Araştırma Makalesi (Research Article)

Postmenopozal Vulvovajinal Atrofi Saptanan Kadınlarda Fraksiyonel CO_2 Lazer (Femilift™) Tedavisinin Etkinliği: Türkiye'den Tek Bir Merkezin Ön Sonuçları

The Efficacy of Fractional CO_2 Laser (Femilift™) Treatment in Postmenopausal Females with Vulvovaginal Atrophy: Preliminary Results From A Single Center in Turkey

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Özet

Amaç: Etyolojisinde hipoöstrojenemi olan Vulvovajinal atrofiye (VVA) bağlı gelişen vajinal laksite, kuruluk, disparoni, kaşıntı, yanma, idrar kaçırma gibi semptomlar postmenopozal kadınlar arasında sık görülen ve yaşam kalitesini azaltan durumlardır. Bu çalışmamızda bu olgularda uyguladığımız CO_2 lazer tedavisinin etkinliğini ve bu tür tedaviyle ilgili olası yan etkileri değerlendirmeyi amaçladık.

Gereç ve Yöntemler: 48-72 yaşları arasında VVA şikayetleri olan ve buna yönelik 4-6 hafta ara ile toplam 3 seans CO_2 lazer tedavisi uyguladığımız 30 hastanın klinik muayene ve tedavi kayıtları retrospektif olarak incelenmiştir. Tüm hastaların ilk lazer seansından once ve son seanstan 4 hafta sonra VVA semptomları görsel analog skala (VAS) kullanılarak değerlendirilmiştir.

Bulgular: Olguların VVA semptomları olarak kuruluk, ağrılı cinsel ilişki, vajinal yanma, kaşıntı ve vajinal introitus ağrısı açısından VAS skorları değerlendirildiğinde her 5 semptom için de tedavi sonrası skorlarda istatistiksel olarak anlamlı düzeyde düşüşler tespit edilmiştir.

Sonuç: VVA şikayetleri olan ileri yaş olgulara yönelik yapılan CO_2 lazer tedavisi şikayetlerde kayda değer oranda yan etki görülmeden anlamlı düzeyde azalma sağlar. Böylece uzun süreli lokal östrojen kremleri kullanmak istemeyen ve meme ve genital jinekolojik kanser geçmişi olup lokal östrojen kullanması kontrendike olan hastalarda güvenilir bir alternatif olabilir.

Anahtar Kelimeler: Vulvovajinal atrofi, CO_2 lazer tedavisi, Hipoöstrojenemi, Postmenopozal kadınlar

Abstract

Objective: Symptoms, such as vaginal laxity, dryness, dyspareunia, itching, burning, and urine leakage, associated with vulvovaginal atrophy (VVA) with hypo-osteogenesis etiology, are frequently seen in postmenopausal females, and they diminish quality of life. This study aimed to evaluate the efficacy of CO_2 laser treatment in these cases and to evaluate the potential side-effects related to this type of treatment.

Material and Methods: A retrospective examination was made of the clinical examination and treatment records of 30 patients, aged 48–72 years, who presented with VVA complaints and underwent CO_2 laser treatment for a total of three sessions at intervals of 4–6 weeks. The VVA symptoms of all the patients were evaluated using a Visual Analog Scale (VAS) before the first laser session and 4 weeks after the final session.

Results: The VVA symptoms of dryness, painful sexual relations, vaginal burning, itching, and vaginal introitus pain were evaluated with VAS scores; a statistically significant reduction was determined in all five symptoms after CO_2 laser treatment.

Conclusion: A significant reduction was obtained in the VVA complaints with no significant side-effects following the application of CO_2 laser treatment for VVA cases in the postmenopausal females. Thus, this treatment can be considered to a reliable alternative for patients who do not wish to use local estrogen creams long-term, those with a history of breast or gynecological cancer, and those with contra-indications for the use of local estrogen.

Keywords: Vulvovaginal atrophy, CO_2 laser treatment, Hypo-oestrogenemia, Postmenopausal females

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INTRODUCTION

Conditions, such as menopausal genitourinary syndrome and vulvovaginal atrophy (VVA), are frequently seen in menopausal females (1). Both structural and functional changes occur due to a decrease in estrogen in the vulva and vagina, including thinning of epithelial tissue, decreased elasticity of the vaginal walls, a significant increase in pH, proliferation of pathogenic bacteria, and an increased risk of infections. Women in this age group may present with one or more clinical symptoms, such as vaginal laxity (71%), dryness (83%), dyspareunia (42%), itching (26%), burning (14%), urine leakage (30%), infections (17%), vaginal introitus pain (11%), and recurrent bleeding (15%) (2).

