Quality of life and sexual function in patients with genitourinary syndrome of menopause: focus on laser remodeling therapy

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SUMMARY (Abstract)

Objective: To evaluate the quality of life and sexual function in patients with genitourinary syndrome of menopause prior to and following laser remodeling using the fractional microablative CO2 laser remodeling therapy (SmartXide2 V2LR Monalisa Touch; DEKA (Florence, Italy)).**Study Design**: An open, multicentre, comparative, independent, prospective study.**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 (n = 30) included women of similar age who did not have a verified diagnosis of postmenopausal atrophic vaginitis.For objectification, the clinical manifestations of GSM in study patients were scored using a 5-point D. Barlow scale and the vaginal health index was calculated (G. Bachmann, 1995). The quality of life and sexual function in the study cohort were evaluated using the following tools: Female Sexuality Index (SSI), 5-point Likert scale, and SF-36 quality of life questionnaire. The pain intensity in patients suffering from GSM-related dyspareunia was measured using a Visual Analogue Scale (VAS). The efficacy of therapy was evaluated 3 and 12 months after laser remodeling procedures. For statistical analysis, the results were processed using IBM SPSS v.23.0 and StatTech software.**RESULTS:** The mean age of patients in the study cohort (n=105) was 52 ± 1.3 years. 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. 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. Following the laser remodeling procedure, patients in groups I and II experienced a significant decrease in GSM symptom intensity 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. A similar positive trend was observed in scores obtained using the D.Barlow scale: 3.8-fold (2.74 ± 1.23 versus 0.72 ± 0.7; $p < 0.001$) and 4.11-fold (2.92 ± 1.14 vs. 0.71 ± 0.66; $p<0.001$) 3 and 12 months after the treatment, respectively. Following the laser remodeling procedure, there was a significant improvement in quality of sexual life of 1.33-fold (Female Sexuality Index (SSI), 19.58 ± 6.88 versus 26.02 ± 4.81; $p < 0.001$) and 1.25-fold (21.4 ± 6.76 versus 26.76 ± 4.9; $p < 0.001$) after 3 months and 1.58-fold (19.58 ± 6.88 versus 30.98 ± 3.12;

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p < 0.001) and 1.46-fold (21.4 ± 6.76 versus 31.16 ± 3.3; p < 0.001) after 12 months, respectively. Following the laser remodeling procedure, patients demonstrated a significant decrease in intensity of GSM-related dyspareunia of 1.6-fold (4.44 ± 2.18 versus 2.76 ± 1.4; p < 0.001) and 1.75-fold (4.24 ± 2.08 versus 2.42 ± 1.26; p < 0.001) after 3 months and 4.83-fold (4.44 ± 2.18 versus 0.92 ± 0.75; p < 0.001) and 5.44-fold (4.24 ± 2.08 versus 0.78 ± 0.69; p < 0.001) after 12 months, respectively.The quality of life measured using SF-36 was also found to improve significantly, i.e., 1.35-fold (48.18 ± 20.06 versus 65.02 ± 16.45; p < 0.001) and 1.31-fold (53.2 ± 21.1 versus 69.64 ± 15.96; p < 0.001) after 3 months and 1.59-fold (53.2 ± 21.1 versus 84.64 ± 9.78; p < 0.001) after 12 months, respectively. The analysis of quality of life measured using the Likert scale demonstrated a significant decrease in the scores of 1.66-fold (2.82 ± 0.98 versus 1.7 ± 0.97; p < 0.001) and 1.76-fold (2.62 ± 0.87 versus 1.49 ± 0.84; p < 0.001) 3 months after and 4.03-fold (2.82 ± 0.98 versus 0.7 ± 0.54; p < 0.001) and 3.82-fold (2.62 ± 0.87 versus 0.685 ± 0.58; p < 0.001) 12 months after the laser remodeling procedure, respectively.**conclusions:** In summary, it can be concluded that the use of the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy), regardless of the parameters of the selected ablation regimen in the treatment of GSM symptoms, has a beneficial effect on the quality of life and sexual function in patients with genitourinary syndrome of menopause.

Key words: vulvovaginal atrophy, genitourinary syndrome of menopause, vaginal dryness, laser treatment, quality of life, dyspareunia.

Background

Genitourinary syndrome of menopause (GSM) is a symptom complex associated with a decrease in estrogens and other sex steroids, which includes changes in the vulva, perineum, vagina, urethra, and bladder [1]. Genitourinary symptoms due to estrogen deficiency are characterized by physiological and anatomical changes [1,2]. Genitourinary syndrome of menopause (GSM) is an extremely common condition with a wide range of incidence rates among postmenopausal women, namely from 24% to 84% of individuals worldwide [3]. It is important to note that based on the prospective cohort study by Monteleone P. et al. (2018), the presence of symptoms of urogenital atrophy, as well as their intensity depend on ethnic, geographical and individual factors [1,2,3,4,5].

Such a high incidence of this condition highlights the relevancy of scientific research in this area aimed at developing new methods of treatment and improvement of the quality of life of patients.

