Laser therapy for the restoration of vaginal function

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A B S T R A C T

Laser therapy has a therapeutic role in various medical conditions and most recently has gained interest as a non-hormonal treatment for genitourinary syndrome of menopause (GSM) and as a non-invasive option for stress urinary incontinence (SUI). Several therapies are available to alleviate GSM symptoms, including hormonal and non-hormonal products. Both microablative fractional CO2 laser and the non-ablative vaginal Er:YAG laser (VEL) induce morphological changes in the vaginal tissues, and data from non-randomized clinical trials suggest that laser therapy can alleviate vaginal dryness and dyspareunia. VEL has been reported to improve SUI as well as vaginal prolapse. Although large randomized trials have not been reported, the evidence suggests that VEL can be offered as a safe and efficacious alternative to hormone replacement therapy (HRT) for GSM, as well as a first-line treatment for mild to moderate SUI, before surgical procedures are resorted to. Randomized studies are needed to compare laser treatments with other therapies, as well as to assess the duration of the therapeutic effects and the safety of repeated applications. Research is presently evaluating both an automated robotic probe for VEL treatments and an intraurethral probe for the treatment of severe and type III SUI.

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The word ‘LASER’ is an acronym for ‘light amplification by stimulated emission of radiation’. Lasers generate a beam of photons released from the laser medium; the medium determines the specific wavelength of the light emitted and also typically gives the type of laser its name. Current medical lasers emit wavelengths from the ultraviolet to the mid-infrared portions of the spectrum. The medium is activated with some form of energy, which is usually either light or electricity. The stimulated emission of photons occurs in the medium, which is then amplified in the laser cavity. The cavity consists of the medium bounded in the front and rear by mirrors. The photons emitted are of identical wavelength and are precisely synchronised in phase, temporally and spatially. Moreover, the beam is more or less parallel, a feature known as collimation. The sum of these three characteristics of laser light is termed ‘coherence’, and it is coherence that gives a laser beam its

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uniquely high photon intensity and allows it to be focused on very small areas. Biological tissues such as blood and substances such as melanin and water generally have very different absorption spectra (i.e. they optimally absorb light of different wavelengths). Laser treatment has been long been used safely and effectively used in many areas, such as dermatology, dentistry, ophthalmology and cosmetic medicine. More recently, several innovative publications on the use of laser in gynaecology have also appeared.

This paper reviews the use of laser therapy for the treatment of genitourinary syndrome of menopause (GSM). An extensive search was performed using EMBASE and PubMed Central (PMC)-NCBI for scientific publications written in English, with keywords including genitourinary syndrome of menopause (GSM); vulvovaginal atrophy (VVA); atrophic vaginitis; postmenopausal symptoms; and vaginal laser therapy. All publications reviewed were in English and were published within the last 8 years. The present review is based on a total of 20 prospective studies and 1 randomized controlled study; reported only in an abstract. In addition: 11 review articles and 11 in vitro studies were found to meet the inclusion criteria. The characteristics of the full-length studies published in scientific journals and included in our review are presented in Table 1.

1. Genitourinary syndrome of menopause (GSM)

Genitourinary syndrome of menopause (GSM) includes a constellation of symptoms related to a decline of circulating ovarian hormones, such as vaginal dryness, dyspareunia, recurrent urinary tract infections and urinary incontinence. GSM replaces the term ‘vulvo-vaginal atrophy’, as agreed by the joint terminology conference sponsored by the North American Menopausal Society (NAMS) and the International Society for the Study of Women’s Sexual Health (ISSWSH) [1–5]. All these symptoms may interfere with sexual function and quality of life [6–11].

Several therapeutic options are available to alleviate GSM symptoms, including hormonal and non-hormonal products. Moisturizers and lubricants tend to provide only temporary relief, whereas local vaginal estrogen administration offers long-term relief and so is the treatment of choice [12–17]. However, some women may not wish to take HRT long term or have contraindications to estrogen therapy [12–17]. Recently osmophotons has been introduced as an oral medication for the treatment of dyspareunia. It provides an alternative to oral and local estrogen therapies [18–20]. New management strategies for GSM mean that women can choose from a wide range of options, with due consideration to the benefits and risks associated with each. One such option is laser therapy, which can be used to stimulate tissue repair and to restore normal vaginal function.

