

The effect of conjugated estrogens vaginal cream and a combined vaginal cream of vitamins D and E in the treatment of genitourinary syndrome

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ABSTRACT

Background and Aim: Genitourinary syndrome occurs due to a decrease in ovarian hormones; this can have a significant negative impact on women's interpersonal relationships and sexual function. The present study aimed at comparing the therapeutic effect of conjugated estrogens vaginal cream and a combined vaginal cream of vitamins D and E in the treatment of genitourinary syndrome in postmenopausal women. **Methods:** This study was conducted as a double-blind randomized clinical trial (RCT). As many as 64 postmenopausal women suffering from genitourinary syndrome were randomly divided into study and control groups. The study group was treated with a combined vaginal cream of vitamins D and E, and the control group was treated with conjugated estrogens vaginal creams for 12 weeks. The patients were visited at the beginning of being admitted, the fourth week, the 12th week, and four weeks after the treatment and their information was recorded by checklists and a sexual function questionnaire. The data were finally analyzed by SPSS-25 at a significant level of 0.05. **Result:** At four visits, libido, orgasm, and frequency of sexual intercourse, as well as vaginal symptoms such as burning, itching, dryness, and dyspareunia were improved in both groups ($P < .05$). However, there was no difference between the two groups in terms of the frequency of severity of these symptoms during the four visits ($P > .05$). Investigating the female sexual function index showed that using vitamin D and E vaginal creams, like the use of conjugated estrogens vaginal creams, improves sexual function in women ($P < .01$). **Conclusion:** According to the results, it can be concluded that the combined vaginal cream of vitamins D and E is a suitable alternative to vaginal estrogens in relieving the symptoms of genitourinary syndrome in postmenopausal women, especially those who are unable to use hormone therapy or have little compatibility with this therapy.

Keywords: Combined vaginal cream of vitamins D and E, conjugated estrogens vaginal cream genitourinary syndrome, menopause

Introduction

Health of middle-aged women is one of the major concerns in public health throughout the world.^[1] Menopause is a natural and important stage in the life of every woman, which is characterized by infertility and amenorrhea in women.^[2] Nowadays, especially

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in developed countries, women spend one-third to one-half of their lives in menopause.^[3] Generally speaking, menopause in women occurs either naturally or due to surgery.^[4] Many women experience menopausal complications that affect their sexual function and quality of life.^[5,6]

Menopause is associated with a variety of problems such as hot flashes, sweating, depression, sleep disorders, sexual problems, urinary incontinence, and urinary atrophy as well as symptoms such as vaginal dryness, itching, dyspareunia, and bleeding,^[7] which is called genitourinary syndrome and occurs as a result of decreased ovarian hormones.^[8] It is the second most common complaint in postmenopausal women after hot flashes and is considered an annoying complication that is required to be diagnosed early, and its treatment should begin before atrophic changes become irreversible.^[9,10] The prevalence of genitourinary syndrome in postmenopausal women is over 50%.^[11] Moreover, only 56% of postmenopausal women with vulvovaginal symptoms reported their problem to healthcare providers^[12] According to studies conducted, 40–50% of women complain of dyspareunia due to decreased blood circulation and vaginal dryness.^[13,14] In addition, as many as 75% of postmenopausal women experience vaginal dryness.^[15] This can especially affect couples' sexual intimacy, their ability to have a romantic relationship, and their overall quality of life.^[16,17]

Researchers have indicated that sexual activity is essential for the health of old women.^[18] Sexual dysfunction is more common in postmenopausal women than in premenopausal women and occurs in 43% of postmenopausal women. Women suffering from genitourinary syndrome are four times more likely to suffer from sexual dysfunction than women with normal vaginal tissue.^[19] Suffering from sexual dysfunction occurs 3.84 times more in postmenopausal women with vulvovaginal atrophy (VVA), these complications include problems with libido, arousal, and orgasm.^[20] In an international study conducted on 4246 middle-aged women, the results indicated that 39% of postmenopausal women suffered from moderate-to-severe symptoms of vaginal atrophy and 42% had no information about treatments for vaginal atrophy.^[21]

