aesthetic medicine

Original Article

Use of intravaginal device based on photobiomodulation for the treatment of vaginal dryness: a pilot study

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Running head: Photobiomodulation to Treat Vaginal Dryness

Abstract

Purpose: this study aimed to evaluate the use of a treatment based on photobiomodulation, for the improvement of vaginal dryness associated with or without menopause.
Methods: this prospective non-placebo-controlled study included women who had reported vaginal dryness associated with or without menopause and had not received any physical or chemical aesthetic treatments. All patients underwent several treatment sessions with the MILTAPLUS intravaginal probe, a therapeutic device for genital restoration, based on non-invasive photobiomodulation and magnetic field techniques, and followed up 1 and 12 months after the last session. Vaginal tissue revascularization, the improvement of dryness symptoms, tissue characteristics of secretion/fluid and lubrication, the percentage of lubrication and pain variation and mean value of the patient's overall amelioration level of symptoms were assessed.
Results: twenty women with a median age of 44.8 (SD 7.4) years were included. Efficacy outcomes were: (1) vaginal tissue revascularization (34.6%); (2) reduction of dryness, stinging and dyspareunia measured using MBS (50%, 100%, and 50% respectively); (3) improvement of tissue characteristics using VHIS (16.1%); (4) mean amelioration of lubrication (94.6% [SD 8.7]) and pain (79.5% [SD 16.8]) one month after treatment using FSFI. The mean value of patients' overall amelioration level of symptoms was 7.5 (SD 1.1). The treatment was safe and no adverse effects were reported.
Conclusion: the use of photobiomodulation for the treatment of vaginal dryness provided excellent results, with the improvement of most symptoms of this condition. However, more research is required to determine the most suitable protocol for maintaining these outcomes.

Keywords

Vaginal dryness, photobiomodulation light-emitting diode, magnetic field, vaginal restoration, low-level laser therapy

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Introduction

Oestrogen deprivation has a significant impact on vaginal wall structure and function, affecting connective tissue components, including collagen, elastin, and smooth muscle, resulting in the degeneration of these structures and leading to vaginal atrophy (VA)[1].
The following major changes occur: (1) the vaginal epithelium becomes less cellular and thinner; (2) glycogen production - responsible for vaginal secretion - gradually declines and stops completely; (3) blood flow to the vagina is also reduced, which is associated with decreased fluid secretion during sexual arousal. These changes cause a variety of symptoms and vaginal dryness in particular, as a result of decreased natural lubrication[2-5]. Other symptoms include a burning sensation, irritation, discomfort or pain, and dysuria. VA symptomatology may vary from bothersome to debilitating, thus making treatment essential. VA makes vaginal dryness a common condition, particularly during menopause, which in turn often leads to dyspareunia (pain during intercourse)[6].
Vaginal dryness can affect patients' quality of life and sexual relationships[7]. The choice of therapy depends on the severity of symptoms, effectiveness and safety, always in accordance with patient preferences. All treatments are addressed to improve genital symptoms and restore the vaginal environment to a healthy condition[8]. The introduction of new medical devices for non-pharmacological therapies offers the possibility to improve treatments, for better results and greater patient satisfaction. Light in the visible-to-far-infrared spectrum has been applied to the female genital tract for nearly 50 years. Photobiomodulation (PBM) therapy is tissue exposure to visible and near infrared light sources (laser, LED, etc.), based on non-thermal and non-cytotoxic biological effects.
PBM therapy has been proposed as an alternative for use in managing the genitourinary syndrome of menopause (GSM) and stress urinary incontinence (SUI)[8].
The main biological effects are reduced tissue repair, greater inflammation, infection, and pain[9]. Some studies have reported the use of Er:YAG or fractional CO2 thermal laser for vaginal atrophy[10-12], for the reduction of pain, edema, and inflammation. Other studies have used devices based on light-emitting diodes (LEDs)[13], as well as therapy combining LED phototherapy with thermal laser procedures[14,15], to reduce thermal laser side effects, such as pain and edema. The rationale behind LEDs is based on their reported efficacy at a cellular and subcellular level, particularly for 660-nm and 850-nm wavelengths. Phototherapy with LEDs has been proven to reduce the production of pro-inflammatory cytokines, allogenic factors, and increases the production of procollagen and collagen[16]. It may also reduce collagen degradation, due to the enhanced trophicity of subcutaneous and submucosal muscle tissue[8].
Other observed benefits of phototherapy with LEDs are improved blood flow and neovascularization, as well as the inhibition of apoptosis[17]. LED treatment also reduces pain, including postoperative pain and edema, along with many types of inflammation[14,18]. The study aimed to assess the effectiveness and safety of a new photobiomodulation- based device in the improvement of vaginal dryness symptoms in women with or without menopause.

Methods

Study Design

This was a prospective non-placebo-controlled pilot study carried out at Clinica Elite Laser, (Madrid, Spain). Study participants were women (n=20) with symptoms of dryness associated with VA, with or without menopause. The complete treatment course included 12 sessions of photobiomodulation (one session of 5 minutes per week for 12 weeks). Patients were followed up at one and twelve months after the last treatment session.
The study was conducted in accordance with principles set forth in the current revised version of the Declaration of Helsinki, Good Clinical Practice (GCP), and in compliance with all applicable laws and regulatory requirements for medical device use in Spain. All patients signed an informed consent form in order to participate in the study, before undergoing any procedures.

Subjects

Consecutive patients were invited to participate in the study and their need for treatment was confirmed. Participants were women >18 years old with vaginal dryness associated or not associated with menopause. Exclusion criteria were: previous hormonal or other treatments for VA in the last six months; women with an active sexually transmitted disease or infection; neurological disorders; morbid obesity; current or attempted pregnancy; diabetes; breastfeeding or lactating; previous vaginal surgery or toning therapy; a history of cancer, chemotherapy or radiation therapy; vesicoureteral reflux; bladder calculi or tumor.