2. The CO2 laser: first-generation laser treatment for GSM

The carbon dioxide laser (CO2 laser) was one of the earliest gas lasers developed, and is still one of the most commonly utilized lasers in various industrial and medical applications [21,22]. The CO2 laser emits light at 10,600 nm, the only chromophore for which is water, the major constituent of mucosal tissues. Ablative-pulsed CO2 lasers are used to treat vaginal atrophy [23–35]. In 2011, Gaspar et al. [23] first demonstrated that vaginal fractional CO2 laser treatment induced a significant improvement in the clinical and histological signs of vaginal atrophy. Subsequently, in seminal observational paper, Salvatore et al. [24] reported a 12-week study where symptoms were analysed before and after 3 sessions (one per month) of fractionated CO2 laser. In the sample of 49 patients, vaginal dryness was improved in 43 women (86.0%), vaginal burning in 45 (90.0%), vaginal itching in 40 (80.0%) and dysuria in 37 (74.0%). Dyspareunia was improved in all women who were sexually active. Similar results were obtained in younger women suffering from VVA due to treatment for endometriosis [25]. The effects of microablative fractional CO2 laser therapy on VVA led to an improvement of both sexual function and quality of life [26].

These studies started a new era for the non-hormonal treatment of GSM. The effects of CO2 laser were also evaluated on ex vivo vaginal specimens from postmenopausal women, and the samples showed remodelling without damage to surrounding tissue [27]. Zerbinati et al. [28] published elegant studies that produced histological evidence of the restoration of vaginal mucosal structure following microablative fractional CO2 laser treatment, as well as increased collagen and extracellular matrix production, together with an increase in the thickness of the vaginal epithelium, with the formation of new papilla [28]. Microablative fractional CO2 laser technology has since been presented extensively to healthcare practitioners and directly to consumers. There are now some other CO2 laser systems marketed for the treatment of GSM, using different machines and technologies, with claims of similar effects [23–35]. However, at present no efficacy and safety data are available for GSM treatment with different CO2 lasers.

Recently, Perino et al. [35] reported that fractionated CO2 laser therapy might also improve overactive bladder in post-menopausal women. No data are available about the possible effects of CO2 laser therapy on SUI. No data from randomized trial (sham versus treatment) have been produced and no data on the duration of treatment effects are available.

3. Vaginal erubium laser (VEL®) treatment

The non-ablative 2940 nm Er:YAG (so-called because it uses an erubium yttrium-aluminum-garnet medium) laser uses precisely controlled, sequentially packaged bursts of long pulses, termed SMOOTH® mode. In this paper vaginal erubium laser (VEL) refers to SMOOTH technology. Studies of its thermal effects on human soft tissue have shown deep collagen remodelling and new collagen synthesis [36–44]. Exposure of tissues to an appropriate controlled temperature increase result in a rapid contraction of collagen fibres, leading to the contraction and shrinking of the exposed tissue [38]. The increased temperature elicits collagen remodelling, resulting in the generation of new collagen and an overall improvement in the tightness and elasticity of the treated tissue [44]. In one study of the application of laser therapy to the genital tract, the high success rate for the treatment of multifocal lesions, excisions and tissue coagulation with Er:YAG lasers was accompanied by an interesting and unexpected effect, on vaginal tightening, which in turn resulted in an enhanced sexual experience [43]. This observation inspired further research in the direction of developing a minimally invasive, non-surgical and non-ablative laser treatment [44–73]. Tightening of the vaginal canal and consequently the improvement of sexual gratification have been observed [44–48]. Specific vaginal probes have been designed to enable a uniform and well-controlled VEL distribution on the whole length and circumference of the vaginal canal. The use of erbium SMOOTH technology for vaginal tightening and incontinence has spread around the world and many additional studies have been initiated to further assess this technology and treatment approach. We have to underline that much of the published evidence has been obtained using the non-ablative solid-state Er:YAG laser with a wavelength of 2940 nm. The SMOOTH mode allows the use of a full beam and patterned handpieces to deliver laser energy with different influences on vaginal tissue.