Since atrophy of the genitourinary tract leads to a significant decrease in quality of life of a woman due to inability for her to have sex, frequent inflammatory diseases of the vagina and urethra, as well as dysuria, the time from the onset of the first symptoms of urogenital atrophy to the moment of treatment is of great importance in the event of signs of estrogen deficiency in postmenopausal individuals. It is also important that the symptoms of urogenital atrophy, in contrast to other symptoms associated with estrogen deficiency, progress over time, which is also accompanied by a significant deterioration in the health and quality of life of a woman [8]. Taking into account the pathogenesis of the disease, topical estrogen therapy is considered the "gold standard" treatment for GSM [9].

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 (RR 1.65) [5,6,8]. However, even these seemingly optimistic data do not allow treating patients with GSM who have contraindications to 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 remodeling therapy, the clinical and morphological efficacy and safety of which justify the need for high-quality studies.

Objective

To evaluate the quality of life in patients with genitourinary syndrome of menopause prior to and following laser remodeling using the fractional microablative CO2 laser remodeling therapy (SmartXide2 V2LR Monalisa Touch; DEKA (Florence, Italy)).

Study Design

An open, multicentre, comparative, independent, prospective study.

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 a change of the place of residence (n = 4). Therefore, 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 the 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 (n = 30) included women of similar age who did not have a verified diagnosis of postmenopausal atrophic vaginitis (ICD N.95.2).

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

A gynecological examination included an examination of the external and internal genital organs with a detailed examination of the mucous membrane of the vagina and cervix. 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).

The quality of life was evaluated in each patient in the study cohort using the following tools: Female Sexuality Index (SSI), 5-point Likert scale, Visual Analogue Scale (VAS; to assess a dyspareunia intensity) and SF-36 quality of life questionnaire.

The pain intensity in patients suffering from GSM-related dyspareunia was measured using the Visual Analogue Scale (VAS).

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 was assessed using non-parametric criteria. i.e., the Mann-Whitney U-test and the Kruskal-Wallis H-test.

To compare the study groups, the t-test was used 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 the 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 groups (p = 0.974). 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 groups (p = 0.418, p = 0.314, p = 0.935, respectively).

For objectification, the clinical manifestations of GSM in patients in the study cohort were scored using the D. Barlow scale. The baseline scores were as follows: 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 groups (p = 0.418, p = 0.314, p = 0.935, respectively).

The Female Sexuality Index (SSI) is one of the main measures. Baseline SSIs in groups I and II were 19.58 ± 6.88 and 21.4 ± 6.76, respectively. Following the laser remodeling procedure, there was a significant improvement in quality of sexual life of 1.33-fold (19.58 ± 6.88 versus 26.02 ± 4.81; p < 0.001) and 1.25-fold (21.4 ± 6.76 versus 26.76 ± 4.9; p < 0.001) after 3 months and 1.58-fold (19.58 ± 6.88 versus 30.98 ± 3.12; p < 0.001) and 1.46-fold (21.4 ± 6.76 versus 31.16 ± 3.3; p < 0.001) after 12 months in groups I and II, respectively. However, there were no statistically significant differences between the groups (p= 0.175, p= 0.435, p= 0.771, respectively).

The assessment of intensity of pain associated with GSM-related dyspareunia in patients in the study cohort is also important. It was carried out using the Visual Analogue Scale (VAS). The mean baseline algological scores were as follows: 4.44 ± 2.18 and 4.24 ± 2.08 in groups I and II, respectively. Following the laser remodeling procedure, patients in groups I and II experienced a significant decrease in pain intensity of 1.6-fold (4.44 ± 2.18 versus 2.76 ± 1.4; p < 0.001) and 1.75-fold (4.24 ± 2.08 versus 2.42 ± 1.26; p < 0.001) after 3 months and 4.83-fold (4.44 ± 2.18 versus 0.92 ± 0.75; p < 0.001) and 5.44-fold (4.24 ± 2.08 versus 0.78 ± 0.69; p < 0.001) after 12 months, respectively. However, there were no statistically significant differences between the groups (p = 0.625, p = 0.192, p = 0.327, respectively). The SF-36 questionnaire represents another extremely important tool to assess the quality of life in patients in the study cohort. The baseline scores were as follows: 48.18 ± 20.06 and 53.2 ± 21.1 in groups I and II, respectively. Following the laser remodeling procedure, there was a

significant increase in these scores of 1.35-fold (48.18 ± 20.06 versus 65.02 ± 16.45; p < 0.001) and 1.31-fold (53.2 ± 21.1 versus 69.64 ± 15.96; p < 0.001) after 3 months and 1.7-fold (48.18 ± 20.06 versus 81.78 ± 10.48; p < 0.001) and 1.59-fold (53.2 ± 21.1 versus 84.64 ± 9.78; p < 0.001) after 12 months, respectively. However, there were no statistically significant differences between the groups (p = 0.215, p = 0.148, p = 0.152, respectively). The 5-point Likert scale was used in all patients as an additional and specifying measure of the quality of life. Baseline scores in groups I and II were 2.82 ± 0.98 and 2.62 ± 0.87, respectively. Following the laser remodeling procedure, patients in groups I and II showed a significant decrease in these scores of 1.66-fold (2.82 ± 0.98 versus 1.7 ± 0.97; p < 0.001) and 1.76-fold (2.62 ± 0.87 versus 1.49 ± 0.84; p < 0.001) after 3 months and 4.03-fold (2.82 ± 0.98 versus 0.7 ± 0.54; p < 0.001) and 3.82-fold (2.62 ± 0.87 versus 0.685 ± 0.58; p < 0.001) after 12 months, respectively. However, there were no statistically significant differences between the groups (p = 0.267, p = 0.239, p = 0.893, respectively).

