Vaginal health and quality of sexual life of postmenopausal women on hyaluronic acid and Biosaccharide Gum-1 vaginal gel

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Abstract

Background: To evaluate the efficacy of daily vaginal gel containing hyaluronic acid (HA) and Biosaccharide Gum-1 (BG-1) on vulvovaginal atrophy (VVA) and on sexual function and quality of life (QoL).

Methods: One hundred-four postmenopausal women with VVA were enrolled in the nonrandomized comparison cohort study. Of them, 50 women on HA/BG-1 participated in the study group and 54 women on lubricants/moisturizers on-demand as a control group.

The primary endpoint was the efficacy of the vaginal gel on VVA evaluated by the Vaginal Health Index (VHI) score. Secondary endpoints included sexual behavior by the self-administered female sexual function index (FSFI) questionnaire and quality of life (QoL) by the Short Form-36 questionnaire (SF-36).

Results: All symptoms of AVV improved after 12 weeks of treatment in women on HA/BG-1. The VMI, although improved at the 12-week follow-up compared to baseline, indicated a low estrogenic stimulation value. Sexual function improved significantly in women on HA/BG-1. Moreover, women reported a significant improvement in the somatic aspects of QoL. No benefits were obtained by the women in the study group.

Conclusions: Treatment with HA/BG-1 could be used in postmenopausal women who complain of vaginal dryness. The amelioration of VVA-related signs could improve sexual function and QoL.

Introduction

Postmenopausal women are likely to have vulvovaginal disorders due to the cessation of ovarian estrogenic activity[1]. Approximately 50% of postmenopausal women experience vulvovaginal atrophy (VVA) with moderate or severe symptoms affecting their quality of life and sexual function[2–4].

The discomforts most reported by women are dyspareunia, vulvovaginal burning, foul-smelling vaginal discharge, bleeding during intercourse, or dysuria[5], which are symptoms of genitourinary syndrome (GSM)[6].

Symptoms can be more disabling if menopause has been induced for medical reasons, such as following chemotherapy, anti-estrogen therapies, or oophorectomy[7]. Additionally, metabolic disease or reduced sexual intercourse are risk factors for VVA. Symptoms are strictly due to changes in trophism, microbiota, and vaginal pH[8].

Sexual function can have a dysfunctional reason, following dyspareunia, which not infrequently affects sexual desire. In fact, women suffering from dyspareunia could experience libido reduction[9].

Medical treatments are usually based on the administration of estrogen[10,11] or DEHA[12] by the vaginal route or on oral selective estrogen receptor modulators (SERMs)[13].

However, postmenopausal women do not always accept hormonal treatments, choosing natural approaches where possible[14]; the use of moisturizers and lubricants, frequently on demand, is widely adopted by women who are afraid of using hormonal treatments or who have contraindications to using them[15,16].

In this case, nonhormonal treatments via the vagina should usually be effective and well tolerated, and this depends not only on their composition but also on osmolarity and pH and on having a physiological appearance similar to that of natural vaginal secretions. Hyaluronic acid (HA) is a common component of nonhormonal aids because of its ability to repair the processes of vaginal atrophy and dystrophy and to allow sufficient vaginal hydration[17,18].

The aim of this nonrandomized comparison cohort study was to evaluate the efficacy of vaginal gel containing HA and Biosaccharide Gum-1 (BG-1) (Vidermina Intima Mucus ®, Istituto Ganassini SpA, Milan, Italy) in postmenopausal women with VVA (primary endpoint) and the effects on the vaginal maturation index (VMI), sexual function and quality of life (QoL) (secondary endpoints). HA is characterized by a high molecular weight that does not allow it to penetrate deeply into the vaginal epithelium. Therefore, it carries out a moisturizing and protective film action on the surface of the vaginal epithelium, reducing genital dryness. In fact, thanks to its ability to distribute itself on the surface, it forms a film that hinders the loss of trans-epidermal water. It also assists the repair processes of the vaginal mucosa in cases of atrophy and reduces symptoms such as itching and burning. These activities are supported by both an osmolarity of less than 380 mOsm/kg and a pH of 4.2, as recommended by the Advisory Note “Use and procurement of additional lubricants with male and female condoms: WHO/UNFPA/FHI360”[19]. BG-1 is a film-forming polysaccharide rich in L-fucose, D-galactose, and galacturonic acid. BG-1 stimulates the production of Sirtuin-1, an inhibitor of the synthesis of inflammatory mediators. In association with L-fucose, it inhibits neurogenic inflammation[20]. It gives the gel soothing and moisturizing properties. Other ingredients include gelling agents, preservatives, and water.

Methods

The study was conducted at the Menopause Service of the Gynecological Clinic, Department of General Surgery and Medical Surgical Specialties, University of Catania, Italy. The study protocol complies with the guidelines of the Declaration of Helsinki of 2013 and was approved by the Ethics Committee Catania 1, n. 84/2020/PO.