Recent publications suggest that VEL may provide non-ablative, second-generation laser photothermal vaginal therapy [48–73]. Vaginal laser has profound effects on the vaginal epithelium and lamina propria [47,48]. Gaspar et al. [49] presented seminal data on the effects of VEL in comparison with estrogen vaginal administra-
tion. Other groups reported an improvement in GSM in VEL-treated patients [50–52]. In a prospective study of women with GSM, VEL was compared with vaginal estriol administration, a standard treatment of GSM [52]. Signs and symptoms were evaluated subjectively by a visual analogue scale (VAS) and objectively by the Vaginal Health Index (VHI) [52]. Three applications of VEL every 30 days induced a significant improvement both in subjective symptoms of vaginal dryness and dyspareunia, and in the objective evaluation (VHI score). These changes matched those induced by the 3 months of estriol administration [52]. In both groups the VAS scores for vaginal dryness and dyspareunia, from basal values of 8.3 ± 1.3, and 8.2 ± 1.3 cm, respectively, showed a significant (p < 0.01) decrease, to 2.7 ± 0.7 and 2.8 ± 1 cm, after the third VEL treatment or 12 weeks of estriol. In the estriol group a reduction of efficacy was seen 12 weeks after the end of treatment. Conversely, in the VEL group the same positive results were maintained throughout the study period, up to the 6-month follow-up. In that study [52] the VEL treatment was performed in post-menopausal women (PMW) suffering from GSM without any previous or concomitant treatment with estrogens or even non-hormonal vaginal creams. Therefore, the effects of VEL are independent of any pretreatment, suggesting that VEL can be proposed in PMW that cannot be treated with hormones, as in breast cancer survivors, as reported in a small pilot study [51]. The effect of VEL in PMW suffering from GSM has now been demonstrated to be practical, effective, and safe in three non-placebo-controlled clinical trials [50–52].

4. Stress urinary incontinence (SUI) VEL treatment in eight non-placebo-controlled clinical trials has been reported to induce a significant decrease in clinical symptoms for women suffering from stress urinary incontinence (SUI) [53–60]. These effects are ascribed to collagen remodelling. Collagen is an important component of the pelvic floor, making up more than 80% of protein content of the endopelvic fascia. Ageing is associated with a decrease in the synthesis of new collagen, resulting in decreasing collagen content and functional damage of the pelvic floor; damage may also be caused by the process of childbirth. SUI is more frequent in women with reduced collagen content in their anterior vaginal wall and pubocervical fasciae [61,62].

Radiofrequency (RF) energy has also been used for the thermal non-surgical treatment of SUI. It has been reported that, using transurethral probes, RF thermal shrinkage and remodelling of collagen can be achieved in the bladder neck and proximal urethra, with success rates of up to 80% [63,64]. However, RF heating decays rapidly with depth and increasing RF power increases thermal coagulation and superficial tissue impedance, further restraining RF penetration. Consequently, RF probes for SUI therapy require the insertion of needles into the urethral wall and submucosal tissue for localized heating, collagen denaturation, and shrinkage, with saline irrigation of the mucosa to prevent overheating. Thus, RF procedures for SUI may require anaesthesia and may be more invasive than other non-surgical treatments [65–68].

Conversely, Er:YAG laser light is strongly absorbed in water, and may increase tissue temperature, leading to the initiation of neo-collagenesis [69–71]. A specifically designed sequence of SMOOTH Er:YAG laser pulses can be delivered to the vaginal tissue in order to achieve controlled heating of the collagen in the deeper mucosa layers, without ablation or over-heating of the mucosal surface. As a result of the temperature increase, the intermolecular cross-links that stabilize collagen’s triple-helix structure are broken, leading to collagen shrinkage and greater tissue rigidity. Fistonic et al. [53] were the first to evaluate the efficacy and safety of VEL in women with SUI. They assessed the impact of SUI using the Incontinence Questionnaire – Urinary Incontinence Short Form (ICIQ–UI SF). In post-menopausal women with moderate or severe symptoms of SUI, treatment with VEL was associated with a significant improvement in ICIQ–UI SF scores (p < 0.01). They evaluated the short-term effect of VEL treatment, and correlated good results other risk factors such as age and body mass index (BMI). They concluded that there was a significantly higher correction of SUI in women with a BMI < 25 (67%) than in overweight women (25%) and results were better in women under 39 years (100%) than in those over 60 years (8%) (p < 0.001). In that clinical trial no serious adverse events were reported [53].