Over time, vaginal atrophy can worsen and quality of life may be negatively affected, with 75% of women reporting a significant worsening in quality of life (3). Distancing from their social network has been reported by 13% of women with vaginal atrophy, loss of confidence has been reported by 26% of these women, and greater difficulty in sexual intercourse has been reported by 40% of these women (3, 4).

There are different treatments for urogenital syndrome and especially for VVA. Although vaginal estrogen is the gold standard treatment for atrophy, it is contraindicated in estrogen-sensitive women with a history of breast or gynecological cancer. Selective estrogen receptor modulators that have an effect on the vaginal wall, vaginal lubricants, and hyaluronic acid-based creams are other widely-used treatments (5).

In the past 10 years, CO_2 laser treatment has been used as a new, non-hormonal approachapproved by the US Food and Drug Administration (FDA) for the prevention and treatment of VVA. Fractional CO_2 laser treatment re-stimulates collagen and extracellular matrix synthesis. The micro-ablative effect of fractional CO_2 laser treatment stimulates the interaction of heat shock proteins that activate fibroblasts for the production of other extracellular matrix components, such as proteoglycans and glycosaminoglycans (6). Of the factors stimulating angiogenic activity with the effect of the CO_2 laser, there is an increase in transforming growth factor beta (TGF-β) and epidermal growth factor (EGF) (7).

The renewal process associated with the laser light begins within 48–72 hours (early phase) after laser treatment; in the progressive phase, which occursin the next 30 days, collagen and extracellular matrix production begins. After approximately 40 days, collagen fibers and new elastic fibers are combined in the remodeling stage (8). Thus, repair and renewal occur in the vaginal mucosa and in the connective tissue surrounding the mucosa; consequently, the VVA symptoms can be decreased.

The present study aimed to determine the efficacy of CO_2 laser treatment in postmenopausalfemales with clinical findings and symptoms of VVA, and to evaluate the possible side-effects of this type of treatment.

MATERIAL and METHODS

The study was planned according to the principles of the Helsinki Declaration. Approval for the study was granted by the local Ethics Committee. A retrospective examination was made of the clinical examination and treatment records of 30 patients, aged 65–77 years, who presented with VVA complaints, such as vaginal burning, pain, itching, painful sexual intercourse, and vaginal dryness, and who underwent CO_2 laser treatment. If urinary or vaginal infections were determined, they were addressed with medical treatment before the CO_2 laser treatment began.

The VVA symptoms (dryness, painful sexual intercourse, vaginal burning, itching, and vaginal introitus pain) of all the patients were evaluated using a Visual Analog Scale (VAS) before the first laser session and 4 weeks after the final session. The patients were instructed to indicate the intensity of the symptoms with VAS scoring on a scale of 0 to 10, where 0=no discomfort and 10 = maximum discomfort.

Informed consent was obtained from all the patients. Three CO_2 laser treatment sessions were administered using a FemiLift CO_2 laser (Alma Laser, Caesarea, Israel) with micro-ablative CO_2 laser energy (30-Watt Dot power, 1000 μm Dot spacing). The laser treatment was applied to the vagina three times during each treatment session. After each full rotation of the probe, it was turned and withdrawn 1 cm to ensure application of the treatment to the entire vaginal canal. No unbearable pain was reported by any patient. Each treatment session lasted approximately 15 mins. Following the procedures, the patients were advised to avoid sexual intercourse for 1 week. The same protocol was applied in the second and third sessions, which were administered at 4–6-week intervals. No creams or vaginal lubricants were recommended during or after the laser sessions. None of the patients required local anesthesia. The patients were instructed to report any bleeding, discharge, or pain in the period following the treatment.