The study was carried out from May 2020 to July 2021. Each woman was informed in advance about the objectives of the study. Each woman was asked to read and sign the study's informed consent form; none of them received any monetary compensation.

Postmenopausal women for 1 year or women with amenorrhea for 6 months with menopausal values of estrogen and FHS, symptoms and signs of VVA and disorders of sexual function were invited to participate in the study.

Surgical or pharmacological postmenopausal women or women with abnormal vaginal bleeding; diagnosed with endometrial thickening ≥ 4 mm, by transvaginal ultrasound; who had been on hormonal treatment up to 3 months before enrollment; who had contraindications to the use of local treatments due to previous intolerance; or with a partner suffering from sexual dysfunction were excluded from the study.

One hundred four women gave consent to participate in the nonrandomized comparison cohort study. Of these, 50 were allowed to take part as a study group, and 54 refused the use of the daily vaginal gel, choosing to use lubricants/moisturizers on demand. The latter gave their consent to participate as a control group.

Instruments

The vaginal health index (VHI) was used for the objective investigation of vaginal hydration and secretions, the elasticity and appearance of the vaginal mucosa, and finally for the detection of vaginal pH[21]. Changes in vaginal pH greater than 5.0 have been associated with a decrease in serum estradiol[22]. Indeed, a pH of 5-5.49 could be indicative of mild atrophy, a pH of 5.5–6.49 of moderate atrophy, and a pH above 6.5 of severe atrophy in the absence of infection[23]. Each of these 5 items is evaluated by means of a scale from 1 (none) to 5 (excellent), and then the average of the scores is calculated. A value of ≤ 15 (= cut-off) is generally considered for the diagnosis of low vaginal health.

The vaginal maturation index (VMI) was used to quantify the parabasal, intermediate and superficial cells of the vaginal epithelium by means of vaginal cytological sampling with the subsequent calculation of the percentage of the cell type[24]. The VMI is obtained through the formula [1 (% superficial cells)] + [0.6 (% intermediate cells)] + 0.2% (parabasal cells)]. Values from 20 to 49 indicate low, 50 to 64 moderate, and 65 to 100 high estrogenic stimulation[25].

Sexual behavior was assessed using the self-administered female sexual function index (FSFI) validated in the Italian gynecological population of childbearing age[26]. The FSFI consists of six domains, namely, desire, arousal, lubrication, orgasm, satisfaction and dyspareunia, which are measured on a five-point Likert scale, ranging from 0 (no sexual activity) or 1 (never/very low) to 5 (always/very high). A score is calculated for each of the six domains, and the total score is obtained by adding all the elements. The total score ranges from 2 to 36. A value of ≤ 26.55 (= cutoff) is generally considered for the diagnosis of sexual dysfunction. In addition, to confirm sexual dysfunction, it is necessary for it to cause significant personal distress to the woman.

Therefore, the 12-item Female Sexual Distress Scale (FSDS) questionnaire was used, with a maximum score of 48. An FSDS score ≥ 15 corresponds to clinically significant distress[27]. In summary, women with

an FSFI score of ≤ 26.55 are considered to have sexual dysfunction if they have an FSDS score ≥ 15.

Quality of life (QoL) was assessed by the Short Form-36 questionnaire (SF-36)[28]. The questionnaire contains 36 questions that group four categories of somatic aspects [physical activity, physical role, somatic pain, and general health] and four mental aspects [vitality, social activity, emotional role, and mental health]. The women were asked to enter a score on a scale of 0 to 100 for each item that best matched their awareness. Subsequently, the sum of all the elements of each category was calculated. As a result, total somatic and mental health scores were obtained; higher scores indicate better QoL.

Each woman had a diary in which to note the frequency of sexual activity and any new event that they wanted to report.

Each questionnaire or instrument was used at enrollment (baseline) and at the 12th week of treatment (follow-up).

Treatment

Each woman in the study group was asked to self-administer 2 doses of 3 cm of vaginal gel, equivalent to 0.5 g, daily. In addition, women were asked to self-administer a total of 12 cm of gel, equivalent to 1 g, before intercourse. The control group consisted of women who were using lubricants or moisturizers on demand.

Statistical analysis

The ^{2} and ANOVA tests were used to compare the demographic and clinical data between the two groups at baseline, respectively. The difference was estimated with a 95% confidence interval (CI). Paired Student's t-test was used to compare the values obtained at baseline with those of the follow-up from the VHI, VMI, FSDS and SF-36 domains. For comparisons of the values obtained from the FSFI items between baseline and the follow-up, the nonparametric Wilcoxon rank-sum test with z values was used. Correlation analyses with Pearson's r coefficient were performed to examine the relationships between the VHI and FSFI scores. Scores are presented as the mean ± SD. The result was statistically significant when $p < 0.05$. Statistical analysis was carried out using the Primer of Biostatistics statistical computer package (Glantz SA, New York, USA: McGraw-Hill, Inc. 1997).

Results

Table 1 shows the demographic characteristics of the study group and control group at baseline. Women in both groups were used to using on-demand lubricants or moisturizers ($p = 0.51$).