Fistonic et al. [59] demonstrated that the numerical modelling of the temperature distribution obtained with the SMOOTH mode corresponds to the in vivo temperatures of the vaginal mucosa determined using a thermal camera. They were able therefore to demonstrate that the VEL the treatment with the SMOOTH mode results in a non-ablative temperature increase in the range of 60–70 °C required to achieve collagen contraction, initiating neo-collagenesis in vivo [70,71]. That is, the VEL treatment increased the tissue temperature up to the optimal range, but did not exceed the threshold for ablation or irreversible tissue damage. In this way, VEL can increase the density of the connective tissue, stimulating collagen remodelling and neoangiogenesis, leading to a suburethral reinforcement to correct mild to moderate SUI. After a single VEL treatment, patients can experience significant improvement in symptoms associated with SUI, including incontinence, overactive bladder, and dyspareunia. The benefits of VEL may persist for up to 12 months, making it a valuable option for women with SUI who do not wish to undergo more invasive procedures. 

Table 1
Characteristics of the full text published studies included in this review; the level of evidence is referred as in http://apps.who.int/medicinedocs/en/d/Jwhozip42e/13.1.html.

<table>
<thead>
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<th>Paper (Ref.)</th>
<th>year</th>
<th>Publication type</th>
<th>Number of patients</th>
<th>Level of evidence</th>
<th>Study design</th>
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treatment a reduction of 4–6 points in the ICIQ-Ul score has been reported [53,54], while after 3 sessions VEL can induce a decrease of more than 6 points in the ICIQ-Ul score, and the results are maintained 6 months after treatment [52]. The effectiveness of VEL has been confirmed in a randomized clinical trial vs. sham treatment [54]; further, in a trial comparing VEL with pelvic floor muscle training, VEL also reduced the post-void residual urine volume and Q-tip angulation [56].

The Ogircn study [58] enrolled a sample of 175 women with urinary incontinence. Scores on the Incontinence Severity Index (ISI) were significantly reduced after two sessions of VEL, and there was an improvement of SUI symptoms in all age groups [58]. At variance with other reports, age did not influence the final outcome. After one-year follow-up, the majority of the SUI patients (77%) were improved. However, only 34% of the patients diagnosed with mixed urinary incontinence improved; the difference between these two groups was statistically significant [58]. After one year, 62% of all patients were cured (dry). This study clearly shows that patient selection is vital in order to predict the effectiveness of VEL in treating urinary incontinence.

In the study conducted by Pardo et al. [60], 42 women with mild to severe SUI were treated with two VEL sessions, with a 21–28-day interval between sessions. In this study [60], more than 78% of the women reported improvement, which was not related to age or the number of vaginal deliveries. In 38.1% of the study population a complete cure of SUI was achieved after the two VEL sessions [59]. The results of this study indicate that VEL can effectively reduce the symptoms of SUI, even in patients with severe SUI [59]. In addition, the sexually active women reported greater sexual gratification [60]. A positive effect of VEL on sexual activity was confirmed in a study conducted by Tien et al. [74]. In that study, scores on the ‘desire’ domain of female sexual function improved following VEL treatment, with a concomitant improvement on measures of health-related quality of life [74]. In addition, Tien et al. [74] reported a success rate (cure and improvement rate determined by measuring pad weights before and after VEL treatment) for SUI of all grades of 79%. Of the women with mild SUI, 50% were cured and 27.8% exhibited improvement at 6 months [74]. However, in this study no differences in urodynamic values between baseline and post-treatment time points were found [74]. The authors suggested that this apparent paradox might be a consequence of a possible effect of tighter and more elastic collagen acting as a ‘hammock’, preventing urine leakage and reducing pad weights [74]. In patients suffering from mixed urinary incontinence, Tien et al. [74] reported an apparent improvement in overactive bladder symptoms after VEL treatment, as described by Perino et al. [35] using the CO2 laser.

