

Fractional CO₂ Laser: the new frontier for the treatment of vulvo-vaginal atrophy symptoms

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SUMMARY: Fractional CO₂ Laser: the new frontier for the treatment of vulvo-vaginal atrophy symptoms.

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The vulvo-vaginal atrophy (VVA) is a chronic condition characterized by gradual involution of the mucous membranes and vulvo-vaginal tissues, which is manifested in the climacteric phase. Numerous therapeutic options, hormonal and non-hormonal, have been proposed to alleviate the symptoms related to VVA, but to date none of them is able to guarantee long-term effects. The use of Fractional CO₂ Laser technology applied to the vulvo-vaginal area represents an innovative procedure to make a real "regeneration treatment" of the vaginal tissues. In fact, it is possible to spread the laser energy in the various layers of the vaginal wall, reactivating the synthesis of extracellular matrix and collagen, with the recovery of tissue tropism and improved VVA-related disorders.

RIASSUNTO: Laser CO₂ Frazionato: la nuova frontiera del trattamento dei sintomi da atrofia vulvo-vaginale.

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L'atrofia vulvo-vaginale (AVV) è una condizione cronica progressiva caratterizzata da un' involuzione delle mucose e dei tessuti vulvo-vaginali che si manifesta con la fase climaterica. Numerose opzioni terapeutiche, ormonali e non-ormonali, sono state proposte per alleviare i sintomi correlati all'AVV, ma ad oggi nessuna di esse riesce a garantire un effetto a lungo termine. L'uso della tecnologia del Laser CO₂ Frazionato applicata all'area vulvo-vaginale rappresenta una procedura innovativa per effettuare un vero trattamento di rigenerazione dei tessuti vaginali. Infatti è possibile diffondere l'energia del laser nei vari strati della parete vaginale, riattivando la sintesi di matrice extracellulare e collagene, con il recupero del trofismo tissutale e un miglioramento dei disturbi AVV-correlati.

KEY WORDS: Vulvo-vaginal atrophy - Fractional CO₂ Laser - Dyspareunia - Menopause.
Atrofia vulvo-vaginale - Laser CO₂ Frazionato - Dyspareunia - Menopausa.

Vulvo-vaginal atrophy (VVA) is a progressive, chronic condition that manifests as involution of the vulvo-vaginal mucous membranes and tissues due to the menopausal drop in estrogen levels (1).

During the childbearing years, the vagina is composed of thick layers of healthy cells, and estrogen encourages the growth and development of these cells; therefore, the vaginal epithelium remains multi-layered, and the vaginal walls are supple and elastic (2).

The progressive reduction in circulating estrogen,

that occurs following the cessation of ovarian function during menopause induces various metabolic and tissue changes, which are most prominent in the genital tract due to its particular sensitivity to variations in sex hormone levels (2). In particular, the vaginal walls appear less elastic with a loss of rugations; the entire vaginal canal becomes narrower and shorter. The vaginal surface appears friable and often bleeds after minimal trauma (3).

The typical symptoms of VVA include vaginal dry-

ness, itching, burning, irritation, dysuria and dyspareunia (4).

Vaginal atrophy can worsen over the years and negatively influence quality of life (QoL) (5). Approximately 50% of postmenopausal women experience the symptoms of VVA, which can range from mild (*annoying*) to severe (*very bothersome*) (6, 7).

Several therapeutic options are available to alleviate VVA symptoms, including non-hormonal products for mild cases, vaginal hormone therapy for persistent symptoms, and systemic hormonal replacement therapy (HRT) for severe symptoms (1, 8). To date, lubricants and vaginal moisturizers do not provide a long-term solution (9). Systemic HRT may be considered for climacteric symptoms in the absence of contraindications, but it is associated with more side effects (1, 18).

Several clinical trials have demonstrated the efficacy of low-dose local estrogen therapies in women with VVA symptoms. However, limited data are available on the long-term safety of these therapies, and no information is available on high-risk patients, as cancer patients (1, 18). Moreover, the major drawback of this approach is the recurrence of symptoms once treatment has been suspended, and this treatment is only effective in the superficial layer of the vaginal walls (10).

In recent years, clinicians have been a greater demand for a safe, effective and long-term therapeutic option to treat VVA symptoms. In this way, by applying the principles of regenerative medicine (just widely used in dermatology and plastic surgery), the use of a Fractional CO₂ Laser may be extended to the vulvo-vaginal tract (11, 12).

