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This clinical e-newsletter from The North American Menopause Society (NAMS) presents questions and cases commonly seen in a menopause specialist's practice. Recognized experts in the field provide their opinions and practical advice. Chrisandra L. Shufelt, MD, NCMP, the Editor of *Menopause e-Consult*, encourages your suggestions for future topics. The opinions expressed in the commentaries are those of the authors and are not necessarily endorsed by NAMS or by Dr. Shufelt.

Question

My patients are requesting a new laser treatment of the vagina to improve their symptoms of vulvovaginal atrophy. What should I tell them?

Commentary

In September 2014, the SmartXide^2 CO_2 laser from the Italian company DEKA, along with a CO_2 laser from the American company Cynosure, were cleared by the US Food and Drug Administration (FDA) for "incision, excision, vaporization and coagulation of body soft tissues in medical specialties including aesthetic (dermatology and plastic surgery), podiatry, otolaryngology (ENT), gynaecology, neurosurgery, orthopaedics, general and thorasic surgery (including open and endoscopic), dental and oral surgery and genitourinary surgery. The use with the scanning unit is indicated for ablative skin resurfacing."[1] Subsequently, a laser system called the MonaLisa Touch for the treatment of vulvovaginal atrophy (VVA) and other symptoms of the genitourinary syndrome of menopause (GSM) has been marketed using this device.

It's important to understand that the criteria for device clearance are much less stringent than for drug approval and that the clearance for the device was as described above and not specifically indicated for use in VVA. Device clearance does not require the large, double-blind, randomized, placebo-controlled trials with established efficacy and safety endpoints required for the approval of new drugs.

Lasers have become a very costly option for the treatment of symptomatic VVA, without a single trial comparing active laser treatment to sham laser treatment and no information on long-term safety. In all published trials to date, only several hundred women have been studied, and most studies are only 12 weeks in duration.

The treatment for VVA is three, short, 5- to 10-minute procedures spaced 6 weeks apart. Some participants show improvement after one treatment; others after two or three completed procedures. No anesthesia or pain medication is required during the outpatient, office-based procedure.

At the present time, there are a variety of companies in the laser procedure field, including Cynosure (MonaLisa Touch), Fotona (IntimaLase/IncontiLase), and Syneron. Some companies claim that the laser, once activated, removes dried skin and revitalizes and stimulates collagen renewal. Researchers have demonstrated that the laser stimulates collagen synthesis, similarly as the technology does in plastic surgery procedures for the face.

In an abstract presented at the 2011 International Continence Society in Glasgow, Salvatore and colleagues reported on the analysis of eight vaginal specimens from four

women who underwent CO_2 fractional laser treatment.[2] Light and electron microscopic evaluation demonstrated remodeling of vaginal connective tissue without damage to surrounding tissues.

A follow-up pilot study was performed in 50 postmenopausal women with symptoms related to VVA who were dissatisfied with previous local estrogen therapies or who were nonresponders.[3] A three-laser application improved the most bothersome vulvovaginal symptom in this 12-week study. A visual analog scale as well as a Vaginal Health Index score (VHIS) were used. The VHIS assesses elasticity, pH, fluid volume, epithelial integrity, and moisture. However, changes in pH and percentage of superficial and parabasal cellular layers (vaginal maturation index) are not specifically mentioned. This study had a small sample size and short duration, without any long-term follow-up of the patients. In addition, sham laser or active comparator groups were lacking.

In another study published in 2015, Salvatore and associates evaluated 77 women with VVA, assessing their sexual function and quality of life after fractional microablative CO_2 laser using the Female Sexual Function Index (FSFI) and the Short Form-12 patient survey.[4] They assessed participants at baseline and at 12 weeks. Patients were advised to avoid coital sexual activity for at least 3 days after each laser application because of a mild inflammatory reaction that may last up to 48 hours. The researchers reported that only two patients could not be treated because their vaginas were too narrow to accommodate the vaginal probe. A 10-mm visual analog scale was used to measure overall satisfaction with sexual life and the intensity of VVA symptoms (such as vaginal burning, vaginal itching, vaginal dryness, dyspareunia, and dysuria) before and after the study period.