After enrollment, 8 (16%) women in the study group were excluded from the statistical evaluation as they did not complete the study. However, 18 (33.3%) women in the control group dropped out of the study. Consequently, 42 (84%) and 36 (66.7%) women in the study and control groups, respectively, completed the study.

In the study group, 15 (35.7%) women performed a typical administration of the vaginal gel, discontinuing it on average once a week. The remaining 27 (64.3%) women performed perfect administration of the vaginal gel.

Intragroup vaginal health changes are shown in Fig. 1.

The study group had an improvement in the VHI from baseline to follow-up (8.6 ± 3.3 Vs 18.8 ± 2.3, $p < 0.0001$; +118.6% Vs baseline); in contrast, the control group did not obtain any benefit from on-demand administration (9.8 ± 3.2 Vs 11 ± 2.3, $p = 0.28$; +12.2% Vs baseline).

Table 2 shows the changes in each VHI item of both groups and the intergroup statistical analysis at baseline and at the 12-week follow-up.

Particularly, in the study group, vaginal secretion improves more evidently (+ 300%) than, in order, pH (+ 200%), hydration (+ 100%), the appearance of vaginal mucosa (+ 100%), and finally vaginal elasticity (+ 50%). The pH decreased from a value > 6 (severe atrophy) to a value between 5.1 and 5.5 (mild to moderate atrophy). The control group did not experience any benefit in each VHI item.

The VMI had a similar trend (Fig. 2). The women in the study group had an improvement in the total score (32.8 ± 3.1 Vs 47.3 ± 3.4, $p < 0.0001$; +44.2%); however, the score indicated low estrogenic stimulation. The control group underwent no VMI modification (33.6 ± 2.9 Vs 33.9 ± 3.2, $p < 0.41$).

Table 3 shows the VMI intergroup statistical analysis at baseline and at the 12-week follow-up. The study group had a significant reduction in basal and parabasal cells ($p < 0.0001$) and an improvement in intermediate and superficial cells ($p < 0.0001$) at the 12-week follow-up compared to baseline. Specifically, the percentage of parabasal cells was reduced by 50% and that of intermediate cells increased by 80.1% from baseline to the 12-week follow-up. Moreover, the percentage of superficial cells was 7.1 at follow-up compared to 0% at baseline. The control group did not have any benefit.

Figure 3 shows changes in women's sexual function and sexual distress levels at baseline and follow-up. The FSFI score in the study group, although it did not reach the cut-off (≤ 26.55), improved from 17.2 to 22.3 ($p < 0.001$), indicating an improvement of 29.6%.

The items that contributed to the improvement of the FSFI of the study group during the use of the vaginal gel were mainly lubrication ($p < 0.0001$), arousal ($p < 0.009$), dyspareunia ($p < 0.009$) and satisfaction ($p < 0.009$). The level of desire ($p < 0.2$) and orgasmic experience ($p < 0.1$), although improved, did not reach statistical significance (Table 4).

At the same time, the FSDS decreased from a dysfunctional value of 17.8 to a normal value of 13.7 ($p < 0.001$), indicating a 23% reduction. On the other hand, the control group did not have any change in FSFI ($p = 0.21$) or FSDS ($p = 0.83$) scores.

Moreover, the FSFI scores demonstrated a negative correlation with VHI values (r -0.99; $p < 0.004$).

Finally, Fig. 4 shows the QoL, investigated by the SF-36 questionnaire, that fundamentally improved from 57.5 to 65.6 ($p = 0.007$, + 14% Vs baseline) in aspects related to somatic health. The total mental health score in the study group improved to the limit of statistical significance [58.9 Vs 64.5 ($p = 0.05$); +9.5% Vs baseline]. The control group had no somatic health ($p = 0.89$) or mental health ($p = .45$) total score changes.

Each woman recorded her frequency of coital activity in the daily diary. The study group reported an increase from 1 ± 0.5 to 3 ± 0.7 sexual intercourse per month ($p < 0.001$). On the other hand, the control group had no increase in frequency (1 ± 0.7 to 1 ± 0.3, $p = 1$). No women reported adverse events during the administration of the vaginal gel.

Discussion

The current nonrandomized comparison cohort study aimed to measure the effectiveness of HA/BG-1 in a gel formulation administered vaginally to postmenopausal women with VVA. An improvement in both the primary endpoint - vulvovaginal symptoms and vaginal well-being - and the secondary endpoints - vaginal epithelial trophism, quality of sexual function, and QoL- were observed.

The symptoms of VVA showed benefits after 12 weeks of treatment in women using HA/BG-1 vaginal gel compared to the control group. In addition to an overall improvement in the VHI, secretion, pH, hydration, the appearance of the vaginal mucosa, and finally the elasticity - all objective indices - improved significantly.

