New therapeutic option in genitourinary syndrome of menopause: pilot study using microablative fractional radiofrequency

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ABSTRACT

Objective: To evaluate the clinical response of patients with symptoms of genitourinary syndrome of menopause after application of microablative fractional radiofrequency in the vagina and vaginal introitus. Methods: Fourteen patients with symptoms of genitourinary syndrome of menopause underwent three applications of microablative fractional radiofrequency with a 30-day interval, using the Wavetronic 6000HF-FRAXX device and a fractional vaginal electrode. The questionnaires World Health Organization Quality of Life (for quality of life evaluation), Female Sexual Function Index and Quality of Life Adapted Questionnaire in the Domain of Sexual Satisfaction (for sexual function and satisfaction evaluation) were administered before and after the applications (30 to 60 days after the last procedure), in addition to the satisfaction questionnaire after procedure. Results: There was an increase in almost all dimensions on average in quality of life, with statistical significance only in the health domain. There was a significant improvement in the sexual domains in almost all dimensions. All patients stopped using lubricant during intercourse after treatment. In the satisfaction questionnaire after treatment, we observed that the vast majority felt cured or much better (29% and 64%, respectively, total of 92.6%) and were very satisfied or satisfied (43% and 57%, respectively, total of 100%). The only patient who reported little improvement had an 18-year postmenopausal history and was treatment naïve. Conclusion: Microablative fractional radiofrequency was effective in treating symptoms of vaginal dryness and dyspareunia, and eliminated the use of vaginal lubricant during the period observed. Since this is a pilot study with a small number of patients, further studies are required to corroborate our findings and evaluate the long-term effects of microablative fractional radiofrequency on the vaginal tissue.

Keywords: Atrophy; Vagina/pathology; Vulva/pathology; Dyspareunia; Radio waves; Lasers; Female urogenital diseases

RESUMO

Objetivo: Avaliar resposta clínica de pacientes com sintomas da síndrome geniturinária da menopausa após aplicação de radiofrequência fracionada microablativa na vagina e no introito vaginal. Métodos: Quatorze pacientes com sintomas de síndrome geniturinária da menopausa foram submetidas a três aplicações de radiofrequência fracionada microablativa com intervalo de 30 dias, utilizando aparelho Wavetronic 6000HF-FRAXX e eletrodo vaginal fracionado. Foram aplicados os questionários World Health Organization Quality of Life (para avaliar qualidade de vida), Female Sexual Function Index e Quality of Life Adapted Questionnaire in the Domain of Sexual Satisfaction (para verificar função sexual e satisfação) antes e depois das aplicações (30 a 60 dias após último procedimento), além do questionário de satisfação após procedimento. Resultados: Na qualidade de vida, houve aumento na média em geral, com significância estatística apenas no quesito saúde. No domínio sexual, houve melhora significativa em quase todas as dimensões. Todas as pacientes cessaram o uso de lubrificante na relação sexual após o tratamento. No questionário de satisfação após tratamento, a maioria se sentiu curada ou muito melhor (29 e 64%, respectivamente; total de 92,6%) e
Descrição: Agradável perda de rugosidade e alteração da mucosa vaginal e redução. A mucosa pode ser menos elástica, com pele seca e córtico vaginal restrita. Hemodinâmica e estruturas da mucosa vaginal podem sofrer danos (1-4) através de cirurgias, que afetam a produção de estrogênio ovariano ou disfunção hipotalâmica, e também podem ocorrer em condições deamenorréia por atividade excessiva. O uso de agonistas de hormônio de liberação de gonadotropina (GnRH) (por exemplo, no estudo piloto com quantidade de pacientes, mais estudos são necessários para corroborar estes achados e avaliar os efeitos a longo prazo da radiofrequência fracionada microablativa no tecido vaginal.

INTRODUÇÃO

O termo “atrofia vulvovaginal” (VVA) é frequentemente usado para descrever sintomas resultantes de baixos níveis de estrogênio e outros sex hormon levels, que são comuns no sintoma climatérico, incluindo vulvar, vaginal, uretral e mudanças pelúricas. No entanto, o termo “atrofia genitourinária de menopausa” (GSM) tem ganhado notoriedade desde 2012, quando a organização da Sociedade Internacional para o Estudo da Saúde das Mulheres (ISSWSH) e a Administração do Conselho do Conselho Americano do Estudo da Menopausa (NAMS) consideraram a necessidade de revisar a terminologia para VVA, considerando os sintomas genitourinários durante o período pós-menopausal.