Variables Assessed

Objective Assessments: Number of microvessels per mm^2 of the vaginal tissue: this variable was measured using a transvaginal Power Angio-Doppler with a 3.5-5-MHz convex probe(Mindray® Bio-Medical Electronics Co Ltd., Shenzhen, China), at baseline and immediately after the treatment session.
Subjective Assessments: Symptoms were assessed according to the most bothersome symptom (MBS), including dryness, stinging, pain, dysuria, dyspareunia, bleeding during sexual intercourse; the values for each one were described as: none (N), low (L), moderate (M), and severe (S). Tissue characteristics were assessed using the Vaginal Health Index Scale (VHIS) score, consisting of five vaginal parameters: Elasticity, Secretion/Fluid Volume, Vaginal pH, Integrity of the Epithelium, and self-reported Lubrication/Moisture of Vaginal Tissue with a 5-point Likert scale, where 1 indicates "None," 2 is "Low," 3 is "Minimum," 4 is "Moderate" and 5 is "Normal." The sum of the five components can provide a maximum score of 25 and a minimum of 5. A score of ≤15 defines the presence of vaginal atrophy. Pain and lubrication were assessed using the Female Sexual Function Index (FSFI), a 19-item questionnaire with self-reported measures of sexual functioning in women, with a specific focus on six domains of sexual arousal, orgasm, satisfaction, and pain,

as well as a total score. The patient's overall amelioration level of symptoms with the treatment procedure was assessed using a 10-point Likert scale, where 1 indicates "Very Dissatisfied," and 10 is "Very Satisfied."

Procedures

Basal assessments: Before treatment, variables self-assessed by patients were: MBS, VHIS and FSFI; investigators carried out an Angio-Doppler to measure the number of microvessels per mm^2.

Treatment procedure: All patients underwent complete treatment (one 5 minute session per week, for 12 weeks) with the MILTAPLUS intravaginal probe (Physioquanta, Mudaison, France), a non-invasive therapeutic device combining technologies based on photobiomodulation and magnetic fields for vaginal tissue restoration (*Figure 1*), the technical characteristics of which are detailed in *Table 1*. The procedure did not require any anesthesia. Each program, LED and laser, lasted five minutes, therefore a complete session lasted 5 minutes. Immediately after the 12-session treatment: A transvaginal Angio-Doppler was performed to assess the number of microvessels per mm^2 and evaluate tissue neovascularization. One and twelve months after session 12 (end of treatment): MBS, VHIS and FSFI variables were assessed. All patients were asked about the amelioration of their symptoms and pain during the procedure.

***Figure 1** - Miltagynea® (Milta Technologie, Mudaison, France) intravaginal probe.*

Efficacy Outcomes

Efficacy outcomes were: (1) vaginal tissue revascularization, evaluated by a transvaginal Angio-Doppler, using the percentage increase in the number of microvessels per mm^2 from baseline to immediately after the treatment; (2) percentage of improvement of symptoms of dryness, stinging and dyspareunia, measured using MBS; (3) the improvement of tissue characteristics of secretion/fluid and lubrication, assessed using VHIS; (4) percentage of lubrication and pain variation using FSFI; and (5) mean value of overall amelioration level of patients' symptoms.

Safety Data

Treatment safety was assessed by recording all procedure complications and any adverse events that may have occurred during treatment right up until the follow-up visit, as well as by patients' self-perception of pain during treatment.

Statistical Analysis

Quantitative variables were described as the mean, standard deviation (SD) and range, whereas categorical variables were described as percentages.

Efficacy outcomes were assessed as the change of the corresponding variable from baseline to one month after treatment.

For this pilot study, the sample size was set at 20 patients. The statistical analysis also included suitable measures for statistical significance (Student's paired two-sample t-test) using the standard cut-off for significance of $p<0.05$.

Results

Subject Characteristics

A total of 20 women with a median age of 44.8 (SD 7.4; range of 29-53) years, eight with menopause (40%) and 12 without menopause (60%), were enrolled in the study and all of them completed it.

Source	Output Power Density	Output Wavelength	Dimension of LED Active Area
LEDs			
VIOLET (12 LEDs)	2160 mW, or 42 mW/cm^2	415 +/- 5 nm	50.9 cm^2
RED (12 LEDs)	900 mW, or 18 mW/cm^2	660 +/- 6 nm	50.9 cm^2
IR (12 LEDs)	540 mW, or 11 mW/cm^2	850 +/- 15 nm	50.9 cm^2
Laser			
Laser IR (12 diodes) Pulse frequency 10 kHz	120 W peak maximum Order of magnitude of the pulse: 100 ns	850 nm	50.9 cm^2
Constant Magnetic Field	70 mT		

Abbreviations: LEDs, light-emitting diodes; IR, infrared; mW, milliwatt; nm, nanometers; cm^2, square centimeter; mT, milliTesla.

***Table 1** - Technical characteristics of Milta emissions.*

Objective Variables: At baseline, global vaginal tissue vascularization had a median of three microvessels per mm^2 (range of 1-4); after one month of treatment, the median value was four microvessels per mm^2 (range of 1-5); twelve months after the last treatment, the median value was four microvessels per mm^2 (range 1-5).
The number of patients with five microvessels per mm^2 at baseline was 0 (0%), at one month after treatment, five (25%) women had five microvessels per mm^2 (*Figure 2*); 100% of said patients were not in menopause. At twelve months after the last treatment, three (15%) women had five microvessels per mm^2; 100% of these were not in menopause.
Subjective Variables: the most prevalent MBS at baseline with a high severe score percentage was pain (65%) followed by stinging (20%) and dyspareunia (20%), dryness (10%), and dyspareunia (10%); no patients reported bleeding during sexual intercourse. After one month of treatment, symptoms with a high severe score percentage were dryness (5%) and dyspareunia (5%) (50% decrease). After twelve months of treatment, symptoms with a high severe score percentage were dryness (5%) and dyspareunia (5%) (50% decrease).
No severe score was reported for any other symptoms.