With respect to the secondary endpoints, the VMI in the study group reached values showing no estrogen-dependent maturation of the vaginal epithelium. In fact, the maturation index, although improved at the 12-week follow-up compared to baseline, connoted a low estrogenic stimulation value [32.8 Vs 47.3 (< 50)]. This improvement, although significant, may depend, in order, on the effectiveness of the HA and the increased coital frequency (from 1 ± 0.5 to 3 ± 0.7 monthly); the latter in itself promotes an activation/stretching of the vaginal muscle epithelium layers with consequent neurovascular activation[29].

Sexual function improved significantly in the women on HA/BG-1 vaginal gel. However, the total score of the FSFI during treatment reached 22.3, compared to the baseline value of 17.2, remaining below the cut-off, which in the female population of childbearing age is ≤ 26.55 (25). In fact, to date, the FSFI cut-off in postmenopausal women has not been well defined, creating confusion in efficacy studies on sexual function. To validate the therapeutic benefit in postmenopausal women, great importance is given to the values of the sexual distress scores that were calculated by the FSDS. Usually, an improvement in sexual distress results in an improvement in sexual function, even when the FSFI score does not reach the cut-off, as was the case in the current study. With regard to the individual items of sexual function whose scores the FSFI measures, lubrication was the subjective aspect that improved more significantly than the other items. Therefore, it was possible to highlight an overall improvement in vaginal well-being, both

through the VHI - which allows for the measurement of the objective aspects of vaginal health - and through the FSFI - which defines the degree of subjective well-being of sexual health.

Simultaneously, pain syndrome decreased; the reduction in dyspareunia probably promoted an increase in coital frequency that was not due to an increase in sexual desire. Indeed, the level of sexual desire did not change significantly from baseline to follow-up. Interestingly, the reduction in pain syndrome could be due to the synergistic activity between HA trophic effects and BG-1 inhibition of the synthesis of inflammatory mediators and neurogenic inflammation.

The orgasmic experience was also reported to be unchanged, maintaining the characteristics of pretreatment. On the other hand, the arousal and the degree of satisfaction from the sexual experience improved significantly.

To strengthen the effectiveness of the treatment adopted, the women reported a significant improvement in the somatic aspects of QoL. However, although the mental health scores showed an improvement, the values barely reached statistical significance.

None of the benefits obtained by the women on treatment with HA/BG-1 vaginal gel were found in the control group, in which the participants adopted an on-demand regimen of vaginal lubricants or moisturizers.

Some authors obtained similar results to ours with regard to VHI scores and better VMI than us in women on 30 [days 30] or 12 weeks after vaginal HA administration[31]. However, we could not fully compare our results with those obtained by other authors, as only HA vaginal administration was used in their studies. Regardless, in these studies, the authors reported a moderate estrogenic stimulation index even after 30 days of treatment, meaning that HA had immediate effects on the vaginal epithelium, similar to estrogenic [effects30]. Moreover, it was not possible to compare our results to those obtained by some authors regarding FSFI and SF scores, as different analytical methods were used[30]. On the other hand, some authors investigated, by randomized studies, the effectiveness of a vaginal cream containing HA or conjugated estrogen on symptoms of vaginal atrophy and on VMI in postmenopausal women. They observed an improvement after 8 weeks of treatment. HA was found to be more effective than conjugated estrogen for dryness, VMI, and some scores of vaginal symptoms. The authors concluded that HA might be an appropriate alternative for women with medical contraindications or negative experiences in using hormonal treatments[32]. Other authors, by a randomized study, compared the effects of estradiol vaginal tablets with HA vaginal tablets and observed that both treatments improved vaginal symptoms and VMI after 8 weeks of usage, but the improvements were greater in women on estrogen than on HA[33].

In a more recent study, other authors reported similar results. In fact, they claimed that the symptoms of VVA improved in women either on estradiol vaginal or on HA, but the improvement of VMI was significantly higher in the hormonal group than in the nonhormonal group[34].

Finally, in a systematic review including five studies, the authors emphasized the lack of a consensus opinion[35]. In fact, three studies showed that although HA was effective in improving the symptoms of vaginal atrophy, the difference between vaginal HA and vaginal estrogen was not statistically significant[36–38].

Conclusions

Treatment with HA/BG-1 could have an excellent use in postmenopausal women who complain of vaginal dryness, in those who do not want to use hormonal treatments, and again in those who cannot use steroids, following hormone-dependent oncological events. However, first-line treatment of women with VVA consists of nonhormonal therapies such as lubricants and moisturizers, while hormonal therapy with local estrogen products is generally considered the gold standard. Vaginal dryness mainly affects postmenopausal women, even if some VVA symptoms could affect premenopausal women. It would therefore be necessary to identify premenopausal women at risk for VVA so that they could start treatment with vaginal HA. The association of HA and BG-1 synergistically improved the trophism and the inflammatory state of the vaginal epithelium. The investigation of the effects of HA/BG-1 versus HA alone on postmenopausal women with VVA might be the aim of a future randomized study.

Finally, the use of the device in women with AVV secondary to breast cancer treatments should be studied.

