. Nonprescription vaginal lubricants and moisturizers are often offered as first-line therapy for GSM. Although they help some, many women need vaginal (estrogen and dehydroepiandrosterone) and/or systemic (estrogen or ospemifene) prescription therapies.¹ These medications for GSM are very effective but are underprescribed for a variety of reasons, including an underappreciation among professionals of the serious effect of GSM on quality of life, discomfort discussing sexual health, and a lack of education about the efficacy and safety of these products. In addition, the cost of prescription therapies can be a barrier, and some find the vaginal products cumbersome, irritating, or messy. Prescription therapies also may not be an option for certain women with hormone-sensitive cancers. Therefore, there is a need for effective and safe nonpharmaceutical options for the treatment of GSM.

Historic data. The fractional carbon dioxide, or CO₂, laser has been promoted for the management of GSM. The hypothesis behind the fractional CO₂ laser is that the fractionated or split beams of light create a controlled thermal injury to the vaginal mucosa, increasing blood flow and stimulating collagen remodeling and regeneration.² The initial supporting evidence for the CO₂ laser was based on small, uncontrolled studies of histologic changes in the vaginal mucosa, observational studies, and uncontrolled trials. Despite the limited data and lack of sham-controlled clinical trials, laser therapy was widely promoted for GSM. Prompted by concerns about the claims of efficacy and reports of complications, in 2018 FDA issued a warning, stating “that the FDA has

serious concerns about the use of these devices to treat gynecological conditions beyond those for which the devices have been approved or cleared.”³

A clinical trial comparing laser with topical estrogen therapy (estriol) for GSM was published in 2018, several years after these devices were being used for this indication.⁴ It evaluated 42 women randomized to one of three arms: combined laser and vaginal estriol; laser arm with placebo estriol; and estriol with sham laser therapy. The authors concluded that outcomes were similar among the three groups but advised in their discussion that their study was only powered to evaluate differences in the vaginal health index and that “their findings should be interpreted with extreme caution.”⁴

A meta-analysis of studies published up to December 2020 concluded that although the Female Sexual Function Index improved significantly in eight studies, there was only a “clinically relevant” difference in two. In addition, most studies were single center and nonrandomized, and the “quality of the body of evidence” was considered “very low” or “low.”⁵

Consensus statements. A variety of professional organizations have released statements or guidelines regarding the use of laser for GSM. The 2019 Best Practice Guideline from the International Society for the Study of Vulvovaginal Disease and the board of trustees of the International Continence Society recommended against the use of vaginal laser for the treatment of vaginal atrophy outside of “well-designed clinical trials.”² A 2021 American College of Gynecologists and Obstetricians consensus statement concluded: “Additional research is warranted before recommending laser therapy for this indication.”⁶ The National Institute for Health and Care Excellence (updated 2021) states that “evidence on long-term safety and efficacy is inadequate in quality and quantity” and recommends that transvaginal laser for GSM should only be used in appropriately powered randomized, controlled clinical trials (RCTs).⁷ And, according to The Menopause Society’s 2020 Genitourinary Syndrome of Menopause position statement: “Additional randomized, prospective, sham-controlled trials of adequate size and scope are necessary before these therapies can be routinely recommended for treatment of GSM.”¹

New studies. Since these guidelines were published, several studies have evaluated laser therapy for GSM, warranting a reevaluation of the evidence. Two of these studies are randomized, double-blind, sham-controlled trials that also included biopsies for vaginal histology. Li and colleagues randomized participants to three laser treatments spaced 1 month apart or sham procedures, with 78 (91.7%) completing 12 months’ follow-up.⁸ Biopsies were collected at enrollment and at 6 months. There were no differences in symptoms, quality of life, or vaginal histology with the laser versus the sham procedure after 1 year. In 2023, Mension and associates randomized women with breast cancer who were taking aromatase inhibitors to either five sessions of laser therapy, spaced 1 month apart, or sham therapy, with both groups also using a hormone-free vaginal hyaluronic moisturizer.⁹ Vaginal cytology and biopsies were performed at baseline and at 6 months. There were no differences in subjective measures, such as sexual function (the primary outcome) and dyspareunia, or objective measures, including vaginal pH, vaginal maturation index, and thickness and elasticity of the vaginal epithelium for the laser versus the sham procedure at 6 months.⁹

There are other RCTs comparing the CO₂ laser with sham therapy, although vaginal biopsies were not included in these studies. Page and colleagues evaluated the effect of the laser on the most bothersome vaginal symptom of GSM with a sham-controlled, double-blind randomized trial in which participants crossed over to the other therapy at 12 weeks.¹⁰ Fifty-seven participants

completed the study, and there was no difference in treatment response between the groups at 12 weeks postlaser therapy. Although there was a trend toward improvement for those who reported dryness as their main concern, the study was not powered for subgroup analysis, making it difficult to draw conclusions. A smaller randomized, double-blind, sham-controlled trial (N=28) also found no improvement with the CO₂ laser for GSM compared with a sham arm, although the study was underpowered to reach conclusions.¹¹

There are two short-term, randomized, double-blind, sham-controlled trials that have shown evidence of efficacy. However, these studies had shorter follow-up durations (≤ 4 mo) and did not include biopsies to evaluate the effect on histology.^{12,13}

One criticism of some of these RCTs is the failure to treat the vestibule, which can be a source of pain or bothersome symptoms with GSM. Clinical trials are needed to resolve this concern.

Another important consideration is concerns about postlaser histologic changes. Animal data challenges the beneficial effect on the vaginal mucosa, and histologic changes in some earlier reports may be more consistent with “reparative changes after a thermal injury,” as opposed to “restoration of function.”^{2,14} In addition, the two sham-controlled studies that included biopsies failed to find changes in histology with the laser versus sham therapy.^{8,9}

Two consistent findings have emerged from the existing research: The first is that vaginal sham therapy elicits a significant short-term subjective response for those with GSM, so further research that does not include a sham arm is of little value in assessing the benefit of laser therapy for GSM. The second is that serious adverse effects from the vaginal CO₂ laser are uncommon.

Pearls. Although there is an unmet need for nonmedication options for GSM, more studies evaluating the effect of the CO₂ laser on vaginal histology and adequately powered sham-controlled trials are necessary before this therapy can be recommended for the treatment of GSM.

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Disclosures

Dr. Gunter reports no financial relationships with ineligible companies.



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