

# Quality of life and sexual function of naturally postmenopausal women on an ultralow-concentration estriol vaginal gel

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## Abstract

**Objective:** This study aims to evaluate the sexual function and quality of life (QoL) of naturally postmenopausal women affected by genitourinary syndrome of menopause who were treated with an ultralow-concentration estriol vaginal gel (0.005%).

**Methods:** Postmenopausal women with vulvovaginal atrophy symptoms and sexual disorders were enrolled in a case-control study. Women were treated with vaginal gel (containing 50 µg of estriol) daily for 3 weeks and then twice weekly up to 12 weeks. Determination of vaginal maturation index, evaluation of vaginal pH, and assessment of vaginal atrophy symptoms were carried out. QoL, sexual function, and distress were investigated using the Short Form 36, Female Sexual Function Index, and Female Sexual Distress Scale questionnaires. Changes between baseline and week 12 were assessed.

**Results:** Sixty-eight women were included in the study group, and 42 women were included in the control group. Women on estriol vaginal gel had a significant increase in vaginal maturation index and improvement of vaginal pH compared with baseline ( $P < 0.05$ ). Mean total Female Sexual Function Index score improved, and Female Sexual Distress Scale score decreased from baseline to follow-up. Results from the Short Form 36 questionnaire showed a significant improvement in the overall index of somatic aspects ( $P < 0.05$ ). The control group showed no changes from baseline evaluation ( $P = NS$ ).

**Conclusions:** Estriol vaginal gel (0.005%) therapy significantly improves the trophism of the vaginal mucosa and the sexual health and QoL of naturally postmenopausal women. These results confirm that low doses of vaginal estrogen must be considered as the first choice for the initial treatment of postmenopausal genitourinary symptoms.

**Key Words:** Estriol – Genitourinary syndrome – Postmenopausal – Quality of life – Sexual function – Vaginal dryness.

Postmenopausal women may experience genitourinary syndrome of menopause (GSM), whose etiology is attributable to reduced estrogen stimulation of specific tissue targets such as the vaginal epithelium and the trigone of the bladder.<sup>1</sup> Vulvovaginal atrophy (VVA) usually becomes clinically evident a few years after menopause, and vaginal dryness and dyspareunia are the most bothersome symptoms.<sup>2</sup> Furthermore, women may experience vaginal burning, itching, and irritation.<sup>3</sup> Changes in objective and subjective symptoms are present in 25% to 50% of all postmenopausal women.<sup>4</sup> In fact, cohort studies reported a 27% to 55% prevalence of VVA in postmenopausal women and estimated that such symptoms

persist in 10% to 25% of women receiving systemic hormone therapy.<sup>5,6</sup>

Endocrinological and biological postmenopausal changes contribute to development of female sexual dysfunction (FSD; including dyspareunia)<sup>7</sup> and worsening of quality of life (QoL).<sup>8</sup> Moreover, urinary symptoms are frequent in postmenopausal women and are intimately related to atrophy, which engages the whole genitourinary system; in fact, estrogen deficiency can be traced to irritative urinary symptoms such as frequency, nocturia, enuresis, and urge incontinence—all attributable to increased contact of sensitive nerve endings with urine caused by thinning of the bladder.<sup>9</sup>

Data from two large studies—VIVA (Vaginal Health: Insights, Views & Attitudes)<sup>10</sup> and REVIVE (REal Women's VIEWS of Treatment Options for Menopausal Vaginal Changes),<sup>11</sup> which were carried out by direct interviews with postmenopausal women—are extremely important to understanding the multidimensionality of this disorder, how it can influence relationships, and, more generally, how it impacts on QoL. Currently, the lowest local dose of estrogen for the shortest period may be prescribed to women experiencing vaginal symptoms.<sup>12</sup> In fact, a new ultralow-dose estriol vaginal gel formulation (0.005% estriol vaginal gel) that significantly enhances estriol

Received February 21, 2015; revised and accepted April 2, 2015.

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Funding/support: None.

Financial disclosure/conflicts of interest: None reported.