Declarations

The research protocol was approved by the institutional review board of the Ethics Committee of the University Hospital Polyclinic, Catania, Italy, registered n. 84/2020/PO.

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Author contributions

Conception and Design: All authors

Acquisition of Data: SC; SDP; GM; GC

Analysis and Interpretation of Data: SC; GP; GC

Drafting the Article: SC; EB; GC;

Revising It for Intellectual Content: All authors

Final approval of the completed article: All authors

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Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available to maintain the privacy of the participants but are available from the corresponding author upon reasonable request and with permission of the Ethics Committee.

Ethics approval and consent to participate

Ethics Committee Catania 1, University Hospital Polyclinic, Catania, Italy, approved the study protocol. It conformed to the ethical guidelines of the 2013 Helsinki Declaration. Informed consent was obtained from all the study participants.

The research protocol was approved by the institutional review board of the Ethics Committee of the University Hospital Polyclinic, Catania, Italy, registered n. 84/2020/PO.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Tables

Table 1. Demographic and clinical characteristics at baseline

	Study Group (n=50)	Control Group (n=54)	P
Mean Age (±SD)	55.6±4.2	54.9±4.1	0.39 (ANOVA)
BMI, kg/m^2 (±DS)	26.8±4.8	25.7±5.6	0.28 (ANOVA)
Age at menopause (years)	51.5±3.6	50.7±2.6	0.74 (ANOVA)
Years from menopause	5.3±1.9	5.6±1.4	0.35 (ANOVA)
Parity, n. (%)			(^{2} test)
One child	9 (18)	11 (20.3)	0.03
Two or more children	41 (82)	43 (79.6)	0.9
Smoking habit, n. (%)			(^{2} test)
Never smoked	36 (72)	38 (70.3)	0.88
Smoker	11 (22)	10 (18.5)	0.8
Ex smoker	3 (6)	6 (11.2)	0.09
Lubricants/Moisturizers, n. (%)			(^{2} test)
On demand	32 (64)	41 (75.9)	0.51
Hormonal treatment in the past, n. (%)	7 (14)	5 (9.3)	(^{2} test) 0.39
Systolic blood pressure (mmHg)	131.5±11.8	130.2±15.8	0.63 (ANOVA)
Diastolic blood pressure (mmHg)	78.9±8.2	81.6±7.8	0.08 (ANOVA)
Heart rate (x min)	68.7±11.2	67.9±10.1	0.7 (ANOVA)

Table 2. Intergroup statistical analysis of each vaginal health index (VHI) item at baseline and 12-week follow-up.

VHI Items	Baseline			12-month follow-up		*P**
	Study Group n.50	Control Group n.54	*P**	Study Group n.42	Control Group n.36	
Moisture	2±1.1	2.2±1.6	0.46 95% CI, -0.73 to 0.33	4±1.5	2.1±1.2	<0.001 95% CI, 1.20 to 2.59
Secretion	1±0.8	1.1±0.5	0.44 95% CI, -035 to 0.15	4±1.2	2.2±0.9	<0.001 95% CI, 0.94 to 2.65
Elasticity	2±1.2	1.9±1.3	0.68 95% CI, -0.38 to 0.58	3±1.1	1.6±1.1	<0.001 95% CI, 0.85 to 1.94
Appearance	2±0.5	1.8±1.2	0.27 95% CI, -0.16 to 0.56	4±1.6	1.5±1.1	<0.001 95% CI, 1.78 to 3.21
pH	1±1.2	1.1±0.7	0.60 95% CI, -0.47 to 0.27	3±1.4	1.2±0.5	<0.001 95% CI, 1.22 to 2.37

* two-sided t test; CI= Confidence Interval

Table 3 Intergroup statistical analysis of the vaginal maturation index (VMI) at baseline and at the 12-week follow-up.

VMI % Cells	Baseline			12-month follow-up		
	Study Group n.50	Control Group n.54	*P**	Study Group n.42	Control Group n.36	*P**
Basal	7.2±1.9	6.8±1.6	0.24 95% CI, -0.28 to 1.08	0.1±1.1	5.2±2.8	<0.0001 95% CI, -6.06 to -4.13
Parabasal	57.1±4.2	58.3±4.8	0.17 95% CI, -2.96 to 0.56	28.5±3.9	57.5±3.7	<0.0001 95% CI, -30.9 to -27.1
Intermediate	35.7±2.5	34.9±2.9	0.13 95% CI, -0.25 to 1.85	64.3±5.6	37.3±3.1	<0.0001 95% CI, 26.69 to 29.4
Superficial	0	0	1 95% CI, -0.18 to 1.18	7.1±1.6	0	<0.0001 95% CI, 6.38 to 7.81

* two-sided t test; CI= Confidence Interval

Table 4. Intragroup statistical analysis of sexual function investigated by the female sexual function index (FSFI)

