SEXUAL MEDICINE REVIEWS

Sexual Function in Women Suffering From Genitourinary Syndrome of Menopause Treated With Fractionated CO_2 Laser

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ABSTRACT

Introduction: Genitourinary syndrome of menopause (GSM) has a significant impact on the trophism of the genital and lower urinary tracts and can considerably impair sexual function. Fractional CO_2 laser has a regenerative effect on vulvovaginal tissue trophism after menopause.

Aim: To review the available literature on the effect of fractional CO_2 laser on the sexual function of postmenopausal women affected by GSM.

Methods: A database search was carried out using the terms *CO_2 laser, vaginal atrophy, sexual function, dyspareunia,* and *genitourinary syndrome of menopause* and excluding studies using other types of laser or including breast cancer survivors with vulvovaginal atrophy. For statistical analysis, the estimated overall laser effect was computed (when at least two studies were involved) and data type of generic inverse variance was computed using inverse variance as the statistical method, a random-effects model, and the difference in means as an effect measurement.

Main Outcome Measures: Different methods of evaluating sexual function were reported and studies were grouped and analyzed accordingly. Subjective assessment for dyspareunia was evaluated with a 10-point visual analog scale. Patient-reported outcome for an overall perception of sexual function was evaluated with a Likert scale. The Female Sexual Function Index was used as a condition-specific questionnaire.

Results: Six articles were considered for this review. A total of 273 women (mean age = 57.8 years) were treated with the same protocol in all studies. Compared with baseline, at the end of the treatment, dyspareunia significantly decreased in severity ($P < .001$), and the patient's perception of overall sexual function showed a statistically significant improvement ($P < .001$). At the last follow-up visit, the Female Sexual Function Index score for each single domain and overall score was significantly better than at entry ($P < .001$).

Conclusion: Fractional CO_2 laser can improve sexual function in postmenopausal women affected by GSM by restoring a better trophism in the lower genitourinary tract. **Salvatore S, Pitsouni E, Del Deo F, et al. Sexual Function in Women Suffering From Genitourinary Syndrome of Menopause Treated With Fractionated CO_2 Laser. Sex Med Rev 2017;X:XXX–XXX.**

Key Words: CO_2 Laser; Genitourinary Syndrome of Menopause; Sexual Function; Quality of Life

INTRODUCTION

In 1916 Albert Einstein[1] introduced the concept of stimulated emission for energy balance, the primary principle of the laser (acronym for light amplification by stimulated emission of radiation). However, although the first functioning laser was described by Maiman[2] in 1960, the first scientific report of laser medical use was in dermatology and described by Goldman et al[3] in 1963.

The interaction between an electromagnetic wave and biological tissue depends on the wavelength and on the optical properties of the tissue; different light sources are commonly used in medicine with specific wavelengths. The CO_2 laser is in the infrared spectrum, with a wavelength of 10,600 nm and high water absorption, giving it superficial action.

The laser mode of delivery can be continuous or fractionated; the latter avoids possible tissue damage secondary to overheating.

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Tissue modifications produced in this way can vary depending on the machine setting and can include vaporization, ablation, coagulation, collage shrinkage, or collagen neo-synthesis and remodeling. Studies on laser skin resurfacing have demonstrated that shrinkage of collagen fibers, after they have been denatured by laser-generated heat, is the primary mechanism of skin tightening, although vaporization of intracellular water and ablation also contribute. The wound-healing phase is initiated by extremely high levels of collagenases (matrix metalloproteinases), which degrade the fragmented collagenous matrix. Rapid reconstitution of the epidermis from adjacent epidermal cells contrasts with healing after traditional resurfacing in which new epidermis is derived from cells that migrate from adnexal structures. A prolonged period of new dermal collagenesis of up to at least 6 months follows.[4–7]

Because of its regenerative tissue properties, the fractional CO_2 laser was used first in dermatology for many conditions including scars and changes caused by acne and aging, among other indications, and then in many other medical fields. Different studies have described the successful effect of fractional CO_2 laser in treating aging-related and atrophic conditions.[8–12] In 2003 Capon and Mordon[13] reported the mechanism of action of CO_2 laser in regenerating atrophic tissue through micro-ablative and thermal effects. The former induces tissue regeneration, whereas the latter induces some changes in cell metabolism. The heating shock induces the production of some proteins called *heat shock proteins.* Heat shock protein 70 stimulates the action of transforming growth factor-β in activating fibrocytes to become fibroblasts that are responsible for the synthesis of the new extracellular matrix, new collagen, and new elastic fibers. This process of tissue remodeling takes 30 days to occur.