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delivery to vaginal tissue, compared with existing formulations, has been developed, thus allowing the use of much lower doses of estriol to treat vaginal atrophy. Moreover, estriol has lower estrogenic potency than estradiol (ranging from 1:10 to 1:100)<sup>13</sup> and greater relative affinity for estrogen receptor- $\beta$  than for estrogen receptor- $\alpha$ , thus minimizing extravaginal effects.<sup>14</sup>

The aim of the current study was to evaluate the QoL and sexual activity of postmenopausal women with VVA on a low-concentration estriol formulation (0.005% estriol vaginal gel) and the effects of treatment on the maturation of the vaginal epithelium.

## METHODS

The study was performed at the Menopause Service of the Department of General Surgical and Medical Surgical Specialties, School of Medicine, University of Catania (Catania, Italy).

All participants gave their written informed consent form before participation in the study, which was conducted in accordance with the Declaration of Helsinki and with the approval of the institutional review board of the department research committees.

One hundred twenty-one heterosexual women aged 48 to 61 years (mean [SD] age, 54.5 [8.2] y) who were living with a partner without sexual dysfunction, have had 2 years of amenorrhea attributable to natural postmenopause, and were affected by GSM received counselling on the benefits of using estriol vaginal gel. At enrollment, physical and gynecological examinations were performed by a gynecologist expert in endocrinology and menopausal gynecology. Moreover, medical, surgical, and medication history were assessed to ensure study eligibility. Women who were using medications or were affected by a long-term medical illness were excluded from the study. Women with a body mass index of 35 kg/m<sup>2</sup> or higher; with endometrial thickness of 4 mm or greater (measured by transvaginal ultrasound before study initiation) and/or abnormal uterine bleeding; with hormone-dependent malignancies; with a history of thromboembolic disease, liver disease, and/or hormone therapy use for less than 3 months; or who had received phytoestrogens within 1 month before the start of the study were excluded from the study. Finally, we excluded women who were living with a partner affected by a sexual disorder and women who had a conflict with their partner (based on sexual history interview).

Women with genital dryness; irritation/burning/itching of the vulva or vagina; decreased lubrication with sexual activity; discomfort or pain with sexual activity; postcoital bleeding; decreased arousal, orgasm, or desire; and/or dysuria were included in the study.

## Instruments

VVA symptoms, including vaginal dryness and dysuria, were evaluated. The severity of each symptom was self-assessed and rated on a four-point scale (0, *none*; 1, *mild*; 2, *moderate*; 3, *severe*). At baseline and end of treatment, participants were instructed to rate each of the VVA symptoms

as *not present*, *mild*, *moderate*, or *severe*. Change in severity was used to evaluate symptomatic improvement. To evaluate the effects of estriol vaginal gel on the vaginal epithelium, we used the vaginal maturation index (VMI). To calculate the VMI, we took vaginal smears by scraping the upper third of the vaginal wall with a spatula. Samples were fixed, stored, and sent to the Cytological Laboratory of the Institute of Pathological Anatomy for staining using the Papanicolaou technique, followed by analysis. All samples were evaluated by the same cytologist. The index quantifies the percentages of parabasal, intermediate, and superficial cells by using the formula:  $VMI = [1(\% \text{ superficial cells})] + [0.6(\% \text{ intermediate cells})] + [0.2(\% \text{ parabasal cells})]$ <sup>15</sup> (0%-49%, low estrogenic stimulation of the vaginal epithelium; 50%-64%, moderate estrogenic stimulation of the vaginal epithelium; 65%-100%, high estrogenic stimulation of the vaginal epithelium). In addition to the VMI, vaginal pH was measured by inserting a pH test strip into the upper wall of the vagina. Vaginal pH changes greater than 5.0 were associated with decreased serum estradiol and menopause.<sup>16</sup> In fact, a pH of 5 to 5.49 could be indicative of mild atrophy, a pH of 5.5 to 6.49 could be indicative of moderate atrophy, and a pH higher than 6.5 could be indicative of severe atrophy.<sup>17</sup>

The Short Form 36 (SF-36) questionnaire was used to assess QoL.<sup>18</sup> The questionnaire contains 36 questions grouped into four categories in somatic aspects (physical activity, 10 items; physical role, 4 items; bodily pain, 2 items; general health, 6 items) and four categories in mental aspects (vitality, 4 items; social activity, 2 items; emotional role, 3 items; mental health, 5 items). Women were instructed to place a mark for each item that best corresponded to their feelings (on a scale of 0-100; from the lowest to the highest score of a given category of QoL). Thereafter, the sum of all items of each category was determined. Mean values were calculated based on individual items within a given category. Consequently, eight scale scores were obtained, with higher scores indicating better functioning.