Statistical Analysis: Data obtained in the study were analyzed statistically using IBM SPSS for Windows, vn 22.0 software (IBM Corporation, Armonk, NY, USA). Quantitative data were stated as median±standard deviation (SD) and median ± interquartile range (IQR) values. In the variance analysis of repeated measurements, the Repeated Measures ANOVA with Bonferroni test was used, and in the comparisons of the paired groups, Tukey's Honestly Significant Difference (HSD) test was used. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The demographic data of the 30 patients in the study, such as age, age at menopause, and natural or surgical menopause, are shown in **Table 1**. In the evaluation of the VAS scores before the first laser session and 4 weeks after the final laser session, a statistically significant decrease was found in the scores after treatment for all five VVA symptoms: dryness, painful sexual intercourse, vaginal burning, itching, and vaginal introitus pain ($p<0.001$, for all) (**Table 2, Figure 1**). In the evaluation of side-effects, 10 patients reported vaginal discharge at a level giving discomfort starting a few days after the procedure.

Table 1. Demographic characteristics of the patients

Patients enrolled	30
Median age (Years)	57(54-67)
Median age of menopause (Years)	47.7 ±6.34
Parity	3.76 ±3.12
Patients with natural menopause (%)	27/30 (90 %)
Patients with surgically menopause (%)	3/30 (10 %)

Table 2. Symptoms pre- and post-treatment

	Pre-treatment VAS score	Post-treatment VAS score after two sessions	P value
Vaginal burning	6,1	1,3	<0.001
Pain at the vaginal orifice	8	2,9	<0.001
Itching	6,7	1,5	<0.001
Dyspareunia	8,7	3,5	<0.001
Dryness	8,1	2,9	<0.001

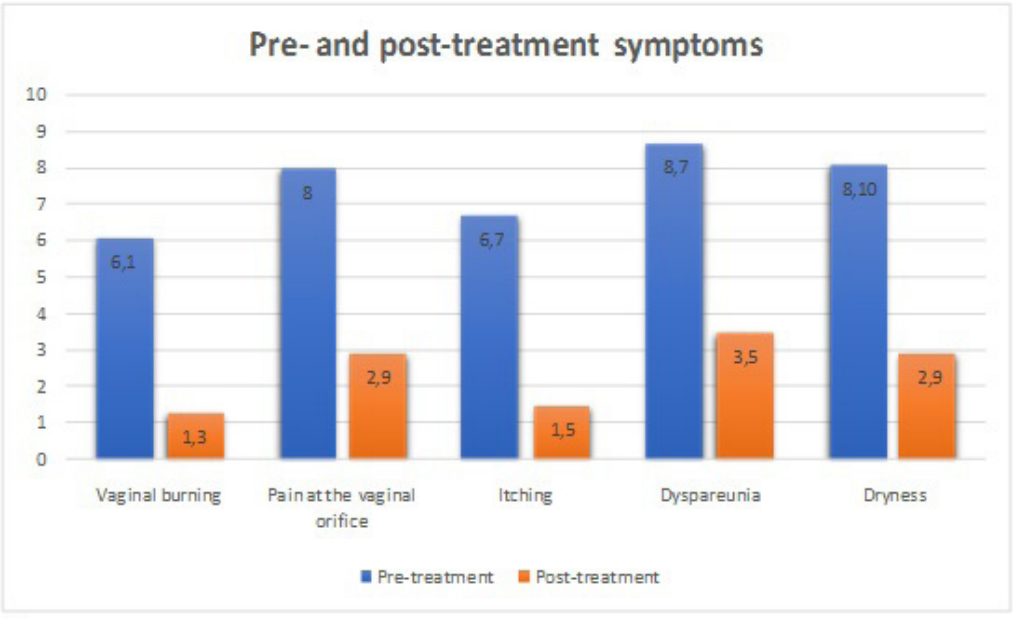

Figure 1. VVA symptoms before and after CO_2 laser treatment.

DISCUSSION

The results of this study showed CO_2 laser treatment significantly reduced all the VVA symptoms. The micro-ablative fraction CO_2 laser uses water in the tissue as a chromophore to create heat in the genital mucosa, and this heat induces the formation and remodeling of collagen and elastin. The heat also increases neovascularization in the vaginal wall and stimulates some tissue growth factors. Consequently, vaginal epithelial thickening starts in the first month of treatment, and in the connective tissue below the epithelium, formation of papillae entering the epithelium begins. The increasing angiogenesis in epithelial cells provides an increase in glycogens.