Table 2 (click here) shows global results obtained with MBS throughout the study and according to menopause condition: Dryness, stinging, pain, dysuria, dyspareunia, and bleeding during sexual intercourse. VHIS at baseline had a mean value of 19.9 (SD 2.4; range of 16-23); one month after treatment, the mean value was 23.0 (SD 2.0; range of 19-25); twelve months after treatment, the mean value was 22.3 (SD 2.6; range of 17-25).
Table 3 (click here) shows the global results of VHIS and FSFI, variables assessed and their results throughout the study; *Table 4 (click here)* shows the results of VHIS and FSFI for patients with or without menopause.

Efficacy Outcomes

For vaginal tissue revascularization, the number of microvessels per mm^2 from baseline and one month after treatment increased by 34.6% (SD 23.5); differences were statistically significant (p=0.0008). At 12 months after the last treatment, the number of microvessels per mm^2 from baseline increased by 23.8% (SD 23.6); differences were statistically significant (p=0.0144). Symptoms of dryness, stinging, and dyspareunia, measured using MBS, improved by 50%, 100%, and 100% respectively, at one month after treatment; the same results were obtained 12 months after the last treatment.

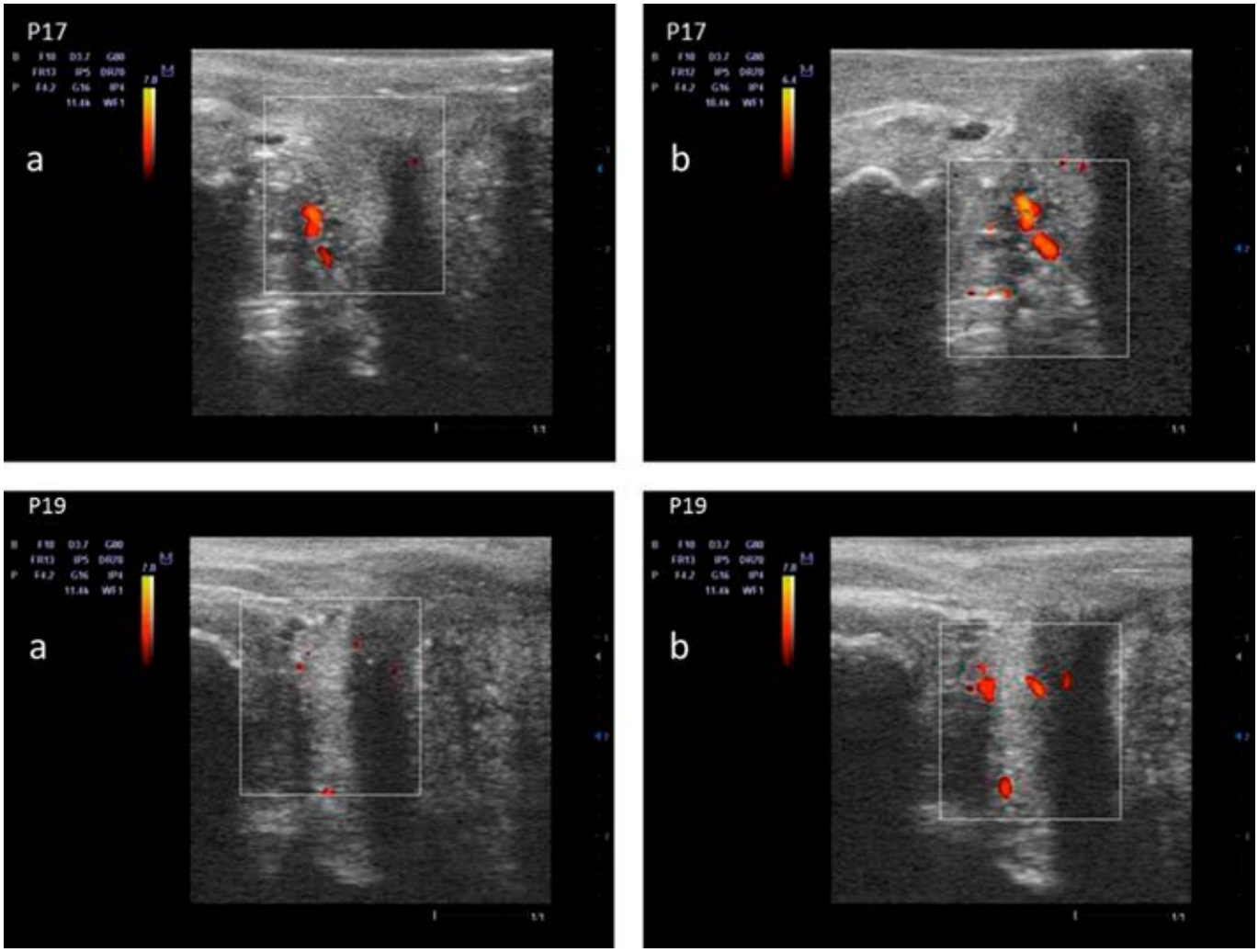

Figure 2 *- Example of a patient's Power Doppler at baseline and at one month after the last treatment session. a: Pre-treatment; b: At one month after the treatment.*

Table 2 shows all differences obtained for each MBS measurement from baseline to one month and 12 months after treatment for all patients and according to menopause condition. The improvement of tissue characteristics at one month after the last treatment, assessed using VHIS, was 16.1%. After one month of treatment, this improvement was significant (p=0.0003). *Figure 3* shows the mean of tissue characteristics at baseline and one month after the last treatment session, for each variable. 12 months after the last treatment session, a 12.5% tissue improvement was recorded, which was significant (p=0.0062).