A sexual history interview was adopted to investigate the quality of sexual function of women and their partners. To define FSD, we used the revised definition and classification of the International Consensus Development Conference on FSD.<sup>19</sup> Sexual behavior was assessed using the self-administered Female Sexual Function Index (FSFI) validated in the Italian gynecological population.<sup>20</sup> The FSFI consists of six domains—desire (two items), arousal (four items), lubrication (four items), orgasm (three items), satisfaction (three items), and pain (three items)—answered on a five-point Likert scale (0, *no sexual activity*; 1, *never/very low*; 5, *always/very high*). A score is calculated for each of the six domains, and the total score is obtained by summing all of the items. Total score ranges from 2 to 36. A cutoff score of 26.55 or lower is usually accepted for diagnosing sexual dysfunction in women within a wide age range. Moreover, in diagnosing sexual dysfunction, an essential element is that the condition causes significant personal distress to the woman. Therefore, the Female Sexual Distress Scale (FSDS) was used.<sup>21</sup> The

FSDS consists of 12 items, and the maximal score is 48. An FSDS score of 15 or higher corresponds to clinically significant distress. Women with FSFI scores lower than 26.55 were considered to be affected by sexual dysfunction if they also had FSDS scores of 15 or greater.

Furthermore, women received a diary to record daily sexual events and adverse events during treatment. The diary was presented in months divided into days; women had to report daily vaginal gel administration, sexual activity, and adverse events in the boxes for each day, specifying the type of adverse event in a specific space.

After baseline evaluation, each enrolled woman was prescribed 1 g of vaginal gel (containing 50 µg of estriol) daily for 3 weeks and then twice weekly for a complete treatment cycle of 12 weeks. Women were invited to self-administer the gel at night by inserting the applicator deep into the vagina. All assessments were made at baseline and at the 12th week follow-up. Endometrial thickness was measured at baseline and end of study by the same sonographer-gynecologist at the outpatient menopause service, using transvaginal ultrasound (Voluson 730; GE Medical Systems Kretztechnik, Tiefenbach, Austria).

### Statistical analysis

Paired Student's *t* test was used to compare SF-36 domain scores, VMI, and vaginal pH values obtained at baseline with those obtained on follow-up. To compare FSFI values between baseline and follow-up, we used nonparametric Wilcoxon rank sum test with *z* values. The independent Student's *t* test was used to compare demographic and clinical data between the study group and the control group. We estimated the difference with 95% CI.

The statistical correlation of age with SF-36 score and FSFI score was calculated by Pearson's correlation. Scores are presented as mean (SD). The result was considered statistically significant when  $P < 0.05$ . Statistical analysis was carried out using the Primer of Biostatistics statistical computer package (Glantz SA, New York, NY).

## RESULTS

Among 121 enrolled white women who had requested examination/consultation at the Service of Menopause for their genitourinary symptoms, 42 refused estriol vaginal gel treatment and were invited to participate in the study as the control group; 79 women constituted the study group. Table 1 shows the demographic characteristics of both groups at baseline. There were no significant differences between the groups ( $P = \text{NS}$ ). However, based on the daily diary, 10 women (13.9%) in the study group discontinued therapy—mainly during the first week (4 women, 5.1%) and the second week (6 women, 7.6%)—because of vaginal itching and/or burning, and 1 woman (1.2%) discontinued (during the second week) because of bleeding from external hemorrhoids, which was not correlated to the use of the drug. Nevertheless, during the first 2 weeks, three women (3.6%) reported vaginal itching and six women (7.6%) reported vaginal itching and irritation without discontinuing treatment. Consequently, 68 participants were included in the analysis. In the control group, 6 women (14.3%) were lost to follow-up; therefore, 36 women were included in the analysis.