Fractional CO_2 laser also has been used in dentistry for severe conditions such as oral leukoplakia.[14] In all these conditions, the regenerative effect of CO_2 laser can be used to remodel the affected tissue to create healthy tissue.

Genitourinary syndrome of menopause (GSM) is a new terminology used to describe symptoms that occur secondary to vulvovaginal atrophy (VVA).[15] The recent change in terminology from "vulvovaginal atrophy" or "atrophic vaginitis" to "genitourinary syndrome of menopause" stems from a consensus panel consisting of the Board of Directors of the International Society for the Study of Women's Sexual Health and the Board of Trustees of the North American Menopause Society (NAMS). Based on a terminology consensus conference in May 2013, they determined that "genitourinary syndrome of menopause" is a more accurate, all-encompassing, and more publicly acceptable term to indicate the collection of genital, urologic, and sexual sequelae caused by hypoestrogenism after menopause. Premenopausal women also can develop an estrogen deficiency with similar sequelae, in particular those treated with hormonal therapies and chemotherapy for breast cancer.

Regardless of its origin, the hypoestrogenic state results in anatomic and physiologic changes in the genitourinary tract.[16] A loss of superficial epithelial cells, decreased collagen content and hyalinization, decreased elastin, altered appearance and function of smooth muscle cells, and fewer blood vessels are common histologic findings. Then, there is a loss of vaginal rugae and elasticity that results in a narrowing and shortening of the vagina. The vaginal epithelium becomes much thinner and more fragile, resulting in tears that can lead to bleeding and fissures, especially during sexual activity. There also is a loss of subcutaneous fat from the labia majora and these changes can result in narrowing of the introitus, fusion of the labia majora, and shrinkage of the clitoral prepuce and urethra. The vaginal pH becomes more alkaline, which can alter the vaginal microbiota and increase the risk of urogenital infections (specifically, urinary tract infections). Vaginal secretions, largely transudate, from the vaginal vasculature also decrease over time. These menopause-related changes in the genitourinary tract can lead to debilitating symptoms whose prevalence, unlike vasomotor symptoms, tends to increase with the number of years since menopause.

Genital complaints include vaginal or vulvar dryness, burning, and irritation. Lack of lubrication, discomfort, or pain considerably impairs sexual function. Because the urethra and the bladder trigone are derived embryologically from the same estrogen receptor–dense primitive urogenital sinus tissue, women also might complain of "irritative" bladder symptoms such as frequency of micturition, urgency, dysuria, and recurrent urinary tract infections.[15]

In a postmenopausal woman complaining of these symptoms, examination of the external genitalia might show a pale and shiny vaginal mucosa with possible patches of erythema. Lacerations or lesions, labial fusion, or introital stenosis might be present. After the initial clinical assessment, several laboratory tests can be considered to confirm the diagnosis. Vaginal cytology shows an increase in basal epithelial cells and a decrease in superficial cells, whereas vaginal pH, Pap test, and vaginal culture are useful to detect the presence of genitourinary infections.[17]

According to the NAMS position statement on the management of symptomatic VVA, use of non-hormonal lubricants during intercourse and, if indicated, regular use of long-acting vaginal moisturizers are first-line therapies, whereas estrogens remain the therapeutic standard for symptomatic women with moderate to severe VVA and for those with milder VVA that does not respond to lubricants and moisturizers. Estrogens can be administered vaginally or systemically but low-dose vaginal estrogens should be preferred when VVA is the only menopausal symptom.[18]

As stated in the American Congress of the Obstetricians and Gynecologists' (ACOG) practice bulletin on the management of menopausal symptoms, non-estrogen water-based or silicone-based vaginal lubricants and moisturizers might be particularly helpful in women who do not wish to use hormonal therapies.[19] Vaginal lubricants are used to relieve friction and dyspareunia related to vaginal dryness during intercourse and are applied to the vaginal introitus before intercourse. Vaginal moisturizers are