At one month after treatment, the mean percentage of variation and the SD of FSFI lubrication and pain of 94.6% (SD 8.7) and 79.5% (SD 16.8), respectively. Improvement at one month was significant in both domains (*Table 2*). The mean value of overall amelioration level of patients' symptoms was 7.5 (SD 1.1). *Figure 4* shows the mean value at baseline and one month after the last treatment session, in each domain. At 12 months after treatment, the mean percentage of variation and SD of FSFI lubrication and pain was 71.7% (SD 8.2) and 63.3% (SD 14.7), respectively. Improvement at 12 months was significant in both domains (*Table 2*). The mean value of overall amelioration level of patients' symptoms was 7.0 (SD 1.0).

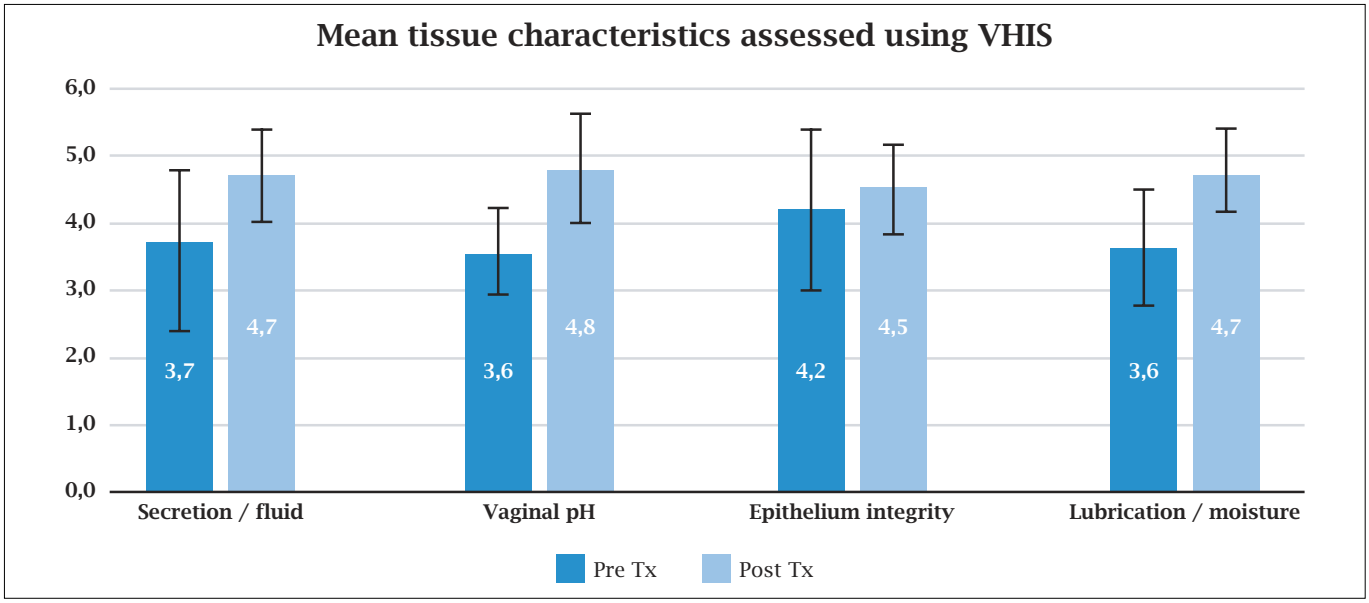

Figure 3 *- Mean of tissue characteristics at baseline and one month after last treatment session assessed using VHIS. Abbreviations: VHIS: Vaginal Health Index Scale; FSFI: Female Sexual Function Index; Tx: treatment.*