Figure 1 shows genitourinary symptoms before and after treatment. At baseline, 4 women (5%), 7 women (8.9%), and 68 women (86.1%) in the study group reported mild, moderate, and severe vaginal dryness, respectively. On the 12th week of follow-up, no woman reported moderate or severe vaginal dryness (−100%; Fig. 1), 61 women (89.7%) reported no symptoms, and 9 women (10.3%) reported mild vaginal dryness ( $P < 0.001$ ). Moreover, at baseline 2 women (2.5%), 4 women (5%), and 30 women (37.9%) were affected by mild, moderate, and severe dysuria, respectively. After 12 weeks of treatment, 31 women (86.1%) had no symptoms, whereas 5 women (13.9%) had mild dysuria ( $P < 0.01$ ); finally, moderate dysuria (−97.2%) and severe dysuria (−94.4%) improved ( $P < 0.001$ ). On the contrary, women in the control group had no change in VVA symptoms ( $P = \text{NS}$ ).

Figure 2 shows VMI changes before and after treatment. At baseline, the percentage of parabasal, intermediate, and

TABLE 1. Baseline demographic characteristics

Characteristic	Study group (n = 79)	Control group (n = 42)	<i>P</i>
Age, y			
Mean (SD)	53.4 (8.4)	55.4 (8.3)	0.21
Range	46-57	48-61	NS
Age at menopause, mean (SD), y	49 (4.7)	50.1 (3.5)	0.19
Body mass index, mean (SD), kg/m <sup>2</sup>	27.3 (4.1)	26.6 (3.1)	0.33
Parity, n (%)			NS
Nulliparous	6 (8.8)	4 (9.5)	
One or more children	62 (91.2)	38 (90.5)	
Cigarette smoking, n (%)			NS
Nonsmoker	49 (72.1)	30 (71.4)	
Current smoker	19 (27.9)	12 (28.6)	
Daily cigarettes, mean (SD)	13.2 (5.7)	12.2 (4.6)	0.32
Current coffee drinker, n (%)	62 (91.2)	42 (100)	
Daily cups of coffee, mean (SD)	3.4 (2.3)	3.7 (1.1)	0.42
Systolic blood pressure, mean (SD), mm Hg	135.5 (10.6)	132.4 (9.7)	0.11
Diastolic blood pressure, mean (SD), mm Hg	78.6 (10.8)	75.4 (9.5)	0.1
Heart rate, mean (SD), beats/min	66.7 (9.5)	67.9 (8.7)	0.49

NS, not significant.

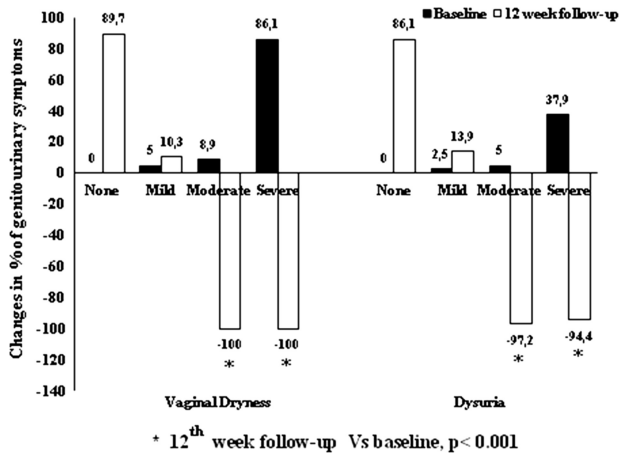


FIG. 1. Vaginal dryness and dysuria in postmenopausal women before and after 12 weeks of estriol vaginal gel treatment. \**P* < 0.001, 12th week follow-up versus baseline.

superficial cells was 19.3%, 75.4%, and 5.2%, respectively; on the 12th week of follow-up, the percentage of parabasal, intermediate, and superficial cells was 4.4%, 83.8%, and 11.7%, respectively. Consequently, the VMI improved from a baseline value of 42.9% ( $\leq 49\%$ , low estrogenic stimulation) to a 12th week follow-up value of 53.7% (50-64%, moderate estrogenic stimulation; *P* < 0.05). Figure 3 shows improvement of vaginal pH on the 12th week of follow-up (mean [SD], 4.3 [0.7]) compared with baseline (6.1 [0.7]) (*P* < 0.001). No change was observed in the control group (*P* = NS).

Figure 4 shows changes in QoL. On the 12th week of follow-up, women showed improvement in baseline values for somatic categories (*P* < 0.05). The somatic index improved from 63.11 (at baseline) to 74.26 (on follow-up; *P* < 0.05). No statistically significant change was observed for the mental categories (*P* = NS). Table 2 shows an intergroup statistical comparison analysis of QoL between baseline and 12th week follow-up values. At baseline, no difference was observed between groups (*P* = NS). On follow-up, intergroup difference was statistically significant for all SF-36 somatic categories (*P*  $\leq$  0.04) but not for mental categories (*P* = NS).