Assim, GSM pode incluir, mas não está limitado a, sintomas genitais como vulva, vestibule e vírgula, frieza, sensação de desconforto e vulvovaginal irritação, adicionalmente a sintomas sexuais, como falta de lubrificação e dispureia, levando a desfunção de córtico, e sintomas urinários como urgência urinária, frequente urinação, disúria e infecções urinárias.

Hipoestrogenismo pode ocorrer em outras situações, como cirurgia menopausa, ou o uso de gonadotropin-releasing hormone (GnRH) agonist (por exemplo, no tratamento de endomiocisto e leiomiomia); também, em amenaorrea hipotalâmica devido à excesso de exercício, e distúrbios alimentares. O mesmo ocorre em condições que afetam a produção de estrogênio ovariano ou causam dano ao epitélio vaginal, o suprimento vascular e a anatomia vaginal, como cirurgias, quimioterapia e radioterapia.

Clinicalmente, o epitélio vaginal se torna fino, comum e seca, e pode levar a restrição vaginal e degeneração. O epitélio pode ser menos elástico, com uma perda gradual de rugosidade e alteração do epitélio microbiano vaginal, adicionalmente à redução da circulação sangüínea. In
Radiofrequency is a process of cutting and/or coagulating biological tissues by using a high-frequency alternating current, which instantly raises the intracellular temperature up to 100°C, thus determining cellular membrane expansion and rupture. This phenomenon is known as vaporization, similar to the laser action.

Conventional electrosurgery devices amplify the electrical alternating current provided as 60 cycles/second (60Hertz) and work in the range of 500,000 (500KHz) to 1,500,000 cycles/second (1.5MHz). By reaching the frequency of 4,000,000 cycles/second (4MHz), the FM radio frequency is obtained – giving rise to the name RF electrosurgery. This technology yields effect into biological tissues like the laser technology – gentle, with no trauma, with precise cut and coagulation, through electromagnetic energy in the megahertz (MHz) frequency.(13)

Energy fractionation consists of energy distribution at equidistant points, producing microscopic columns of thermal injuries in the epidermis and upper dermis, resulting in microscopic columns of treated tissue and intervening areas of untreated skin, which in turn achieve faster reepithelialization.(13)

Based on the use of fractional RF on the skin, and of fractionated laser in dermatology and in the genital region, we aimed to study the effects of microablative fractional radiofrequency (MAFRF) with an innovative technique for vaginal application in patients with GSM. Moreover, to evaluate the benefits regarding relief of symptoms as well and the duration of the effects to suggest this technique as a new therapeutic option. A fractional vaginal electrode coupled to the FRAXX platform of the Wavetronic 6000 device was developed for vulvovaginal applications.

OBJECTIVE

To evaluate the clinical response of patients with symptoms of genitourinary syndrome of menopause after application of microablative fractional radiofrequency in the vagina and vaginal introitus.

METHODS

A prospective pilot study conducted in the Department of Gynecology at Hospital Heliópolis, from September 2016 to September 2017. A total of 15 patients with GSM complaints were selected and agreed to be treated with microablative fractional radiofrequency (MAFRF) as a therapeutic alternative. One patient withdrew after the first application, for personal reasons.

The inclusion criteria were patients with symptoms of GSM; vaginal, vulvar and/or urinary complaints; perimenopause; surgical menopause; other hypoestrogenic conditions (except for those resulting from chemotherapy, radiation therapy); and cervical citology test negative for cancer within the routine period recommended by the Brazilian Ministry of Health. The exclusion criteria were use of hormone therapy (either systemic or topical) or long-acting moisturizers within the last 60 days prior to the initial assessment; patients with active or recurrent genital infection (e.g. genital herpes, candidiasis); patients with human immunodeficiency virus; recurrent urinary tract infection; pelvic radiation therapy or brachytherapy; reconstructive pelvic surgery. Other chronic diseases, such as diabetes, hypertension and deep venous thrombosis were not exclusion criteria.