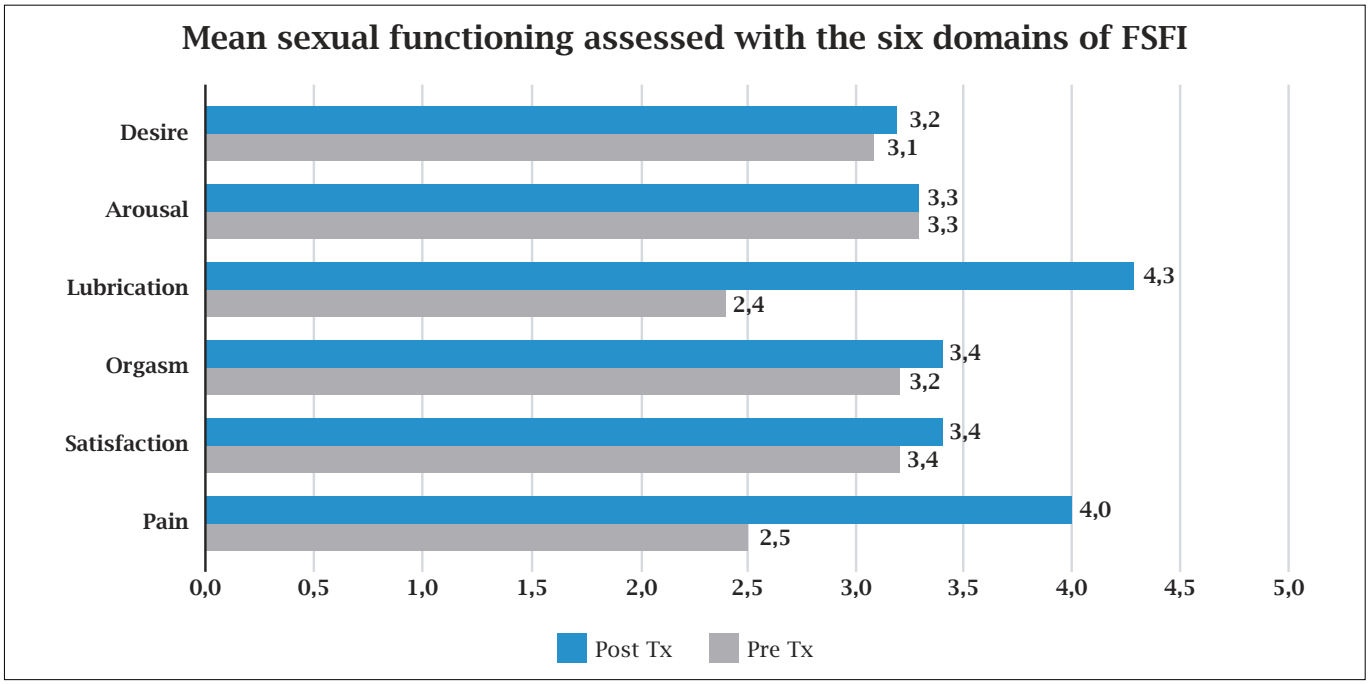

Figure 4 *- Mean patients' sexual functioning at baseline and one month after the last treatment session assessed using the six domains of FSFI. Abbreviations: FSFI: Female Sexual Function Index; Tx: Treatment.*

Safety Outcomes

The procedure did not require analgesia/anesthesia. No pain, complications or side effects were reported during treatment.

Discussion

Study results showed that the combination of LED, soft laser and magnetic field treatment was associated with improved vaginal health and VA symptoms, resulting in better vaginal tissue vascularization immediately after the treatment protocol (34.6%, SD 23.5; p=0.0008) (*Figure 2*) and after 12 months (23.8%, SD 23.6; p=0.0144). Patients' vaginal and sexual symptoms also improved, with decreased severity at all follow-ups. MBS symptoms with a sharp decrease (100%) in severity were: stinging, pain and dysuria at one month of treatment, and stinging and dysuria at twelve months after the last treatment session (see *Table 2*). A significant improvement of the following VHIS symptoms was reported: secretion and lubrication, both with a significant increase (p<0.0001) (*Table 3*). The VHIS score at one month and 12 month after the last treatment, showed a significant improvement compared to baseline (p=0.0003 and p=0.0062 respectively). An improvement in all FSFI components was observed at all follow-up visits. The "lubrication" and "pain" domains showed a significant improvement (*Table 3*). The overall value of patients' self-perceived amelioration of symptoms at one month was 7.5 (SD 1.1), and 7.0 at 12 months after the last treatment session (SD 1.0). All patients resumed usual activities after the treatment session.

Patients without menopause had better outcomes than patients with menopause, however improved conditions were observed in both groups. VHIS score variables remained, with amelioration at twelve months after treatment, in both groups (*Table 4*).

Since no similar studies can be found in literature, results must be compared with previous studies conducted by us. In 2018 we carried out a study with an intravaginal device using only LED technology, for the treatment of vaginal atrophy; increased vaginal tissue revascularization, measured by a transvaginal Angio-Doppler; results were not significant however (p=0.3369); regarding VHIS, the FSFI domains of "lubrication" and "pain" improved, and results were statistically significant[13]. In another study with Erbium YAG (Er:YAG) or carbon dioxide (CO2) lasers and LEDs, the number of microvessels was higher immediately after treatment, and results were statistically significant (p<0.0001)[15]. On the basis of our experience with a combination of photobiomodulation-based technologies, the perception is that this synergy (magnetic field, LED, soft laser) primarily enables greater depth of photon penetration in soft tissues, acting directly on the target area and obtaining better benefits from these technologies, promoting optimal tissue regeneration without side effects. In this study, the added benefit is that the device includes all three technologies in one device, facilitating the professional's handling of the procedure and providing more patient comfort.

Despite considerable improvement in all variables assessed in this study, our results should be considered in the context of the limitations of the study design, i.e. a low number of participants. Thus, unlike other studies previously mentioned, ours was not randomized and did not compare the efficacy of the investigation device with that of a sham device. The study aimed to relieve symptoms that are experienced subjectively by individual patients and thus patient self-assessment was deemed a good representation of treatment effectiveness.

In short, the combined use of these three technologies (LEDs, soft laser, and magnetic field) for the treatment of vaginal dryness provided excellent results for tissue regeneration and symptom amelioration. However, future randomized, double-blind studies with sham devices and a more significant number of patients will be necessary to confirm these results.

Conflicts of Interest and Disclosure

The authors have no conflicts of interest or financial ties to disclose.

Role of funding source

This study did not receive any funding.

Ethical Approval

The study was conducted in accordance with the principles set forth in the current revised version of the Declaration of Helsinki, Good Clinical Practice (GCP), and in compliance with all applicable laws and regulatory requirements for the use of medical devices in Spain. The authors do not have a formal ethics review committee.

Informed Consent

Before undergoing any procedures, patients signed an informed consent form in order to participate in the study.

Acknowledgments

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Table 2. MBS results at baseline, 1 and 12 months after treatment session.