This laser consists of a CO₂ ray (infrared ray), which generates heat and vaporizes the water content of target cells. This effect is specific to the superficial layer of skin and does not cause damage to the surrounding tissue.

The first data about the laser CO₂ effect on the application tissues (6) have been identify that the generation of supra-physiologic levels of heat induce a local *Heat Shock Response*, which is a temporary and rapid change in cellular metabolism; this response is characterized by the massive production of heat shock proteins (HSPs), a group of proteins that play a role in the coordinated expression of many growth factors, such as TGF-beta, which is a key element in the inflammatory response and fibrogenic process (12).

It is a real “regeneration” treatment, that improve the vaginal mucosa status with a minimally invasive procedure. The application of the laser, using a specific

probe designed for the vagina, stimulates the synthesis of new mature collagen and matrix substance components in the treated site. In this way, laser treatment improve the elasticity and hydration of the vaginal walls and relieve discomfort in menopausal women.

In particular, we can identify 3 phases of vaginal remodelling: **acute thermal damage** phase (first 48-72 h from application); **proliferation** phase (successive 30 days), with recall of fibroblasts and new collagen and extracellular matrix production; **remodeling** phase (after 40 days) characterized by the placing of new collagen fibers and mature elastic fibers.

It is a non-invasive treatment, that is performed in outpatient setting, without any anesthesia/analgesia. The recent clinical experiences suggest to perform 3 sessions of treatment for each patient, with an interval time of 30-45 days between the treatment sessions.

The vaginal status of the patients was evaluated using the *Vaginal Health Index - VHI score* (obtained using colposcopic vision), which consisted of the following 5 parameters: elasticity, fluid volume, pH, epithelial integrity and moisture. Each parameter was graded from 1 (worst condition) to 5 (best condition) (Figure 1). A total score < 15 is usually associated to a severe vaginal atrophy status.

The first study on the results of fractional CO₂ laser applied to the vulvo-vaginal area, was published by Gaspar et al. in 2011, that evaluated the effects of fractional microablative CO₂ laser in combination with platelet-rich plasma in vaginal biopsy specimens. They demonstrated a significant histological improvement on treated specimens, with beneficial effects in the 3 layers of the vaginal wall (13).

Recently, Salvatore et al. published a pilot study on the treatment of VVA in postmenopausal women using a fractional CO₂ laser, with attention to the clinical improvement of these patients (14). Their results supported the Gaspar’s data, with a significant improving of VVA symptoms and VHI scores at a 12-week follow-up.

Certainly, different “open” questions need to be clarify. First, the duration of the vaginal changes that were induced by the laser application, although many studies at the skin level and on the vaginal specimens supported the long-term duration of the obtained effects (15). Moreover, comparison studies with a control group of patients, which use traditional local estrogen therapy are actually lacking. So, it should important to realize new randomized case-control studies, with large sample size of women and long-term follow-up.

For the treatment of women with severe urogenital

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Score	1	2	3	4	5
Elasticity	none	poor	fair	good	excellent
Fluid Volume (Pooling of Secretion)	none	Scant amount, vault not entirely covered	superficial amount, vault entirely covered	moderate amount of dryness (small areas of dryness on cotton tip applicator)	normal amount (fully saturates on cotton tip applicator)
pH	≥ 6.1	5.6 - 6.0	5.1 - 5.5	4.7 - 5.0	≤ 4.6
Epithelial Integrity	petechiae noted before contact	bleeds with light contact	bleeds with scraping	not friable – thin epithelium	normal
Moisture (Coating)	none, surface inflamed	none, surface not inflamed	minimal	moderate	normal

Figure 1 - Vaginal Health Index (VHI) score.

symptoms who do not benefit from lifestyle changes, vaginal moisturizers or local estrogen therapy, clinicians should consider the use of the vaginal fractional CO₂ laser treatment.

Furthermore, in the future, fractional CO₂ laser could provide a response for patients with estrogen-dependent malignant disease and who often complain of severe symptomatic VVA. In fact, these patients have relevant contraindications to hormonal treatments, and although

today the most common approach is represented by local administration of estrogen at low doses, there are no clear guidelines regarding the administration of these therapies in patients with breast or genital tract cancer (4).

The vaginal treatment with fractional CO₂ laser, may in this sense be a valid “non-hormonal therapy” for this group of patients, providing a safe and well tolerated alternative.

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