5. Vaginal relaxation syndrome and pelvic organ prolapse

Because of its effects on collagen and pelvic floor tissue, VEL could represent an effective non-surgical method of treating not only female SUI but also other disorders resulting from diminished pelvic floor support, such as vaginal relaxation syndrome (VRS) and pelvic organ prolapse (POP), with or without SUI. VRS is a clinical condition, not well defined, where the relaxing of the vaginal wall leads to physical and psychological problems mainly related to decreasing sexual satisfaction for both the woman and her partner. VRS can be assimilated with stage 1 POP.

The efficacy of VEL treatment for POP of grade II or higher has been assessed using the Baden-Walker scale [46,47,72]. At the final follow-up, the large majority of patients had their prolapse reduced by at least one grade, 30–45% by two grades and approximately 10% by three grades. Twelve-month follow-up data after the last VEL treatment are available [72]. Treatment discomfort was low (the maximum score was 3 on a 10-point scale) and a large majority of the patients reported improvement. No adverse events were reported. A significant improvement in vaginal laxity was reported by partners (76.6%) as well as in sexual satisfaction (70.0%).

6. Clinical and cost issues

Although data from large randomized trials are not available, the results from observational studies are encouraging. The effect of laser treatment appears to be comparable to that exerted by local hormone treatment in postmenopausal women suffering from GSM. Vaginal laser treatment may be appropriate for women who cannot or do not want to be treated with hormones, as well as for women who reject the long-term use of moisturising/lubricant because of its interference with sexual activity. The data on vaginal laser procedures from non-randomized clinical trials appear to suggest that they are safe and well accepted, with no major side-effects or adverse events reported.

The cost of laser treatment is 2–4 times that of local lubricants/moisturizing products for one year of therapy. Currently, the laser costs may vary from €1000 to €1500. Some private insurance companies are now providing coverage of VEL treatments for SUI in order to avoid or limit or postpone the costs of surgical interventions. Future investigations should compare long-term compliance and costs with the use of vaginal hormonal/non-hormonal vaginal therapy and the costs of laser therapy.

7. Future research

Different aspects of vaginal laser treatment need further investigation. The possible difference in the outcomes of VEL treatment with or without estrogen pretreatment or the current use of estrogenic or non-hormonal therapies should be examined in randomized studies. No data on the duration of laser treatment effects after 6–12 months are currently available. There is also the question of when laser procedures should be offered. Large, long-term and well-controlled studies are required to explore the use of vaginal laser so that alternative procedures can be offered, possibly in association with established therapies. VEL treatment of SUI needs to be tested not only in women who are not suited for surgery, but also in those who are candidates for surgery. A novel robotic probe is under evaluation, the G-Runner™, an automated control system that allows optimization of the treatment time and avoids operator manual positioning of the handpiece. The G-Runner™ is fully automatic and so improves the targeting of vaginal mucosa and shortens treatment time. In addition, an erbium laser intraurethral probe is being developed to treat severe and type III SUI. Both new probes are being tested in large clinical trials.

8. Conclusions

Studies suggest that laser treatment for the restoration of vaginal function might improve the quality of life of millions of women. Cohort prospective studies show that the procedure is effective and safe, if appropriately applied, and no serious adverse effects have been reported. For GSM, the clinical changes are similar to those induced by estrogen administration. The second-generation SMOOTH VEL treatment may provide not only an effective ablative procedure for the treatment of GSM, but also for mild to moderate SUI and VRS/POP. Further randomized studies are needed to evaluate the laser treatments in comparison with other therapies, as well as to assess the duration of their therapeutic effects and the safety of repeated applications.
Contributors

The authors participated equally in the preparation of this article.

Conflict of interest

MG has received research support, grants and occasional honoraria as a symposium speaker or advisory board member from Bayer, MS&D, Gedeon Richter, Novo Nordisk, Pfizer, Shionogi and TEVA.

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Provenance and peer review

This article has undergone peer review.

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