	Baseline (%)			One Month After Treatment (%)			Twelve months After Treatment (%)			%Δ 1Month-Baseline (%)			%Δ 12 Months-Baseline (%)		
	Total (N=20)	M (N=8)	NM (N=12)	Total (N=20)	M (N=8)	NM (N=12)	Total (N=20)	M (N=8)	NM (N=12)	Total (N=20)	M (N=8)	NM (N=12)	Total (N=20)	M (N=8)	NM (N=12)
Dryness															
Severe	10	5	5	5	5	0	5	5	0	-50	0	-100	-50	0	-100
Moderate	20	5	15	0	0	0	0	0	0	-100	-100	-100	-100	-100	-100
Low	70	30	40	15	10	5	35	30	5	-78.6	-66.7	-87.5	-50	0	-87.5
None	0	0	0	80	5	55	60	5	55						
Stinging															
Severe	20	10	10	0	0	0	0	0	0	-100	-100	-100	-100	-100	-100
Moderate	65	20	45	5	0	5	20	15	5	-92.3	-100	-88.9	-69.2	-25	-88.9
Low	15	10	5	50	30	20	40	20	20	233.3	200	300	166.7	100	300
None	0	0	0	45	10	35	40	5	35						
Pain															
Severe	65	25	40	0	0	0	15	15	0	-100	-100	-100	-76.9	-40	-100
Moderate	20	5	15	0	0	0	5	5	0	-100	-100	-100	-75	0	-100
Low	0	0	0	25	15	1	20	10	10						
None	15	10	5	75	25	50	45	10	50	400	150	900	300	0	900
Dysuria															
Severe	20	0	20	0	0	0	0	0	0	-100		-100	-100		-100
Moderate	0	0	0	0	0	0	0	0	0	0					
Low	20	5	15	10	0	10	15	5	10	-50	-100	-33.3	-25	0	-33.3
None	60	35	25	90	40	50	85	35	50	50	14.3	100	41.7	0	100
Dyspareunia															
Severe	10	10	0	5	5	0	5	5	0	-50			-50	-50	
Moderate	30	15	15	10	10	0	15	15	0	-66.7	-33.3	-100	-50	0	-100
Low	60	15	45	10	10	0	15	15	0	-83.3	-33.3	-100	-75	0	-100
None	0	0	0	75	15	0	65	5	60		-50				
Bleeding during sexual intercourse															
Severe	0	0	0	0	0	0	0	0	0	0					
Moderate	0	0	0	0	0	0	0	0	0	0					
Low	10	5	5	0	0	0	5	5	0	-100	-100	-100	-50	0	-100
None	90	35	55	100	40	60	95	35	60	11.1	14.3	9.1	5.6	0	9.1

Abbreviations: M, menopausal; NM, no menopausal; SD, standard deviation; MBS, Most Bothersome Symptoms; N, number of patients; %Δ, percentage of difference.

Table 3. Global results of **VHIS** and FSFI results at baseline, 1 and 12 months after treatment session.

Variables Assessed	Baseline (N=20)		1 Month AT (N=20)		12 Month AT (N=20)		%Δ 1 Month-B		%Δ 12 Months-B		*p* 1 Month-B	*p* 12 Months-B
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
VHIS Score	**19.9**	**2.9**	**23.0**	**2.0**	**22.3**	**2.6**	**16.1**	**6.0**	**12.5**	**6.9**	**0.0003**	**0.0062**
Elasticity	3.6	1.1	4.3	0.7	4.1	1.0	28.3	36.3	17.5	33.0	0.0214	0.1408
Secretion/Fluid Volume	**3.7**	**0.6**	**4.7**	**0.7**	4.5	0.7	**29.2**	**23.6**	24.2	26.6	**<0.0001**	**0.0092**
Vaginal pH	3.6	1.1	4.8	0.6	4.6	0.7	47.9	58.4	44.2	60.6	0.0001	0.0001
Integrity of the Epithelium	4.2	0.8	4.5	0.6	4.4	0.7	8.3	18.3	6.7	17.4	0.1877	0.4054
Lubrication/Moisture	**3.6**	**0.6**	**4.7**	**0.6**	4.6	0.6	**30.4**	**10.6**	29.2	12.5	**<0.0001**	**<0.0001**
FSFI												
1. Desire: Frequency	3.1	1.3	3.3	1.3	3.2	1.3	7.5	18.3	5.0	15.4	0.6294	0.8091
2. Desire: Level	3.1	1.3	3.2	1.3	3.2	1.3	3.3	17.6	5.0	15.4	0.8091	0.8091
Desire, mean amelioration at one month of 5.4% (SD 3.0) Desire, mean amelioration at 12 months of 5.0% (SD 0.0)												
3. Arousal: Frequency	3.4	1.6	3.3	1.6	3.3	1.6	-1.3	5.6	-1.3	5.6	0.8444	0.8444
4. Arousal: Level	3.2	1.5	3.3	1.5	3.2	1.5	5.0	22.4	0.0	0.0	0.8342	1.0000
5. Arousal: Confidence	3.2	1.4	3.2	1.2	3.2	1.3	6.5	34.1	2.8	23.9	1.0000	1.0000
6. Arousal: Satisfaction	3.4	1.4	3.25	1.4	3.5	1.3	6.1	30.1	5.7	25.3	0.8225	
Arousal, mean amelioration at one month of 4.1% (SD 3.6) Arousal, mean amelioration at 12 months of 1.8% (SD 3.1)												
7. Lubrication: Frequency	**2.2**	**0.8**	**4.1**	**1.0**	**3.8**	**1.2**	**102.1**	**55.3**	**79.6**	**30.2**	**<0.0001**	**0.0015**
8. Lubrication: Difficulty	**2.7**	**0.9**	**4.5**	**0.8**	**4.2**	**1.1**	**82.1**	**52.7**	**61.3**	**35.1**	**<0.0001**	**<0.0001**
9. Lubrication: Frequency of Maintenance	**2.4**	**0.8**	**4.3**	**0.7**	**3.9**	**1.1**	**95.8**	**51.5**	**69.2**	**42.9**	**<0.0001**	**<0.0001**
10. Lubrication: Difficulty	**2.5**	**0.9**	**4.4**	**0.9**	**4.1**	**1.1**	**98.3**	**74.1**	**76.7**	**50.8**	**<0.0001**	**<0.0001**
Lubrication, mean amelioration at one month of 94.6% (SD 8.7) **Lubrication, mean amelioration at 12 months of 71.7% (SD 8.2)**												
11. Orgasm: Frequency	3.4	1.1	3.5	1.1	3.5	1.1	4.6	19.4	4.6	19.4	0.7850	0.7753
12. Orgasm: Difficulty	3.6	1.2	3.7	1.1	3.6	1.2	6.3	22.8	1.3	5.6	1.0000	1.0000
13. Orgasm: Satisfaction	3.4	1.3	3.4	1.3	3.4	1.3	0.3	7.3	0.3	7.3	1.0000	1.0000
Orgasm, mean amelioration at one month of 3.7% (SD3.1) Orgasm, mean amelioration at 12 months of 2.1% (SD2.3)												
14. Satisfaction: with amount of closeness with partner	3.3	1.2	3.5	1.3	3.5	1.3	7.5	17.3	7.5	17.3	0.6161	0.6161
15. Satisfaction: with sexual relationship	3.0	1.2	3.3	1.3	3.3	1.3	14.2	26.5	11.7	25.3	0.4529	0.4529
16. Satisfaction: with overall sex life	2.9	1.1	3.2	1.2	3.1	1.2	12.1	19.8	9.6	17.8	0.4150	0.5859
Satisfaction, mean amelioration at one month of 11.3% (SD 3.4) Satisfaction, mean amelioration at 12 months of 9.6% (SD 2.1)												
17. Pain: Frequency During Vaginal Penetration	**2.3**	**1.2**	**3.8**	**1.2**	**3.6**	**1.4**	**95.0**	**61.1**	**77.5**	**53.2**	**0.0002**	**0.0032**
18. Pain: Frequency After Vaginal Penetration	**2.5**	**1.1**	**4.1**	**1.3**	**3.9**	**1.5**	**81.7**	**72.4**	**65.0**	**62.9**	**0.0002**	**0.0018**
19. Pain: Level During or After Vaginal Penetration	**2.7**	**1.0**	**4.1**	**1.2**	**3.9**	**1.3**	**61.7**	**37.7**	**48.3**	**39.5**	**0.0003**	**0.0023**
Pain, mean amelioration at one month of 79.5% (SD 16.8) **Pain, mean amelioration at 12 months of 63.3% (SD 14.7)**												