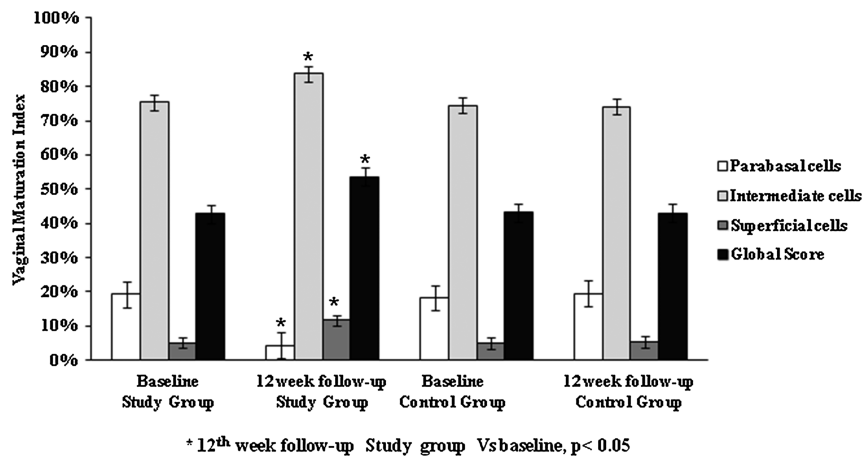


FIG. 2. Vaginal maturation index of postmenopausal women before and after 12 weeks of estriol vaginal gel treatment. \**P* < 0.05, 12th week follow-up versus baseline.

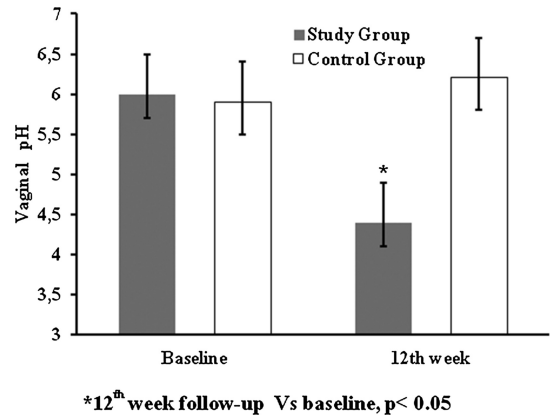


FIG. 3. Vaginal pH of postmenopausal women before and after 12 weeks of estriol vaginal gel treatment. \**P* < 0.05, 12th week follow-up versus baseline.

Table 3 shows statistical comparisons between baseline and 12th week follow-up FSFI scores. On follow-up, sexual desire did not change (*P* = NS); all of the other items improved from baseline scores (*P* < 0.05). At baseline, the total FSFI score was 16.3, and the FSDS score was 19.4; on follow-up, the FSFI and FSDS scores were 21.1 (*P* < 0.003) and 11.4 (*P* < 0.001), respectively. Table 4 shows an intergroup statistical comparison analysis of sexual function index and sexual distress scale between baseline and 12th week follow-up scores. At baseline, no difference was observed between the study group and the control group (*P* = NS). On the 12th week of follow-up, the study group showed improvement in all FSFI items (*P*  $\leq$  0.03), in the FSFI total score (*P* < 0.001), and in the FSDS score (*P* < 0.001)—except for the desire score (*P* = NS)—compared with the control group. Age did not correlate with SF-36 score (*r* = 0) and correlated negatively with FSFI score (*r* = -0.04), with the lowest values correlating with advancing age.

Upon checking of the diaries, 88 women (91.8%) correctly used the vaginal gel; on the other hand, 12 women (8.2%) successfully used the gel in the first 3 weeks but postponed its use by 1 day during twice-weekly administration.

