

Review

Treatment of Female Sexual Dysfunction Due to Dyspareunia with Solid-State Vaginal Laser and Recombinant Platelet-Derived Epidermal Growth Factors: A Viable Possibility?

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Abstract

Objective: To examine the efficacy and safety of non-pharmacological and non-ablative options (or a combination of these) for postmenopausal dyspareunia. **Mechanism:** Narrative review on non-pharmacological and non-ablative options (or a combination of these) for postmenopausal dyspareunia. **Findings in Brief:** Dyspareunia is the most bothersome symptom of the genitourinary syndrome of menopause, often complicated by decreased sexual interest and arousal. Solid-state vaginal laser (SSVL) and recombinant platelet-derived epidermal growth factors (RGFs) are new alternatives that improve female sexual dysfunction resulting from dyspareunia. **Conclusions:** SSVL is a new alternative the treatment of postmenopausal dyspareunia either alone or in combination with other alternatives with efficacy and safety similar to the classical options.

Keywords: female sexual dysfunction; genitourinary syndrome of menopause; dyspareunia; solid-state vaginal laser; epidermal growth factors

1. Introduction

The impact of gradual hormonal deficiency on vulvo-vaginal and urinary tissues after menopause causes signs and symptoms that fall under the category of what is now called genitourinary syndrome of menopause (GSM) [1]. In Europe, more than 80% of postmenopausal women are reported to suffer from GSM, most of whom experience effects on their general health and sexuality in particular, with dyspareunia being the most bothersome symptom, often complicated by decreased sexual interest and arousal [2].

Despite their high prevalence, treating these female sexual dysfunctions is highly complex, mainly due to the need for compliance and continuity, where most pharmacological options usually fail [3]. For other non-pharmacological treatments that do not require daily compliance (ablative lasers), the discomfort caused makes them difficult to access. Other non-pharmacological non-ablative alternatives are still under development, as there is little comparative evidence [4]. However, a literature review showing the degree of efficacy and safety they offer is needed to inform the recommendation of treatments for women with dyspareunia [5].

Therefore, this narrative review will examine the efficacy and safety of other non-pharmacological and non-ablative options (or a combination of these), in particular, solid-state vaginal laser (SSVL) for postmenopausal dyspareunia, giving special consideration to the issue of female sexual dysfunction.

2. Genitourinary Syndrome of Menopause and Sexuality

Vaginal health is “the state of the vagina that maintains age-appropriate conditions without producing local symptoms and allows for a satisfying sexual life”. Vaginal health depends to a large extent on hormonal secretion. Estrogens stimulate the renewal of vaginal tissues by synthesizing collagen and elastic fibers, which facilitate their transudation with acid pH and maintain the vaginal microbiota, while androgens increase cell growth, mucin production, collagen turnover, blood perfusion, neurotransmitter synthesis, and nerve-ending growth [6,7].

Accordingly, the decrease in estrogen and androgen in postmenopausal women leads to anatomical, physiological, and functional changes in the vulvovaginal area. Such changes include shortening, thinning, and decrease in vaginal secretion, atrophy of the skin and vulva with reduction and even disappearance of the labia minora, and stenosis of the introitus responsible for the most bothersome symptom of GSM: dyspareunia.

Dyspareunia is defined as the presence of persistent pain associated with sexual intercourse. It causes discomfort and negatively interferes with sexuality, a problem that is compounded by a lack of sexual desire [5].

Although it is the most common sexual problem in women of any age, there is a peak of increased prevalence of dyspareunia (especially of vestibular origin) and decreased desire after menopause.



As noted in the introduction, adherence to conventional therapies is essential for treating postmenopausal dyspareunia [8]. Some clinical practice guidelines incorporate initiatives to improve adherence, such as *empowered sequential therapy*. The latter is regarded as “sequential” because it is a long-term treatment that evolves according to the woman’s needs, while “empowered” refers to the fact that the woman is involved in the decision-making process for selecting the most appropriate treatment [5,9].

3. Treatments for GSM Sexual Dysfunctions

Following this line of empowered sequencing, most hormone treatments (estrogen, prasterone, or ospemifene) are strongly recommended based on high-quality evidence. Therefore, the decision to choose one type of treatment or another is not algorithmic (there is no first-line treatment) but instead depends on factors related to the particular symptomatology, but, above all, on the individual woman’s preferences [9].