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. The condition associated with GSM symptoms affects a large number of women worldwide, namely 48% of perimenopausal subjects and 53.8% to 90% of postmenopausal individuals [9, 14]. However, in addition to the high prevalence of GSM, it is characterized as a gynecological problem with an extremely adverse impact on the quality of life, including the sexual function of patients in the study cohort. Thus, a large CLOSER study, which included 4100 postmenopausal women with verified GSM, demonstrated that the vast majority of women (62%) began to avoid sexual intercourse, 58% of women experienced a decrease in sexual intercourse frequency due to vulvovaginal atrophy, and 49% of women reported avoidance of intimacy with a partner [8,9].

Once a urogenital atrophy is successfully verified, the main task for the health care professional is to thoroughly stratify patients based on severity of the pathological condition in order to determine the most effective and appropriate treatment strategy [10]. Despite the fact that menopausal hormone therapy is considered the first-line treatment for vulvovaginal atrophy, alternative treatment options may be used in patients with mild GSM, which include laser remodeling of the vulvovaginal region. Moreover, laser remodeling is indicated in individuals with absolute contraindications to topical hormone therapy and considered to be the most promising and modern approach to the treatment of GSM by many authors. MonaLisa Touch CO2-based fractional lasers (DEKA) with a wavelength of 10600 nm are the most widely used devices due to their proven efficacy.

Remodeling of the vaginal mucosa is induced during tissue ablation at temperature of 42 degrees, which activates the processes of neocollagenogenesis, increased glycogen production, fibroblast proliferation, and increased production of local growth factors (VEGF-A), which in turn cumulatively lead to increased proliferation of cells of the stratified squamous epithelium and tightening of the vaginal walls [11,12]. Based on a large systematic review by Le C. et al. (2021), in addition to the above effects of the laser at a wavelength of 10600 nm, there is an increase in colonization of the mucous membrane with beneficial lactic acid bacteria and a shift of vaginal pH to the acidic side [12]. Therefore, it can be concluded that the use of this type of laser is associated with a lot of benefits and no adverse effects. However, currently there are no clear recommendations from the world scientific society on the use of laser technologies for the treatment of vulvovaginal atrophy. Despite this, there is a great number of large studies confirming the beneficial effects of this technology on the mucous membrane of the vulva and vagina [11, 12, 15].

Recently, Bretas T. L. B. et al. (2022) demonstrated a significant beneficial effect of fractional CO2 laser on the tissues of the vulva and vagina. The mean age of subjects in this study was 54.4 ± 4.5 years with the mean postmenopausal period of 7.6 ± 5.1 years. The results of the study showed a thickening of the general and surface layers of epitheliocytes and increase in indices of female sexual function and vaginal health following a course of the laser therapy [13].

In a double-blind, randomized, placebo-controlled study Jason Cruff and Salil Khandwala (2021) evaluated the effect of the fractional CO2 laser (MonaLisa Touch) on GSM. In this study, thirty postmenopausal women with symptoms of GSM received a treatment course consisting of 3 procedures using a fractional laser. The outcomes of the therapy after 6 months were assessed using a visual evaluation of the vaginal mucosa and vulva and various scales, such as: Visual Analogue Scale (VAS), modified Patient Global Impression of Improvement (PGI-I) and Female Sexual Function Index (FSFI). This study demonstrated a decrease in symptoms of GSM following the fractional laser therapy and no adverse effects. However, based on a comparative analysis the differences between two groups were not significant. This study had a significant limitation, namely insufficient proportion of sexually active patients. In light of this, the authors note that further studies are needed to more effectively evaluate this treatment option [14].

The findings from a double-blind, randomized, placebo-controlled study conducted by Salvatore S. et al. (2021), which included 58 postmenopausal women with dyspareunia and vaginal dryness, were as follows: in the study group, where the patients underwent a course of 3 procedures using the

MonaLisa Touch fractional CO2 laser, the rates of symptoms of vaginal dryness, dyspareunia and sexual dysfunction were significantly lower compared to the placebo group without laser treatment ($p < 0.005$) [15].

Based on the results of our open-label, independent, prospective, multicenter, 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

In summary, it can be concluded that the use of the SmartXide2 V2LR Monalisa Touch fractional CO2 laser (DEKA, Florence, Italy), regardless of the parameters of the selected ablation regimen in the treatment of GSM symptoms, has a beneficial effect on the quality of life and sexual function in patients with genitourinary syndrome of menopause.

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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