Abbreviations: M, menopausal; NM, no menopausal; SD, standard deviation; AT, after treatment; VHIS, Vaginal Health Index Scale; FSFI, Female Sexual Function Index; N, number of patients; SD, standard deviation; %Δ, percentage of difference; *p*, *p*-value.

Table 4. VHIS and FSFI results by patients with or without menopause, at baseline, 1 and 12 months after treatment session.

Variables Assessed	Baseline		1 Month AT		%Δ		12 Month AT		%Δ	
	M (N=8)	NM (N=12)	M (N=8)	NM (N=12)	M %	NM %	M (N=8)	NM (N=12)	M %	NM %
	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD
VHIS Score	**18.5 2.1**	**20.8 2.2**	**22.0 1.9**	**23.6 1.9**	**19.3 4.3**	**14.1 6.2**	**20.4 2.5**	**23.6 1.9**	**10.2 7.6**	**14.1 6.2**
Elasticity	3.1 1.1	3.9 1.0	4.0 0.5	4.5 0.7	39.6 41.7	20.8 32.5	3.4 1.1	4.5 0.7	12.5 35.4	20.8 32.5
Secretion/Fluid Volume	3.8 0.5	3.7 0.7	4.4 0.9	4.9 0.3	15.6 12.9	38.2 25.2	3.9 0.6	4.9 0.3	3.1 8.8	38.2 25.2
Vaginal pH	3.5 1.3	3.7 1.0	4.8 0.7	4.8 0.6	59.4 73.1	40.3 48.3	4.4 0.7	4.8 0.6	50.0 79.1	40.3 48.3
Integrity of the Epithelium	3.8 0.7	4.5 0.8	4.0 0.5	4.8 0.5	8.3 15.4	8.3 20.7	3.9 0.6	4.8 0.5	4.2 11.8	8.3 20.7
Lubrication/Moisture	3.6 0.5	3.6 0.7	4.6 0.5	4.7 0.7	28.1 4.3	31.9 13.2	4.5 0.5	4.7 0.7	25.0 10.9	25.0 13.2
FSFI										
1. Desire: Frequency	2.5 0.9	3.5 1.4	2.6 0.9	3.7 1.3	6.3 17.7	8.3 19.5	2.5 0.9	3.7 1.3	0.0 0.0	8.3 19.5
2. Desire: Level	2.5 0.9	3.5 1.4	2.4 0.9	3.7 1.3	-4.2 11.8	8.3 19.5	2.5 0.9	3.7 1.3	0.0 0.0	8.3 19.5
Menopausal: Desire, mean amelioration at 1 month of 1.1 (SD 7.4), and at 12 months of 0.0% (SD 0.0)										
No menopausal: Desire, mean amelioration at 1 month of 8.3 (SD 0.0), and at 12 months of 8.3% (SD 0.0)										
3. Arousal: Frequency	2.4 1.2	4.0 1.5	2.3 1.0	4.0 1.5	-3.1 8.8	0.0 0.0	2.3 1.0	4.0 1.5	-3.1 8.8	0.0 0.0
4. Arousal: Level	2.3 1.2	3.8 1.5	2.4 1.1	3.8 1.5	12.5 35.4	0.0 0.0	2.3 1.2	3.8 1.5	0.0 0.0	0.0 0.0
5. Arousal: Confidence	2.5 1.2	3.7 1.3	2.4 0.9	3.8 1.1	6.3 41.7	6.7 29.9	2.4 1.1	3.8 1.1	-3.1 8.8	6.7 29.9
6. Arousal: Satisfaction	2.9 1.4	3.8 1.3	2.5 1.1	4.2 1.2	-8.8 18.1	16.0 33.0	2.6 1.1	4.1 1.2	-5.6 10.5	13.2 29.6
Menopausal: Arousal, mean amelioration at 1 month of 3.3 (SD 11.0), and 12 months of -2.9% (SD 2.8)										
No menopausal: Arousal, mean amelioration at 1 month of 7.6 (SD 8.0), and at 12 months of 6.6% (SD 6.6)										
7. Lubrication: Frequency	**2.0 1.1**	**2.3 0.7**	**3.6 1.1**	**4.4 0.8**	**107.3 70.4**	**98.6 45.8**	**3.1 1.1**	**4.3 1.0**	**69.8 33.3**	**86.1 27.4**
8. Lubrication: Difficulty	**2.5 1.3**	**2.8 0.6**	**4.0 0.9**	**4.8 0.4**	**91.7 77.2**	**75.7 30.0**	**3.4 1.2**	**4.7 0.7**	**50.0 38.8**	**68.8 31.8**
9. Lubrication: Frequency of Maintenance	**2.1 1.0**	**2.5 0.7**	**3.8 0.7**	**4.6 0.5**	**103.1 71.3**	**91.0 35.8**	**3.0 1.2**	**4.4 0.7**	**46.9 38.8**	**84.0 40.3**