General healthy lifestyle recommendations can be made for all women. Aside from general habits such as regular physical exercise, smoking cessation, and maintaining a healthy weight, it is recommended that women maintain sexual activity and practice specific exercises to improve vaginal tone [10].

Regenerative medicine is an emerging inter- and multidisciplinary field of research and clinical application. This strategy focuses on repairing, replacing, or regenerating cells, tissues, or organs to restore impaired functioning due to any cause, including the effects of aging. All treatment alternatives offered by Regenerative Gynecology can be used alone or in combination with hormonal options for dyspareunia and associated sexual dysfunctions since they promote regeneration and improvement of genital tropisms [11].

Lasers represent a new treatment option for GSM due to their ability to revitalize (“rejuvenate”) vulvovaginal tissues with increased collagen and fibroblastic activity. The mechanism of action of lasers consists of provoking small mucosal/dermal “wounds” that stimulate their healing through the production of collagen and elastin and the inhibition of metalloproteases, resulting in a remodeling of the dermal or mucosal extracellular matrix. The regeneration of atrophy is the first step towards the relief of related symptoms, as well as associated vaginal weakness, stress urinary incontinence, and sexual dysfunctions [12].

The most widely used laser types in the treatment of GSM are CO₂ and Erbium YAG [13], which have collagen-repairing and regenerative properties. Studies comparing the effectiveness of these therapies with local estrogenic treatments have reported similar improvements in lubrication and desire [14–18]. Furthermore, a recent systematic review concludes that CO₂ laser improves sexual function in women with GSM [19]. However, these studies have major methodological limitations (lack of randomization,

blinding, or a control group). A grade analysis provided Level III evidence and a Grade D recommendation. Although the safety of CO₂ lasers has been confirmed in all these series, side effects have also been described, mainly derived from pain/burning of the vagina. Moreover, this therapy is relatively costly and, therefore, unsustainable.

4. Solid-State Vaginal Laser

Other less harmful lasers, such as the SSVL, are being tested to improve sexual symptomatology associated with GSM. SSVL exerts its therapeutic effect through a non-ablative procedure similar to radiofrequency, focusing its action on deep vaginal tissues where the increase in collagen fibers is most effective. Unlike ablative lasers, this avoids superficial damage to the vaginal mucosa. In addition, it uses a more efficient light source that dissipates less heat and thus requires a less powerful cooling system, making it a more sustainable alternative [20].

Thus, an Italian study [20] presented SSVL data similar to those found with other lasers in women who had not responded to estrogen therapy or who did not wish to use hormones. This study reported significant short-term improvements in dyspareunia, urinary continence, and vaginal lubrication, which were maintained during the four months of follow-up. Moreover, the authors found reduced fibrosis, along with increased angioblast fibroblastic activity (angioblast granulation tissue type) and collagen. In addition, tissue inflammation was reduced, observing a total reduction of inflammatory infiltrate of the dermis and vaginal mucosa. However, to our knowledge, only one study has evaluated vaginal histological changes in postmenopausal women treated with fractional CO₂ lasers, showing collagen formation and restoration of the trabecular architecture similar to that found in premenopausal women [21].

An interesting observation to emerge from these studies is that for treatments to be effective, their use must not be delayed for too long; this is particularly evident in women over 75 years of age and those with early menopause who sought medical help too late. Consequently, the best age at which to recommend these treatment options is in the years around menopause.

A special situation is the treatment of GSM in breast cancer patients. The healthy lifestyles recommended for women with GSM are particularly relevant for breast cancer patients. The benefits of maintaining sexual activity to help improve local vascularization and decrease symptoms of GSM should also be reported. While no randomized controlled trial (RCT) data are available for lasers in these women, case series studies have reported favorable results with no apparent contraindications [22,23].

5. Recombinant Platelet-Derived Epidermal Growth Factors (RGFs)

Recombinant platelet-derived epidermal growth factors (RGFs) have shown to be beneficial in treating various

skin and mucosal conditions with excellent safety and tolerability profiles. In addition, laboratory data indicate their efficacy in improving vaginal tropisms. They are regarded as a good alternative for treating GSM due to their ability to augment angiogenesis stimulation, fibronectin synthesis, cell growth, and tissue repair [24].

Experiments in mice have shown that estrogens increase the expression of RGFs and their receptors, which, in turn, act as physiological mediators of the estrogenic effect on the reproductive tract. Moreover, when administered in young female mice, RGFs have been shown to induce early vaginal opening, i.e., they play an important role in vaginal development, supporting the biological plausibility of using these therapies to treat genitourinary atrophy [25].

