Efficacy of laser remodeling treatment in genitourinary syndrome of menopause

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Summary (Abstract)

Objective: To evaluate the efficacy of laser remodeling in genitourinary syndrome of menopause using fractional microablative CO2 laser remodeling treatment (SmartXide2 V2LR Monalisa Touch; DEKA (Florence, Italy)).**Materials and Methods**: This prospective, observational study included 105 patients (n=105) aged 52.0 ± 1.3 years with a verified diagnosis of postmenopausal atrophic vaginitis (ICD N.95.2) who provided voluntary informed consent to participate in this study. Based on the regimens of fractional microablative CO2 laser remodeling treatment using the SmartXide2 V2LR Monalisa Touch laser system (DEKA, Florence, Italy) patients in the study cohort were assigned to either group I (n= 50; 40/1000/1000/1 ST/DP) or group II (n=55; 40/1400/1000/1 ST/DP). The control group for clinical and morphological comparison (n=30) included women of the similar age who did not have a verified diagnosis of postmenopausal atrophic vaginitis, N95.2.For objectification, the clinical manifestations of GSM in patients of the study cohort were scored using a 5-point D. Barlow scale and the vaginal health index was calculated (G. Bachmann, 1995).**RESULTS:** Following the laser remodeling procedure, patients in groups I and II demonstrated a significant increase in the vaginal health index, i.e., 1.25-fold (3.0 ± 0.81 versus 3.74 ± 0.69; $p < 0.001$) and 1.3-fold (3.15 ± 0.65 versus 4.11 ± 0.57; $p < 0.001$) after 3 months and 1.55-fold (3.0 ± 0.81 versus 4.66 ± 0.48; $p < 0.001$) and 1.5-fold (3.15 ± 0.65 versus 4.71 ± 0.46; $p < 0.001$) after 12 months, respectively. However, there were no statistically significant differences between the study groups (p= 0.310, p= 0.003, p= 0.593, respectively). In patients in the study cohort the baseline scores of the clinical manifestations of GSM using the D. Barlow scale were 2.74 ± 1.23 and 2.92 ± 1,14 in groups I and II, respectively. Following the laser remodeling procedure, patients in groups I and II experienced a significant decrease in these scores of 1.49-fold (2.74 ± 1.23 versus 1.84 ± 0.93; $p < 0.001$) and 1.45-fold (2.92 ± 1.14 versus 2.02 ± 0.87; $p < 0.001$) after 3 months and 3.8-fold (2.74 ± 1.23 versus 0.72 ± 0.7; $p < 0.001$) and 4.11-fold (2.92 ± 1.14 versus 0.71 ± 0.66; $p < 0.001$) after 12 months, respectively. However, there were no statistically significant differences between the study groups (p= 0.418, p= 0.314, p= 0.935, respectively). In this study, two regimens (40/1000/1000/1 ST/DP and 40/1400/1000/1 ST/DP) of the microablative laser remodeling treatment using the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy) were found to be similar in clinical efficacy and safety and had no adverse effects associated with burns and/or adhesions to the vaginal mucosa.**conclusions**: Therefore, it can be concluded that the use of the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy) in treatment of GSM is pathogenetically justified and is an effective and safe treatment option in postmenopausal patients with vulvovaginal atrophy.

Key words: vulvovaginal atrophy, genitourinary syndrome of menopause, vaginal dryness, laser treatment

Background

Genitourinary syndrome of menopause (GSM) is a prevalent medical condition associated with rapid atrophy of the epithelial compartment of the genitourinary tract in women with a progressive estrogen deficiency in the pre- or postmenopausal period [1]. Thus, the incidence of GSM among postmenopausal women worldwide varies from 24 to 84% and depends on the study population [2,3].

GSM occurs due to a decrease in the proliferative activity

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of mucosal cells of the genitourinary tract causing characteristic symptoms, such as vaginal dryness, dyspareunia and dysuria [4,5,6]. Along with another significant adverse effect of estrogen deficiency, namely a decreased accumulation of glycogen in vaginal mucosal cells, this leads to an inevitable shift (generally more than 5) to alkaline pH and consequently to impairment of colonization resistance and activation of opportunistic pathogens, and inflammatory diseases [7, 8].