Increasing glycogen results in decreased pH and an increased number of Lactobacillus vaginalis. The increasing submucosal vascularity results in an increase in the collagen and elastin fibers in this region. All these changes eliminate clinically pale and friable mucosa, and vaginal laxity is replaced by a tightened vagina. The lost vaginal rugation is re-formed, lubrication increases, pH decreases, and the vaginal microbiota normalize. Thus, symptoms, such as vaginal dryness, dyspareunia, itching, burning, urine leakage, infections, and vaginal introitus pain, are relieved (9, 10).

Almost all the studies in the literature on CO_2 laser treatment for VVA complaints are case-control studies. To evaluate the efficacy of treatment, three different methods, histopathological examinations (11), physician assessments (12-14), and subjective patient reports (15, 16), have been applied in these studies. In a study by Samuels and Garcia, vaginal biopsies were obtained from postmenopausal women before treatment and 3 months and 6 months after three sessions of treatment for histopathological examination to evaluate treatment success. In the third month, increased collagen and elastin, thicker mucosal epithelium, and a better degree of surface maturation were observed in all patients. In the sixth month, an increase in submucosal vascularity and the amount of collagen and fibrin fibers in the submucosal tissue was seen (11).

We developed a task that assessed treatment success through physician assessments, Athanasiou et al. determined an increase in vaginal pH acidity and an increase from 30% to 79% in Lactobacillus vaginalis in the vaginal flora (12), whereas Sokol et al. reported no change in vaginal pH (13). Bercopi et al. examined the effect of vaginal CO_2 laser treatment on vaginal immunity; they reported an increase in vaginal cytokines and growth factors interleukin (IL)-18, leukemia inhibitory factor (LIF), and macrophage colony stimulating factorM-CSF and a decrease in pro-inflammatory and inflammatory factors IL-1ra, IL-2, IL-7, IL-9, IL-13, eotaxin, GM-CSF, and regulated on activation, normal T cell expressed and secreted (RANTES) after treatment (14).

As in the current study, subjective patient reports have most often been used to evaluate treatment success. Tovar-Huamini et al. (15) and Behnia-Willison et al. (16) evaluated VVA-related genitourinary symptoms on a 10-point VAS, which was also used in the current study. Following three sessions of treatment, significant improvements were determined in both genitourinary symptoms and sexual functions. The only randomized, double-blinded, placebo-controlled study of VVA symptoms in the literature was published in 2018 by Cruz et al. (17). In that study, 45 patients were randomly separated into three groups (15 patients in each): a laser treatment only group, a laser+ local estrogen group, and a local estrogen only group. The Vaginal Health Index (VHI), VAS, Female Sexual Function Index, and Maturation Value of Meisels were used to evaluate the treatment results. Significant improvements in symptoms were determined in all three study groups in the evaluations conducted 8 weeks and 20 weeks after treatment. It was concluded that laser treatment is a reliable and effective treatment option in patients with these types of symptoms for whom estrogen use is contraindicated.

In the literature related to fractional CO_2 laser treatment, vaginal discharge (16), urinary system infections (14, 18), dysuria (11), burning sensation (18, 19), and adverse effects related to the placement and movement of the probe (14) have been reported. However, these adverse effects have been reported at very low rates, and some patients have recovered in a short time with medical treatment and some only required short-term follow-up. In the current series, the only adverse effect observed was vaginal discharge caused by the shedding of epithelial cells from the vaginal mucosa and the accompanying exudate, which was part of the regeneration process. This condition recovered spontaneously in all cases within approximately 1 week without application of any medical treatment.

This study had some limitations. The primary limitation was its retrospective design, as it was not a prospective study with a control group. Another limitation was that there was no histopathological examination of the histological changes in the vaginal walls to show vaginal improvement after treatment. Vaginal pH as another marker of response to treatment was not measured, and the change in the amount of Lactobacillus vaginalis was not investigated. Finally, no long-term results were reported for any of the patients. However, this study only aimed to present the preliminary results of VVA cases in which CO_2 laser treatment was used.

In conclusion, a significant reduction in the VVA complaints was achieved, with no significant side-effects, following the application of CO_2 laser treatment for VVA cases in the postmenopausal females. Therefore, laser treatment can be used as a reliable alternative for patients who do not wish to use local estrogen creams long-term, those with a history of breast or gynecological cancer, and those with contraindications for the use of local estrogen.

Conflict of interest: The authors of the current paper declare no conflict of interest.

Research Contribution Rate Statement Summary: The authors declare that, they have contributed equally to the manuscript.

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