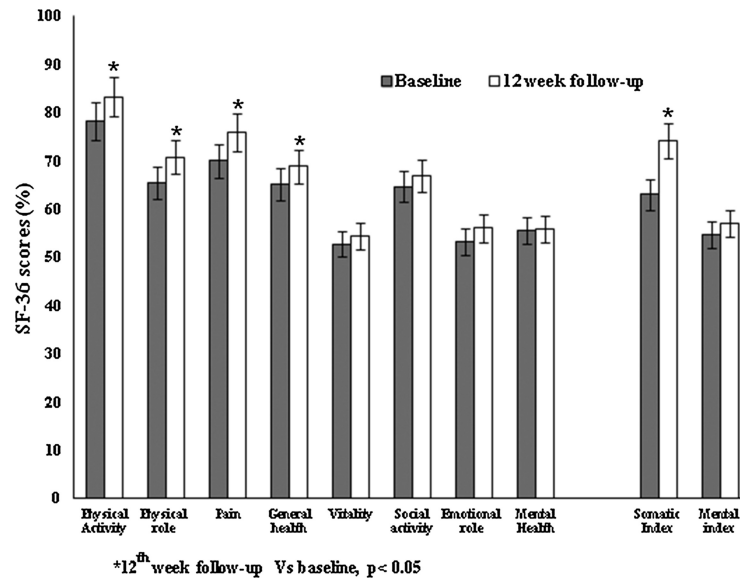


FIG. 4. Quality of life of postmenopausal women before and after 12 weeks of estriol vaginal gel treatment. \* $P < 0.05$ , 12th week follow-up versus baseline. SF-36, Short Form 36.

Endometrial thickness did not change from baseline to 12th week of follow-up among women on estriol (mean [SD], 1.9 [0.9] and 2.0 [1.1] mm, respectively;  $P = NS$ ) and among women in the control group (2.0 [0.8] and 2.0 [0.9] mm, respectively;  $P = NS$ ). Finally, no woman reported abnormal vaginal bleeding.

DISCUSSION

The current study investigated the effects of a low-concentration estriol vaginal gel on the QoL and sexual activity of postmenopausal women affected by GSM. The daily diary recorded sexual activity and adverse events. This instrument, although widely used, has some limitations mainly because of the subjective perception of the evaluation of adverse events and their intensity. On the other hand, it allows us to learn about certain events such as frequency of sexual activity.

To avoid duplication, we did not include VVA symptoms that were usually investigated (such as dyspareunia) because they had been studied by the FSFI and SF-36 questionnaires. After treatment, vaginal dryness and dysuria improved in 88.6% and 77.6% of women, respectively. Furthermore, cytological evaluation showed a significant decrease in parabasal cells and an increase in intermediate and superficial cells; a decrease in pH was simultaneously observed after 12 weeks on estriol vaginal gel. Both improvements were not observed in the control group. Other studies had previously obtained similar results, showing the superiority of estriol vaginal gel to placebo gel for changes in VMI, vaginal pH, and vaginal symptoms after 12 weeks of therapy.<sup>22</sup> An improvement in VMI and pH attributable to estriol could promote the proliferation of lactobacilli, lowering susceptibility to and frequency of urogenital infections. We did not investigate the vaginal microbiota before or after treatment. However, other

TABLE 2. Short Form 36 intergroup statistical comparison analysis between baseline and 12-week values among postmenopausal women on estriol vaginal gel

Short Form 36 scores	Baseline study group (n = 79) vs control group (n = 42) <sup>a</sup>		12-wk follow-up study group (n = 68) vs control group (n = 36) <sup>b</sup>	
	t (95% CI)	P	t (95% CI)	P
Physical activity	0.80 (-1.11 to -2.65)	NS	-6.71 (-7.12 to -3.87)	0.001
Physical role	-0.93 (-2.77 to -0.996)	NS	-8.04 (-7.23 to -4.36)	0.001
Bodily pain	1.26 (-0.49 to -2.25)	NS	-6.67 (-5.18 to -2.81)	0.001
General health	-1.52 (-2.43 to -0.31)	NS	-2.99 (-3.32 to -0.67)	0.003
Vitality	-0.87 (-2.31 to -0.89)	NS	-1.79 (-2.1 to -0.1)	NS
Mental health	1.65 (-0.26 to -2.94)	NS	-1.63 (-2.21 to -0.21)	NS
Social activity	0.74 (-0.94 to -2.08)	NS	-1.21 (-2.63 to -0.63)	NS
Emotional role	-0.37 (-2.51 to -1.71)	NS	-1.39 (-2.42 to -0.42)	NS
Somatic index	-0.88 (-3.06 to -1.16)	NS	9.61 (8.16 to -12.4)	0.001
Mental index	-0.74 (-2.91 to -1.31)	NS	-1.63 (-4.42 to -0.42)	NS

T values were determined by two-sided t test.