FSFI Items	Baseline n.50	12-week follow-up n.42	*P*
Desire	2.9±1.1	3.2±1.3	p<0.2
Arousal	2.7±1.5	3.5±1.2	p<0.009
Lubrication	2.8±1.2	4.5±1.2	p<0.0001
Orgasm	2.9±1.5	3.4±1.3	p<0.1
Satisfaction	3.2±1.3	3.9±1.1	p<0.009
Dyspareunia	2.7±1.9	3.8±1.8	p<0.009

Figures

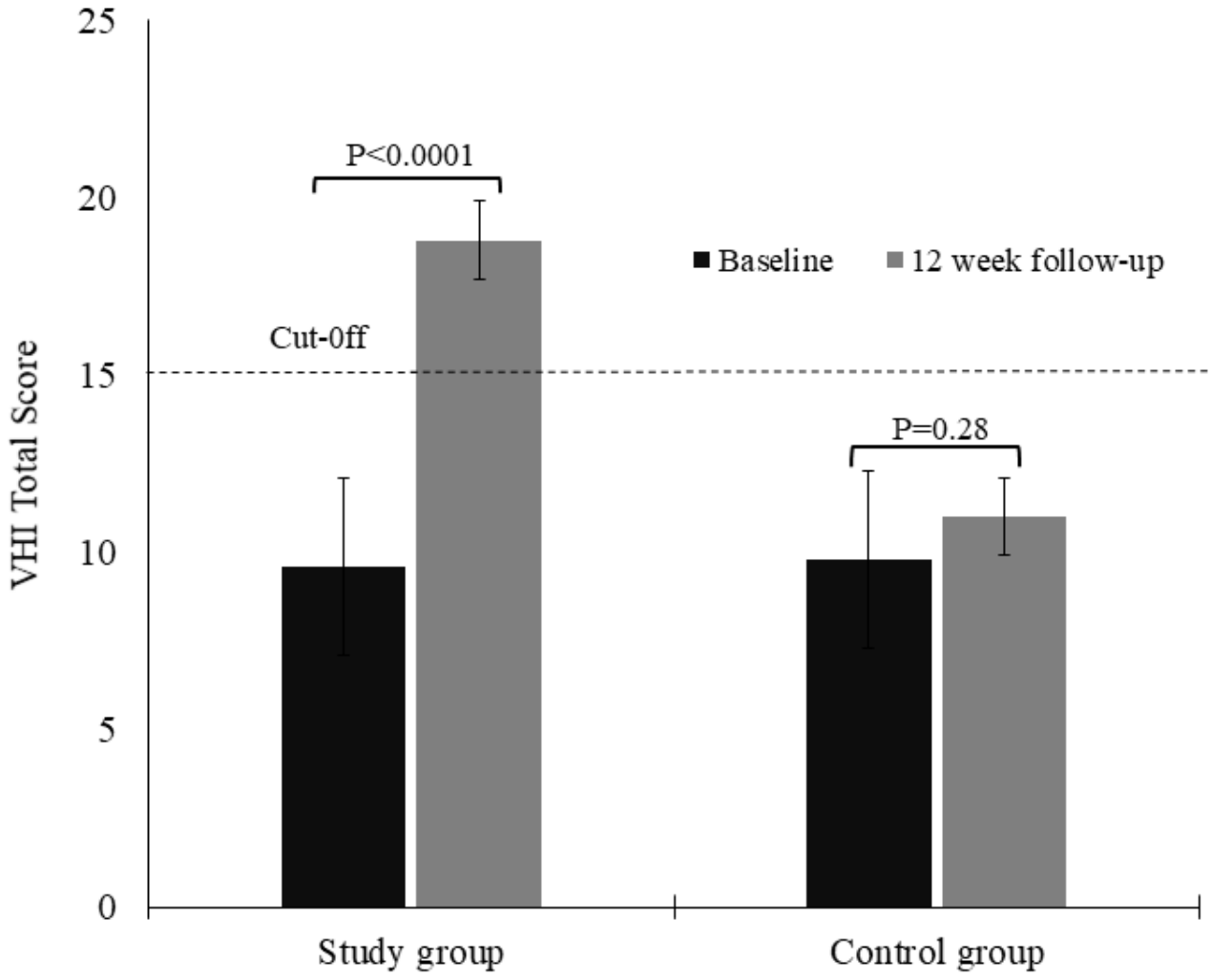

Figure 1

Intragroup comparison of vaginal health index (VHI) of postmenopausal women treated with hyaluronic acid (study group) or using on-demand lubricants or moisturizers (control group)