Undoubtedly, there are absolute reasonable grounds for the topical estrogen therapy to be pathogenetically justified in any atrophic disorders associated with menopause. It is fair to say that having a significantly lower systemic effect compared to estradiol preparations, topically applied estriol improves the blood supply to the vaginal wall, restores the transudative function of the mucous membrane of the genitourinary tract, maintains sufficient thickness and elasticity of the epithelium and the level of glycogen synthesis in the vaginal fluid, and also stimulates the secretion of immunoglobulins, i.e., it prevents vaginitis [5-7].

A Cochrane review based on an analysis of 15 randomized placebo-controlled trials suggested the high efficacy and safety of topical estrogen therapy [7,8]. In addition, currently it can be stated with certainty that topical estrogen therapy is more effective in reducing the risk of recurrent urinary infections, overactive bladder and urinary incontinence in postmenopausal women (level of evidence A) than systemic drugs (HR 1.65) [5,6,8]. However, even these seemingly optimistic data do not allow treating patients with GSM who have contraindications for hormone therapy, have experienced treatment complications or refused this therapy due to hormonophobia. This means that the clinician's arsenal should also include non-pharmacological treatments with comparable efficacy [8]. One of these options is the laser modeling therapy, the clinical and morphological efficacy and safety of which justify the need for high-quality studies.

Materials and methods

A total of 179 postmenopausal patients were randomized in this study. The reasons for non-inclusion (n=75) of patients in the study were: exclusion criteria (n=38), contraindications to laser remodeling therapy (n=25), as well as other reasons associated with non-compliance with the recommendations (n=8), and changing the place of residence (n=4). Thus, this prospective, observational study included 105 patients (n=105) aged 52.0 ± 1.3 years who referred to the clinical sites of the Department of Obstetrics and Gynecology with a course of perinatology of the Peoples' Friendship University of Russia with a verified diagnosis of postmenopausal atrophic vaginitis (ICD N.95.2) and provided their voluntary informed consent for enrollment in this study, namely, collection of biological materials, investigation of clinical, laboratory and instrumental parameters, evaluation of efficacy and safety of the therapy, statistical processing and publication of the results. Depending on the regimens of fractional microablative CO2 laser remodeling treatment using the SmartXide2 V2LR Monalisa Touch laser system (DEKA, Florence, Italy) patients in the study cohort were assigned to either group I (n= 50; 40/1000/1000/1 ST/DP) or group II (n=55; 40/1400/1000/1 ST/DP). The control group for clinical and morphological comparison (n=30) included women of similar age who did not have a verified diagnosis of postmenopausal atrophic vaginitis, N95.2.

For objectification, the clinical manifestations of GSM in patients of the study cohort were scored using a 5-point D. Barlow scale.

All patients underwent pH-metry using a color scale. Based on the above signs, vulvovaginal atrophy was objectified by calculating the Vaginal Health Index (G. Bachmann, 1995).

For statistical analysis, the results were processed using IBM SPSS v.23.0 and StatTech software. The arithmetic means, standard deviations and errors of means were calculated. Statistical significance of differences between values was assessed using non-parametric criteria, i.e., the Mann-Whitney U-test and the Kruskal-Wallis H-test.

The study groups were compared using the t-test with a significance level of $p < 0.05$

Results

The mean age of patients in the study cohort (n=105) was 52 ± 1.3 years with the mean age of 51.78±1.37 and 52.1±1.26 years in the first (n=50) and the second (n=55) study groups, respectively. Meanwhile, there were no statistically significant differences between the study groups and the control group (mean age = 51.17±1.62) ($p = 0.203$).

The mean postmenopausal period was 2.38±0.9 years and 2.26±0.84 years in the first and the second study groups, respectively. There were no statistically significant differences between study groups I and II and the control group (2.14±0.81 years in the control group, $p = 0.463$).