NS, not significant.

<sup>a</sup>df equals 119.

<sup>b</sup>df equals 102.

**TABLE 3.** FSFI and FSDS scores, at baseline and on 12-week follow-up, of postmenopausal women on estriol vaginal gel

FSFI items	Baseline (n = 79)	12-wk follow-up (n = 68)	P
Desire	2.7 (1.3)	2.9 (1)	NS
Arousal	2.3 (1.5)	3.2 (1.7)	0.009
Lubrication	2.3 (1.7)	3.2 (1.6)	0.009
Orgasm	2.8 (2)	3.9 (2)	0.008
Satisfaction	3.6 (1.3)	4.1 (1.4)	0.07
Dyspareunia	2.6 (1.9)	3.8 (1.7)	0.001
FSFI total score	16.3 (7.9)	21.1 (7.4)	0.003
FSDS score	19.4 (2.3)	11.4 (3.6)	0.001

Values are presented as mean (SD).

P values were determined by nonparametric Wilcoxon's rank sum test.

FSFI, Female Sexual Function Index; FSDS, Female Sexual Distress Scale; NS, not significant.

studies have shown that a small quantity of lactobacilli is associated with VVA<sup>23</sup> and that vaginal estrogen allows re-establishment of the vaginal microflora and improves epithelial differentiation and integrity in the urogenital tract.<sup>4</sup> Moreover, lactobacilli in the premenopausal vagina convert epithelial glycogen into lactic acid, which maintains vaginal pH between 3.5 and 4.5. In postmenopause, the vaginal epithelium thins; consequently, glycogen level falls, the population of lactobacilli decreases, and vaginal pH increases.<sup>24</sup> We did not measure serum estradiol levels neither before nor after treatment. In fact, we considered GSM as a mark of hypoestrogenism, confirmed by the VMI and vaginal pH. Studies have shown that a vaginal pH greater than 5.0 is associated with decreased serum estradiol and menopause.<sup>25</sup> Women on estriol experienced changes in QoL and sexual function, which were correlated with objective improvements in vaginal dryness and dyspareunia. The somatic aspects (but not the mental aspects), as measured by the SF-36 questionnaire, improved on the 12th week of follow-up with respect to baseline. Women probably need a longer treatment time before they could experience subjective changes, with their modifications depending on reassuring vaginal health. Furthermore, a complex interplay of individual factors may variably affect well-being.<sup>26</sup> In fact, personal, relationship, familial, and sociocultural aspects could influence the life of postmenopausal women. On the contrary, sexual activity modified all of the dimensions of the FSFI questionnaire, except for

the desire score. Postmenopausal women do have sexual desire, but hypoactive desire may depend on dyspareunia. Many women reported increased libido after using vaginal estrogens as a result of pain relief.<sup>27</sup> In our study, women did not show changes in desire score from baseline levels. On the contrary, arousal, lubrication, orgasmic experience, and satisfaction improved. In some instances, a more detailed psychosexual assessment may be required, including partner assessment, availability, and sexual functioning.<sup>28</sup> Improvement of dyspareunia attributable to the effects of estriol on VVA would be able to modify sexual life; in fact, better vaginal lubrication and reduction in vaginal pH would constitute a state of comfort that positively affects quality of sexual life.

A cutoff score of 26.55 or lower usually indicates a diagnosis of sexual dysfunction in women of premenopause age. The FSFI cutoff score is limited by its validation in postmenopausal women. In fact, postmenopausal women have significantly lower median FSFI full scale scores compared with fertile women.<sup>20</sup> In our current study, the mean (SD) FSFI score improved from 16.3 (7.9) to 21.1 (7.4)—that is, under the cutoff score. Therefore, women with FSFI scores lower than 26.55 were considered to be affected by sexual dysfunction when the condition simultaneously caused significant personal distress (ie, FSDS score  $\geq 15$ ). Women on estriol improved their state of distress from 19.4 to 11.4. Women with FSD are usually more likely to have VVA than women without FSD. In the Menopause Epidemiology Study, women had a fourfold greater risk of experiencing sexual dysfunction when VVA was present.<sup>29</sup>

The relationship between genitourinary symptoms and sexuality is complex, as psychologic factors, interpersonal relationships, and sociocultural influences could play a role in sexual function. Based on the aim of the current investigation, women with partners affected by sexual dysfunction were excluded from the study. Moreover, based on the sexual history interview, no psychosexual disorders other than dyspareunia and vaginal dryness were reported by women.