After history taking and physical examination, patients were selected and instructed about the procedure, and, after giving Informed Consent and authorization for photographic documentation, they answered the following questionnaires: bref version of World Health Organization Quality of Life (WHOQoL-BREF), comprising 26 items, which evaluates the general quality of life considering the broad domains physical health, psychological health, social relationships, and environment; Female Sexual Function Index (FSFI); and International Consultation on Incontinence Questionnaire – Vaginal Symptoms (ICIQ-VS), part of Quality of Life Adapted Questionnaire in the Domain of Sexual Satisfaction. Patients were informed that 30 to 60 days after the last MAFRF application, the three questionnaires would be answered again in addition to a questionnaire on post-procedural satisfaction with Likert scale. Physical examination and new assessments could be carried out every 6 months. The clinical outcome was evaluated by analyzing the questionnaires.

The study was approved by the Research Ethics Committee under number 1769977, CAAE 58353416. 2.0000.5449 and conducted according to the guidelines recommended by the 2000 Declaration of Helsinki, updated in 2008.

Application technique

No anesthetic agent was required for the vaginal procedure. In the vestibule and vaginal opening, 10% lidocaine spray was applied 3 minutes prior to the procedure. The Wavetronic 6000 Touch device is used with the Megapulse HF FRAXX system (Loktal Medical Electronics, São Paulo, Brazil), equipped with an electronic circuit of energy fractionation, connected to a
vaginal pen with 64 microneedles 200μ in diameter and 1mm in length, mounted on a Teflon body and divided into an eight-column matrix with eight needles each (Figure 1). When pressing the activator pedal, the 64 needles are not energized at the same time, and energy delivery is randomized into columns of eight needles in a pre-set sequence in such a way that two underlying columns do not shoot in sequence, thus preventing thermal summation of columns (exclusive random fractionated shot control “Smart Shoot”).

This allows cooling between the points and preservation of the tissues adjacent to the vaporized points for neocolagenesis and neoelastogenesis to take place through fibroblast stimulation. Each shot of the pen performs 64 microablations in the mucosa (Figures 2 and 3).

Vaginal/Introitus Application
Three MAFRF applications were performed in the vagina/vaginal introitus, with a 28 to 40-day interval between each application. The following technique was performed: patient in the lithotomy position; placement of the disposable vaginal speculum, antisepsis with 0.2% aqueous chlorhexidine, and cleaning with sterile 0.9% saline solution, removing excess vaginal contents with gauze. A sequential emission of MAFRF was applied on all vaginal walls under direct vision and moving the vaginal speculum as necessary. In the vestibule, the application was limited to the vaginal introitus, not including the clitoris, clitoral foreskin and labia minora. The electrode was always kept parallel and lightly touching the mucosa at each shot. The average procedure time was 15 to 20 minutes.

For the post-treatment care, the use of 5% dexamethasone solution in the vaginal opening was recommended two to three times a day, for 2 to 5 days, and no intercourse for 10 days.

Statistical analysis
Data are presented as mean and standard deviation, median or percentages. The significance level was set at 0.05, corresponding to a 95% confidence interval. The Student’s t test was used for dependent samples, and significant differences were analyzed (p<0.05).

RESULTS
Fourteen women were followed up and the questionnaires were administered comparing the two periods – pre-
and post-treatment. The main complaints of patients were vaginal dryness (100%); need for lubricant during intercourse (86%); dyspareunia (50%); urinary urgency (29%); mild urinary incontinence (29%); nocturia (29%); urinary tract infection after sexual intercourse (7%); and bleeding during intercourse (7%).

Considering the WOHQoL, we found an increase in almost all dimensions on average, with statistical significance only in the health domain (p=0.0401) (Table 1).

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<tr>
<th>Dimensions of World Health Organization Quality of Life Questionnaire* of women with symptoms of genitourinary syndrome of menopause</th>
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Mean and standard deviation, Student’s t test; significant difference p<0.05.


Table 1. Dimensions of World Health Organization Quality of Life Questionnaire* of women with symptoms of genitourinary syndrome of menopause

In the FSFI, we noticed significant improvement in the overall total (p=0.0065), in almost all dimensions (desire, arousal, lubrication, satisfaction, and pain), except for excitation and orgasm (Table 2).

In the ICIQ-VS, there was a significant improvement in five questions, with statistical significance in the overall total (p=0.0001). All patients stopped using lubricant during intercourse after treatment (Table 3).