Other human and animal studies suggest that RGFs can treat various skin and mucosal diseases and complications (wounds, scars, dermatitis, skin rejuvenation, conjunctival and oropharyngeal mucosa) with good tolerability and safety. For example, at the genitourinary level, they have been used in the treatment of lichen sclerosus (LS), cystitis, and vaginal atrophy, while showing good efficacy in the healing of lesions of the uterine cervix, with a shorter healing time compared with radiofrequency therapy [26–29].

6. Other Alternatives

Hyaluronic acid is effective in treating GSM due to its moisturizing, reparative, antioxidant and anti-aging properties similar to those offered by local estrogens and other vaginal moisturizers.

Treatment with RGFs—in combination with hyaluronic acid (HA)—reduces inflammation and stimulates angiogenesis and collagen synthesis, improving vaginal tropism and restoring a normal caliber [30].

Combining HA and vitamins E and C reduces vaginal damage from radiotherapy and improves vaginal atrophy and related symptoms [31,32].

To evaluate the efficacy and safety of a vaginal gel with HA in treating vaginal dryness in postmenopausal women, its effects were compared with those of an estriol cream using a visual analog scale. In this randomized clinical trial, both the HA vaginal gel and estriol cream significantly improved the clinical symptoms of vaginal dryness, with an improvement rate of 84.44% and 89.42%, respectively, after ten applications, with no statistically significant differences between them [33].

Other studies comparing the efficacy of HA and local estrogens have shown that vaginal atrophy symptoms, itching, maturation index, pH, and vaginal symptom composite score were significantly alleviated with both types of treatment in an Iranian RCT ($p < 0.001$). At the same time, urinary incontinence was only improved in the hyaluronic acid group ($p < 0.05$). Improvement in all these signs and symptoms was superior in HA-treated patients [34].

In a similar Turkish RCT, symptoms of epithelial atrophy, vaginal pH, vaginal maturation indices, and pH were significantly relieved by HA and estrogens (both administered as vaginal tablets) ($p < 0.001$). While symptom relief was superior with estrogens ($p < 0.05$), HA has been shown to be a suitable alternative for women with genitourinary atrophy who do not wish to use hormonal treatments [35].

In a multicenter, randomized, controlled, open-label, parallel-group trial in Switzerland, a vaginal gel with HA was compared with estriol vaginal cream in 144 women with vaginal dryness randomized at a 1:1 ratio every three days for a total of ten applications. The authors concluded that the HA vaginal gel was not inferior to estriol in women with vaginal dryness. Therefore, they suggest using HA vaginal gel as an alternative treatment to vaginal estrogens and recommend considering its general use in women presenting with vaginal dryness resulting from any cause [36].

In a French study, HA significantly improved vaginal symptoms at one month (–25% for dryness and –46% for pain, $p < 0.001$) and at three months –86% and –79%, respectively). Vaginal Health Index (VHS) improved significantly (from 30% at one month to 72% at three months, $p < 0.001$) [37].

These treatments are also particularly useful for BCS women [38] and cervical cancer survivors [39].

7. Combined Laser Therapies

A recent Italian study of 75 women (25 in a Laser group, 25 in a Laser + estrogen group, and 25 in a Laser + moisturizers group) revealed that mean Vaginal Health Index and Vulvar Health Index scores, sexual function or quality of life test scores, as well as genitourinary syndrome of menopause (GMS) symptoms (Pain, Dryness, Burning, Itching, and Dysuria), improved significantly with all options, with no differences between the treatments. However, only lubrication improved significantly in the laser plus moisturizers group [40].

8. Conclusions

Postmenopausal dyspareunia involves genitourinary tissues other than the vagina, and its treatment is one of the current challenges in our clinical practice. SSVL offers a new alternative for treating postmenopausal dyspareunia, either alone or in combination with other treatments with efficacy and safety similar to conventional options. The main limitation is the heterogeneity and low quality of the studies reviewed, their lack of specificity in defining the degree of pain and sexual involvement, and the small sample sizes with high dropout rates. High-quality studies are needed in the form of RCTs with a larger number of participants to increase the level of our recommendations.

Author Contributions

NM and FQ—conception and design of the idea, data interpretation, statement and approved the final version of the manuscript.

Ethics Approval and Consent to Participate

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Conflict of Interest

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