Genitourinary atrophy can significantly impair the QoL of postmenopausal women and may be underdiagnosed. Several therapies, including vaginal lubricants and moisturizers, vaginal

**TABLE 4.** Intergroup FSFI and FSDS statistical comparison analysis between baseline and 12-week follow-up scores among postmenopausal women on estriol vaginal gel

FSFI items	Baseline study group (n = 79) vs control group (n = 42) <sup>a</sup>		12-wk follow-up study group (n = 68) vs control group (n = 36) <sup>b</sup>	
	t (95% CI)	P	t (95% CI)	P
Desire	0.93 (-0.40 to 0.60)	NS	0.90 (-0.23 to -0.63)	NS
Arousal	-1.07 (-0.85 to -0.25)	NS	2.32 (0.11 to -1.48)	0.02
Lubrication	0.00 (-0.60 to -0.60)	NS	2.55 (0.20 to -1.59)	0.01
Orgasm	0.86 (-0.38 to 0.98)	NS	2.71 (0.29 to -1.90)	0.008
Satisfaction	0.37 (-0.43 to -0.63)	NS	2.13 (0.04 to -1.15)	0.03
Dyspareunia	0.28 (-0.60 to -0.80)	NS	3.35 (0.49 to -1.90)	0.001
FSFI total score	-0.13 (-3.12 to -2.73)	NS	3.27 (1.97 to -8.02)	0.001
FSDS score	-0.18 (-1.18 to -0.98)	NS	-11.54 (-9.25 to -6.54)	0.001

T values were determined by two-sided t test.

FSFI, Female Sexual Function Index; FSDS, Female Sexual Distress Scale; NS, not significant.

<sup>a</sup>df equals 118.

<sup>b</sup>df equals 102.

estrogen, and hormone and nonhormone systemic therapies, have demonstrated effectiveness depending on the severity of VVA symptoms.<sup>30</sup> Furthermore, it has been estimated that 40% of women receiving systemic estrogen do not obtain adequate relief from vaginal dryness.<sup>31</sup> Vaginal estrogen formulations are currently the first choice for the initial management of menopause-related vaginal atrophy symptoms.<sup>32</sup> Semisolid preparations for vaginal estrogen treatment include ointments, creams, and gels. A common feature of these preparations is the capability to adhere to surfaces for a therapeutic period.<sup>33</sup> Gels can present several advantages over other vaginal drug delivery systems, such as higher bioavailability, safety, and versatility.<sup>34</sup>

Choice and route of administration of therapy depend on the severity of symptoms, the effectiveness and safety of therapy for individual women, and women's preferences. On the other hand, when low-dose estrogen is administered locally to women with intact uterus, progestogen is not indicated.<sup>35</sup> In our study, endometrial thickness did not change from baseline to 12th week of follow-up among women on estriol. No women on estriol reported vaginal bleeding.

Interestingly, the use of vaginal estrogens with correct counseling encouraging women to have regular sexual activity has been found to be beneficial in preventing vaginal atrophy.<sup>36</sup> In fact, women who participate in regular sexual activity have reported fewer symptoms of vaginal atrophy and show less evidence of atrophy on vaginal examination compared with sexually inactive women.

Strengths of our study include the instruments used to measure the vaginal health and quality of sexual life of women affected by GSM. On the other hand, our study had some limitations, mainly the sample size and the lack of a placebo group. A study based on a large sample—including subgroups of surgically postmenopausal women with GSM—should be carried out.

## CONCLUSIONS

First, the estriol vaginal gel (0.005%) is effective in treating vaginal dryness and in improving VMI, vaginal pH, and dysuria among naturally postmenopausal women. Second, the consequent reduction of dyspareunia—thanks to ameliorated vaginal health—could improve sexual function and QoL.

**Acknowledgments:** We wish to thank the Scientific Bureau of the University of Catania for language support.

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