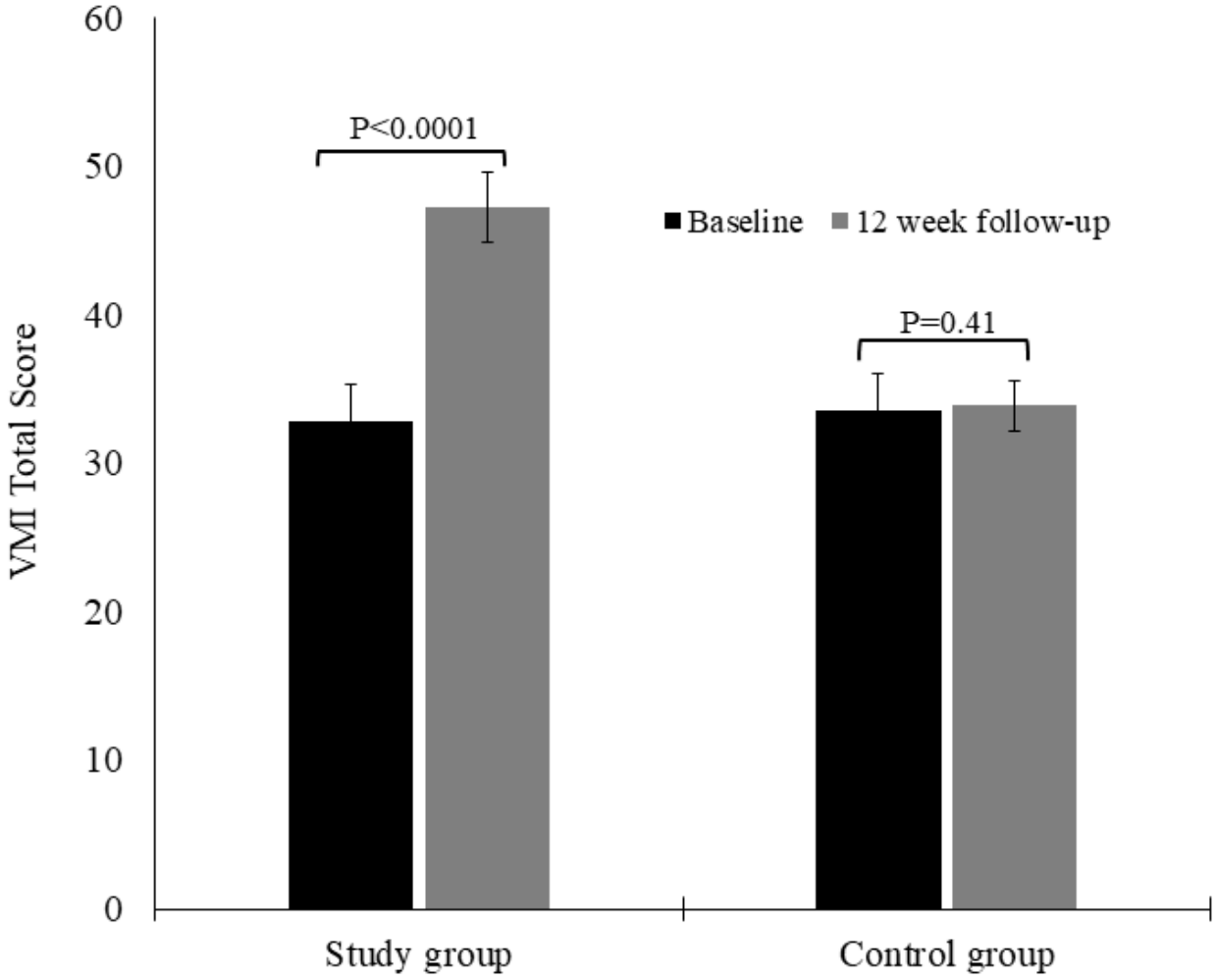

Figure 2

Intragroup comparison of vaginal maturation index (VMI) of postmenopausal women treated with hyaluronic acid (study group) or using on-demand lubricants or moisturizers (control group)