According to the North American Menopause Society, vaginal moisturizing, continued sexual activity, and vaginal lubricants are the first-line treatment for genitourinary syndrome.^[22] In general, topical treatments to increase sexual pleasure at menopausal ages are divided into two main categories: topical hormone therapy (HT) and topical alternative therapies.^[23] First-line treatment in patients suffering from vulvovaginal atrophy is topical treatment of vaginal estrogen, leading to optimized mucosa, increased perfusion, stretched vagina and duct, and reduced sensory threshold, resulting in improved arousal and increased sexual pleasure.^[24]

Topical estrogens may reduce the symptoms and complications associated with genitourinary syndrome in postmenopausal women.^[25] However, there is no doubt that various hormones

in the body can cause problems such as irregular bleeding and thromboembolism. Moreover, the effects of topical estrogens on the endometrium after one year of using have not been investigated. The safety of using topical estrogen by people with a history of breast cancer is unknown as well.^[16] Moreover, based on different reports, topical products containing estradiol or conjugated estrogens are associated with side effects such as pelvic pain, vaginal irritation, vaginal discharge, vaginal bleeding, and breast sensitivity.^[26] As a result, not only patients but also physicians are interested in introducing alternative methods to introduce more effective methods and reduce its related side effects.^[27]

Using herbal medicines and other medical supplements has increased in many countries over the past decade. Herbal medicines, vaginal lubricants, and the use of vitamin E^[28] and vitamin D^[29] can be mentioned as non-hormonal methods.^[14] Vitamin E plays an important role in maintaining estrogen levels and improving menopausal symptoms such as hot flashes, sensitivities, insomnia, dizziness, palpitations, dyspareunia, and vaginal dryness.^[30] This vitamin also keeps arteries flexible and facilitates blood circulation, thereby increasing the metabolism of vaginal connective tissues, increasing the moisture and flexibility of the vaginal walls,^[25] and possibly reducing dyspareunia by healing atrophic ulcers.^[7] Vitamin E does not cause immediate changes in the low reproductive system and has little effect on repairing libido and reaching orgasm, and it seems that long-term use and high doses of vitamin E can relieve up to 50% of age-related vulvovaginal ulcers.^[7,23] Given the prevalence of genitourinary problems in postmenopausal women and its potential ability to cause disability in these people and its progressive trend in society, the aim of this study was to compare the therapeutic effect of conjugated estrogens with combined cream of vitamins E and D for the treatment of patients having the genitourinary syndrome.

Methods

Study design

This study was conducted as a double-blind randomized clinical trial (RCT). As many as 64 postmenopausal women with genitourinary syndrome who had referred to the clinics of Fatemeh Hospital and Omid Clinic in Hamedan in 2021 were randomly and voluntarily entered into the study and control groups. The study group was treated with combined vaginal creams of vitamins D and E and the control group was treated with conjugated estrogen vaginal creams for 12 weeks. The patients were visited the beginning of being admitted, the fourth week, the 12th week, and four weeks after treatment.

Data collection

The data were collected by a researcher-made checklist that included the required information on sexual desire (libido), orgasm satisfaction, itching, vaginal burning and dryness, burning and frequent urination, dyspareunia and urinary

incontinence, and the Female Sexual Function Index Questionnaire, The sexual function index was developed by Rosen *et al.* (2000)^[31] and was validated on a group of women with sexual arousal disorder. This questionnaire includes 19 questions, evaluating women's sexual function in six domains; 1. Desire; 2. Arousal; 3. Lubrication; 4. Orgasm; 5. Satisfaction; and 6. Sexual pain. The cutoff points for the total scale and subscales are as follows: total scale = 28; desire = 3.3; arousal = 3.4; lubrication = 3.4; orgasm = 3.4; satisfaction = 3.8; and sexual pain = 3.8. In other words, scores above the cutoff point indicate good function.

Sample size

The minimum required sample size was calculated by the following sample size formula based on a study by conducted by Sara Ziagham *et al.* in 2012.^[32] The mean (0.65) and standard deviation (0.875) combined score of vaginal symptoms at the end of week 8 in the group treated with vitamin E, and mean (0.15) and standard deviation (0.489) combined score of vaginal symptoms at the end of week 8 in the group treated with hyaluronic acid

$$Z_{1-\alpha/2} = 1.96$$

$$\text{Power} = 80\%$$

$$n = \frac{(Z_{1-\alpha/2} + Z_{1-\beta})^2 * (s_1^2 + s_2^2)}{(m_1 - m_2)^2}$$

$$n = \frac{(1.96 + 0.84)^2 + [0.875^2 + 0.489^2]}{(0.65 - 0.15)^2} = 31.50 = 32$$