10. Lubrication: Difficulty	**2.4 1.1**	**2.5 0.8**	**4.0 1.1**	**4.6 0.7**	**101.0 105.6**	**96.5 48.7**	**3.4 1.3**	**4.5 0.8**	**53.1 44.1**	**92.4 50.4**
Menopausal: Lubrication, mean amelioration at 1 month of 100.8 (SD 6.6), and 12 months of 55.0% (SD 10.2)										
No menopausal: Lubrication, mean amelioration at 1 month of 90.5 (SD 10.3), and 12 months of 82.8% (SD 10.0)										
11. Orgasm: Frequency	2.9 1.1	3.7 1.1	2.9 1.1	3.8 1.0	0.0 0.0	7.6 25.0	2.9 1.1	3.8 1.0	0.0 0.0	7.6 25.0
12. Orgasm: Difficulty	3.0 1.4	3.9 0.9	3.1 1.2	4.0 1.0	12.5 35.4	2.1 7.2	3.0 1.4	4.0 1.0	0.0 0.0	2.1 7.2
13. Orgasm: Satisfaction	2.8 1.6	3.8 0.8	2.6 1.4	3.9 0.9	-2.5 7.1	2.1 7.2	2.6 1.4	3.9 0.9	-2.5 7.1	2.1 0.3
Menopausal: Orgasm, mean amelioration at 1 month of 3.3 (SD 8.0), and 12 months of -0.8% (SD1.4)										
No menopausal: Orgasm, mean amelioration at 1 month of 3.9 (SD 3.2), and 12 months of 3.9% (SD3.2)										
14. Satisfaction: with amount of closeness with partner	2.6 1.3	3.7 0.9	2.6 1.3	4.1 1.0	0.0 0.0	12.5 21.2	2.6 1.3	4.1 1.0	0.0 0.0	12.5 21.2
15. Satisfaction: with sexual relationship	2.3 1.2	3.4 1.0	2.4 1.2	3.9 0.9	6.3 17.7	19.4 30.6	2.3 1.2	3.9 0.9	0.0 0.0	19.4 30.6
16. Satisfaction: with overall sex life	2.4 1.2	3.3 1.0	0.1 0.4	3.7 0.9	6.3 17.7	16.0 20.9	2.3 1.2	3.7 0.9	0.0 0.0	16.0 20.9
Menopausal: Satisfaction, mean amelioration at 1 month of 4.2 (SD 3.6), and 12 months of 0.0% (SD 0.0)										
No menopausal: Satisfaction, mean amelioration at 1 month of 16.0 (SD 3.5), and 12 months of 16.0% (SD 3.5)										
17. Pain: Frequency During Vaginal Penetration	**1.9 1.4**	**2.5 1.1**	**3.3 1.3**	**4.2 1.0**	**106.3 66.5**	**87.5 59.0**	**2.9 1.6**	**4.1 1.1**	**68.8 43.8**	**83.3 59.8**

Variables Assessed	Baseline		1 Month AT		%Δ		12 Month AT		%Δ	
	M (N=8)	NM (N=12)	M (N=8)	NM (N=12)	M %	NM %	M (N=8)	NM (N=12)	M %	NM %
	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD	Mean SD
18. Pain: Frequency After Vaginal Penetration	**2.1 1.4**	**2.8 1.0**	**3.4 1.5**	**4.5 1.0**	**83.3 78.0**	**80.6 72.0**	**3.0 1.8**	**4.4 1.0**	**3.0 1.8**	**77.8 73.2**
19. Pain: Level During or After Vaginal Penetration	**2.5 1.4**	**2.8 0.6**	**3.4 1.5**	**4.5 0.7**	**51.0 41.7**	**68.8 34.8**	**2.5 1.4**	**4.3 0.7**	**26.0 32.9**	**63.2 37.5**
Menopausal: Pain, mean amelioration at 1 month of 80.2 (SD 27.8), and 12 months of 32.6% (SD 33.4)										
No menopausal: Pain, mean amelioration at 1 month of 79.0 (SD 9.5), and 12 months of 74.8% (SD 10.4)										

Abbreviations: M, menopausal; NM, no menopausal; SD, standard deviation; AT, after treatment; VHIS, Vaginal Health Index Scale; FSFI, Female Sexual Function Index; N, number of patients; SD, standard deviation; %Δ, percentage of difference; *p*, *p*-value.

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