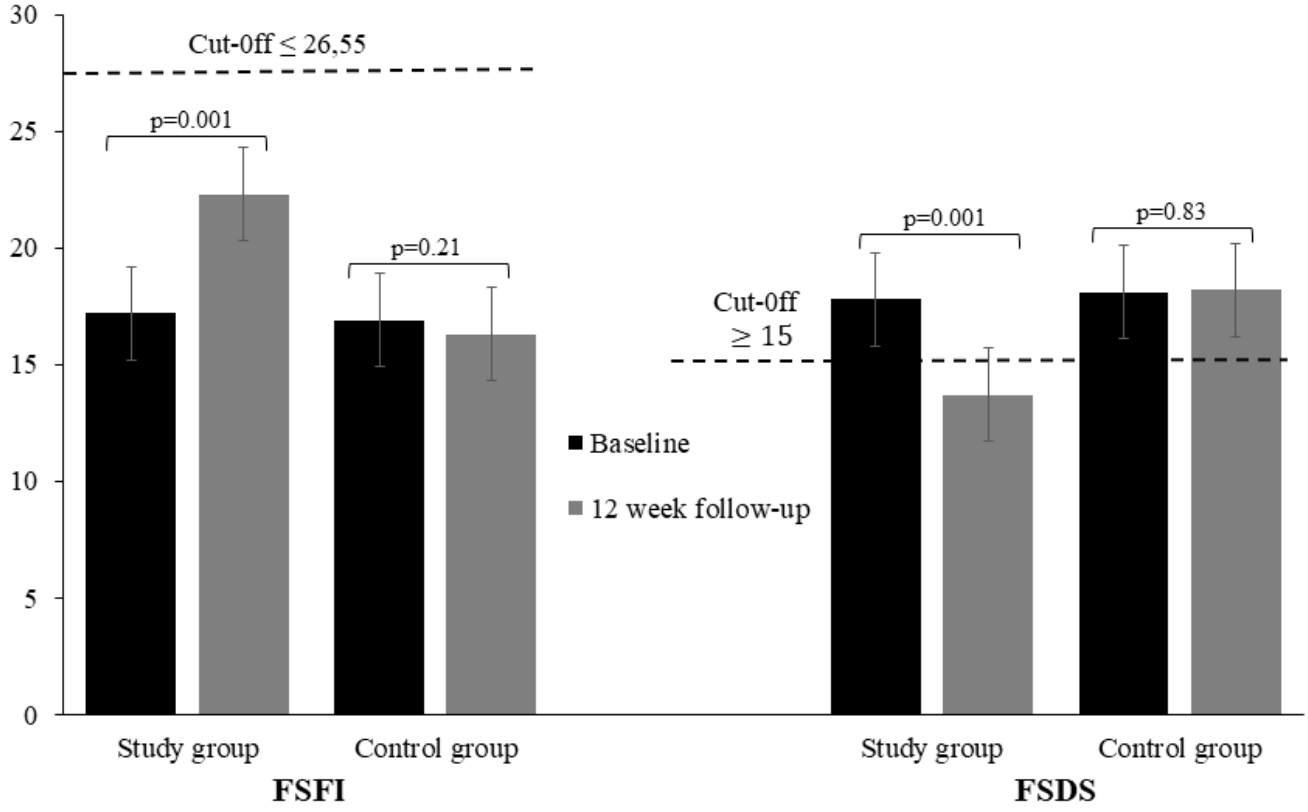

Figure 3

Intragroup comparison of sexual function assessed by the female sexual function index (FSFI) and sexual distress level measured by the female sexual distress scale (FSDS) of postmenopausal women treated with hyaluronic acid (study group) or using on-demand lubricants or moisturizers (control group)

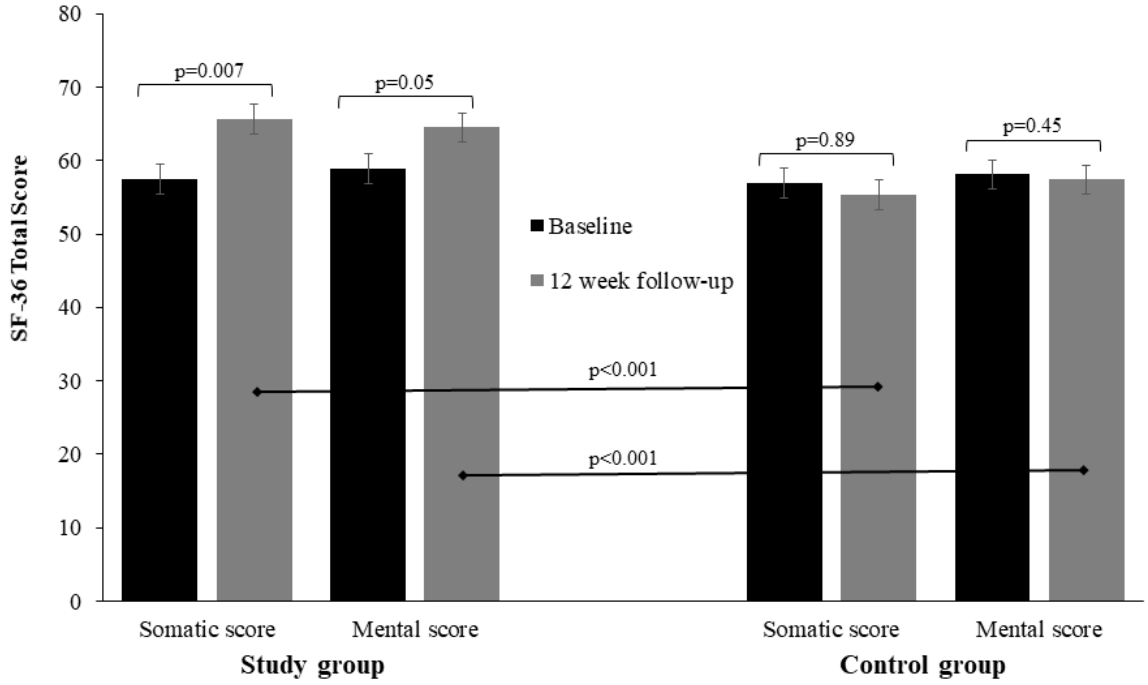

Figure 4

Intragroup and intergroup comparison of the quality of life investigated by the SF-36 questionnaire of postmenopausal women treated with hyaluronic acid (study group) or using on-demand lubricants or moisturizers (control group)