The researchers reported improvement in the total FSFI score and the scores in each specific domain at 12 weeks compared with baseline. Seventeen out of 20 women (85%) who were not sexually active because of VVA severity at baseline regained a normal sexual life at the 12-week follow-up. Serious limitations of this small study include absence of a control arm with a sham laser procedure (given the high placebo response reported in interventional trials on female sexual dysfunction) or with hormone treatment. This open-label study precluded an effective control of potential serious confounding factors (eg, higher motivation for coitus) and selection bias (women who were distressed and more motivated for improvement in their sexual lives). In addition, the authors report that the short follow-up precludes the comprehensive understanding of the duration of the laser effect.

Another limitation of these short-term studies is that the potential risk of long-term complications, such as scarring, is not addressed. Patients were not monitored for concurrent use of intravaginal products or systemic medications that could affect vaginal and vulvar health. Over-the-counter moisturizers, lubricants, prescribed local estrogen products, or systemic hormones could have contributed to the observed improvement with laser treatment.

Another small study of laser treatment with a 12-week follow-up demonstrated improved dyspareunia related to VVA in 15 patients.[5]

Most studies report only “minimal” risks, and the procedure is performed on an outpatient or day-hospital basis. Resumption of intercourse is advocated soon after the procedure. The articles mention that most women report some slight redness and or swelling and “some discomfort” that disappears within 1 to 2 days.

Laser technology should not be confused with, also approved, radiofrequency (RF). Lasers use photon energy in the visible and infrared wavelengths, and the mechanism of action is shallow, with penetration and effect up to 1 mm. Radiofrequency is similar to electrocautery, and the energy waves are less focused.

The focus depth of RF is 2.5 mm, but the energy still penetrates up to 4 mm to 5 mm.

Given the lower bar for device clearance by the FDA compared with drug approval, it is very likely that similar systems will come to market. For example, Fotona, an international company, has released two systems in Europe that it describes on its website (www.fotona.com) as "entirely new, minimally invasive gynecology treatments for incontinence [IncontiLase] and vaginal relaxation syndrome [IntimaLase]" but presents incomplete research regarding long-term efficacy or risk. One good thing about competition is that it will drive prices down. It perhaps also will stimulate meaningful and necessary research into efficacy and risk of laser therapies for these indications.

At the present time, there is no ICD 9/10 code for the procedure, and patients' out-of-pocket costs are estimated to be between $600 and $1,000 per procedure (as high as $2,500 per procedure in some areas) and may vary, depending on the area within the United States. Some laser practitioners are advocating a repeat procedure (for an additional fee) at the 1-year mark. However, there currently are no data to support that this repeat procedure is medically necessary or safe. An initial fee of approximately $4,000 followed by $1,000 annually for repeat procedures is a very costly intervention. By comparison, the average cost of vaginally applied estrogen cream twice weekly is estimated at approximately $30 a month or $360 annually. Laser technology is not only a costly venture for the patient but also for the healthcare professional—the purchase price of the laser is approximately $175,000 USD, although financing programs exist.

It is also of concern that many of the laser companies claim on their websites that the CO_2 fractional laser may be a treatment for a variety of conditions, including vaginal laxity, postpartum/lactational dyspareunia, urinary incontinence, and dyspareunia in women with breast cancer, even though no data have been published on these unique patient populations, nor are there any high-quality clinical trials to support these claims.[6]

Although this FDA-cleared laser technology is being marketed extensively to healthcare practitioners and directly to consumers, large, long-term, randomized, sham-controlled studies are needed to further evaluate the safety and efficacy of this procedure. It is important to understand that FDA clearance for a new medical device and its clinical indication (510[k] mechanism) is a modest clinical study requirement compared with the high bar required for a comparable hormone medication approval (NDA mechanism). The same technology may have been used in plastic surgery on facial tissues, but the potential for adverse effects when used on vulvovaginal tissues must be further studied and elucidated, perhaps in a postapproval registry. To date, no long-term studies are available. Studies comparing this new expensive procedure with the gold standard of low-dose local estrogen treatment also are warranted.

In addition, in the age of shrinking healthcare dollars and financial constraints for all women, a cost analysis may be an important consideration when contemplating a costly fee-for-service procedure.

Although laser technology may hold promise for the future of VVA treatment, further long-term efficacy and safety data should be collected before fully embracing this expensive new technology. In addition, the laser has a broad indication; therefore, further research is required before advocating its use in multiple, random gynecologic conditions.

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What's your opinion on laser treatment for symptoms of VVA and GSM? Visit our Member Forum to discuss the June *Menopause e-Consult*.

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