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<td>Dimension</td>
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<tr>
<td>Q1_ Difficulty in vaginal intercourse</td>
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<td>Q2_ Discomfort or pain in vaginal penetration</td>
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<td>Q3_ Itching, burning, irritation in vagina or around</td>
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<td>Q4_ Is your vagina very dry?</td>
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<td>Q5_ Satisfaction with the appearance of your vulva</td>
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<td>Q6_ Use of lubricant</td>
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<td>Q7_ How vaginal symptoms interfere with your life?</td>
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<td>Q8_ Satisfaction with sexual life in general</td>
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Mean and standard deviation, Student’s t test; significant difference p value <0.05.


In the Satisfaction questionnaire after treatment, we observed that the majority felt cured or much better (29% and 64%, respectively; total of 92.6%) and were very satisfied or satisfied (43% and 57%, respectively; total of 100%). The only patient who reported little improvement had an 18-year postmenopausal history and was treatment naïve (Figure 4).

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**DISCUSSION**

Approximately 40 to 50% of women in physiological menopause may have signs and symptoms of GSM. Early diagnosis and active intervention can prevent the appearance of moderate to severe atrophies, as well as sequelae. Alternative therapies, whether or not associated with local hormone therapy, may contribute to a more complete and appropriate approach to each patient’s situation.
In a study on periorbital rejuvenation, the same Wavetronic HF FRAXX device, version 5000, was successfully used, calibrated at 46W power and 60ms current time. This is the active current time during which the skin is exposed to heat, corresponding to 338mJ/point, so that the thermal lesion is similar to that of a fractionated CO₂ laser, considering the sufficient amount of energy (345mJ) for a safe treatment.\(^{13}\)

Since this study was conducted on the skin, which is keratinized and offers more resistance to electromagnetic wave penetration in relation to the mucosa (not keratinized), we decided to use less energy. The device was set at 45W power and a low energy treatment level, 40ms, which is the current time in milliseconds of each eight-needle column, corresponding to 225mJ per point.

In a pilot study in 2014, Salvatore et al. assessed 50 patients with GSM dissatisfied with local estrogen therapy, who received three vaginal applications of CO₂ laser for 12 weeks. Symptoms were assessed before and after the procedure, using quality of life and sexual function questionnaires. The authors pointed out effectiveness of the treatment proposed as regards the significant improvement of symptoms of GSM among postmenopausal women, and suggested further studies.\(^{16}\)

In the present pilot study, whose design is similar to that of Salvatore et al.\(^{16}\) we used MAFRF in 15 patients with GSM and found analogous results. For our group of patients, this therapy was very effective especially in the treatment of vaginal dryness and dyspareunia, eliminating the use of lubricants during the follow-up period.

In another important \textit{ex-vivo} study, Salvatore et al. compared the effects of microablative fractionated CO₂ laser in the vaginal mucosa of postmenopausal patients using histologic analyses by means of either electronic or light microscopy (hematoxylin and eosin staining), before and after treatment. The authors concluded it could be demonstrated for the first time that fractionated CO₂ laser was capable of producing vaginal connective tissue remodeling with vaginal mucosa reconstitution.\(^{10}\)

The limitations of the present study are related to the small sample size and to the fact that it is based on subjective assessments. This has motivated us to start another research project to assess the presumed histological remodelling of the vaginal mucosa by means of biopsies before and after treatment with three MAFRF applications.

As advantages of the use of MAFRF in the vaginal mucosa in comparison to fractioned CO₂ laser, we point out that the application is performed under direct vision and using a vaginal speculum, thus facilitating the treatment on the vaginal walls and preventing shot overlapping; in addition, the method is easy to learn and less costly.

The procedure proved to be well tolerated, with occasional reports of mild discomfort; patients recovered fast and microablation was no longer visible usually within 3 to 5 days after the application. The adverse effects observed were not significant and none of the participants had any long-term or permanent side effects after the procedure. Most patients reported improvement of the symptoms of dryness and dyspareunia from the first application.

**CONCLUSION**

Microablative fractional radiofrequency was effective in treating symptoms of vaginal dryness and dyspareunia, and eliminated the use of vaginal lubricant during the period observed. Since this is a pilot study with a small number of patients, further studies are required to corroborate our findings and evaluate the long-term effects of microablative fractional radiofrequency on the vaginal tissue.

**REFERENCES**