Two study groups practically did not differ in the mean duration of clinical GSM which was 2.26±0.88 years in the first group and 2.26±0.84 in the second group. There were no statistically significant differences between the study groups ($p = 0.974$).

The structure of complaints reported by patients in the study cohort was found to be very diverse. Thus, all patients had vaginal complaints (irritation, itching, dryness) with all 3 signs reported in half of the subjects (50%) in the first group and in 36.4% in the second group. There were no statistically significant differences between the groups ($p = 0.158$).

Following the laser remodeling procedure, patients in groups I and II demonstrated a significant increase in the vaginal health index, i.e., 1.25-fold (3.0 ± 0.81 versus 3.74 ± 0.69; $p < 0.001$) and 1.3-fold (3.15 ± 0.65 versus 4.11 ± 0.57; $p < 0.001$) after 3 months and 1.55-fold (3.0 ± 0.81 versus 4.66 ± 0.48; $p < 0.001$) and 1.5-fold (3.15 ± 0.65 versus 4.71 ± 0.46; $p < 0.001$) after 12 months, respectively. However, there were no statistically significant differences between the study groups ($p= 0.310$, $p= 0.003$, $p= 0.593$, respectively). In patients in the study cohort the baseline scores of the clinical

manifestations of GSM using the D. Barlow scale were 2.74 ± 1.23 and 2.92 ± 1,14 in groups I and II, respectively. Following the laser remodeling procedure, patients in groups I and II experienced a significant decrease in these scores of 1.49-fold (2.74 ± 1.23 versus 1.84 ± 0.93; p < 0.001) and 1.45-fold (2.92 ± 1.14 versus 2.02 ± 0.87; p < 0.001) after 3 months and 3.8-fold (2.74 ± 1.23 versus 0.72 ± 0.7; p < 0.001) and 4.11-fold (2.92 ± 1.14 versus 0.71 ± 0.66; p < 0.001) after 12 months, respectively. However, there were no statistically significant differences between the study groups (p= 0.418, p= 0.314, p= 0.935, respectively). In this study, two regimens (40/1000/1000/1 ST/DP and 40/1400/1000/1 ST/DP) of the microablative laser remodeling treatment using the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy) demonstrated similar high clinical efficacy and safety in treatment of GSM symptoms and had no adverse effects associated with burns and/or adhesions to the vaginal mucosa.

Discussion

As mentioned above, GSM is indeed a problem of utmost importance requiring a rigorous approach from the clinician both to the verification of atrophic vaginitis and the choice of a treatment strategy in management of GSM. Vulvovaginal atrophy affects a large number of women worldwide, namely 48% of perimenopausal subjects and 53.8% to 90% of postmenopausal individuals [8].

It is important to note that topical hormone therapy using estrogens, besides obvious and undeniable benefits, has a number of contraindications. Thus, in patients with a history of estrogen-dependent reproductive and/or extragenital cancers either systemic or topical estrogen therapy is contraindicated or should be carried out with caution and only after consultation with an oncologist [9,10,11].

Moreover, it is necessary to collect a thorough medical history and elaborate the correct examination algorithm for each patient, which subsequently will allow for a detailed stratification to assign subjects to risk groups.

However, in hormonophobic patients as well as in individuals with absolute contraindications, depending on the severity of GSM alternative treatment options may be used and fully justified. These include laser remodeling therapy using the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy).

Based on this open-label, independent, prospective, single-site comparative study the use of the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy) should be considered a highly effective, safe and promising treatment option in women with GSM.

Conclusions

Therefore, it can be concluded that the use of the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy) in treatment of GSM is pathogenetically justified and is an effective and safe treatment option in postmenopausal patients with vulvovaginal atrophy.

Disclosure of interest

The authors declare that they have no competing interests.

Authors' contribution

The authors declare the compliance of their authorship according to the international ICMJE criteria.

All authors made a substantial contribution to the conception of the work, acquisition, analysis, interpretation of data for the work, drafting and revising the work, final approval of the version to be published and agree to be accountable for all aspects of the work.

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