Inclusion and exclusion criteria

In each of the two control or study groups, as many as 32 individuals and a total of 64 people were investigated. All postmenopausal women with genitourinary symptoms were entered into the study. Also, it was decided to exclude all individuals known or suspected of having endometrial or breast cancer, all individuals with abnormal vaginal bleeding or vaginal infections, all individuals with diabetes mellitus, CKD, arthritis, cardiovascular diseases, active hepatobiliary diseases, all individuals with vitamin D, E or vaginal estrogen allergy, individuals who had been on hormone therapy for the past 12 weeks, and individuals whose spouses suffered from sexual dysfunctions or were sexually inactive.

Participants were randomly divided into two groups (control group "conjugated estrogen vaginal cream" and study group "combined vaginal cream of vitamins D and E"). In this way, before the formation of the samples, a lottery was drawn for the numbers 1 to 64 and one of the two colors of the cream tubes was assigned to each number. Then, while referring to each participant, according to the order of referring to the clinic, one of the numbers 1 to 64 was assigned, and they received the intended drug based on the color of the tube.

Both groups were given the required explanations about the intervention and then informed consent forms were also obtained. In the intervention group, patients treated with a combined vaginal cream containing Vitamin D 1000 IU/dose and Vitamin E 100 IU/dose (2 g of the drug produced by a knowledge-based company called Alvand Pharmed Pars Company equivalent to half of a 4-g applicator) with daily consumption (once a day) for 2 weeks followed by three times a week for 10 weeks (a total of 2 50-g tubes were given to the patient). As for the control group, the patients treated with conjugated estrogen vaginal cream 0.625 gr/dose (1 gram of Estromarin produced by Abu Reihan Pharmaceutical Company, equivalent to a quarter of a 4-g applicator) with daily consumption (once a day) for 2 weeks and then three times a week for 10 weeks. This study was conducted as a double-blind one in which the creams prepared in colored tubes were provided to the patients in two different colors that neither the patients nor the researchers were aware of substances in the cream and only the analyst identified the groups while analyzing the obtained data.

Ethical approval

This study has been approved by the ethics committee of Hamedan University of Medical Sciences, Iran, with the code IR.UMSHA.REC.1399.220 and registered in the Iranian Clinical Trials System with the code IRCT20151123025202N10.

Statistical analysis

SPSS-25 was used to analyze the data, and a significant level of 5% was considered. In the descriptive statistics section, the mean and standard deviation were reported. Friedman and Chi-square tests were used for the abnormal data.

Results

The patients' basic information is provided in Table 1 and Figure 1. It can be stated that the participants are not significantly different and thus similar in terms of age, duration of menopause, and gravidity.

The results related to four weeks after treatment compared to those of first visit indicated that using a combined cream of vitamins D and E improves the number of sexual intercourses, libido, orgasm, and vaginal symptoms including itching, burning, and dryness of the vagina and dyspareunia ($P < .05$) However, at the visit four weeks after the end of the treatment period,

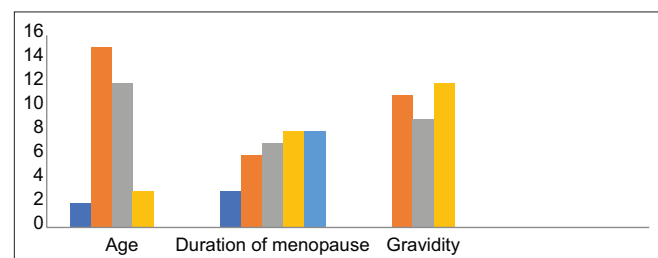


Figure 1: The patients' basic information

Table 1: Frequency distribution of basic information in postmenopausal women having genitourinary syndrome

Variable	Study group	Control group	P
Age			
Age	54.50±7.88	52.97±8.15	0.44*
35-45 years	2	3	0.51*
45-55 years	15	16	
55-65 years	12	11	
Older than 65 years	3	2	
Duration of menopause			
Less than one year	3	8	0.12*
1-3 years	6	8	
3-5 years	7	4	
5-10 years	8	11	
More than 10 years	8	3	0.88**
Gravidity			
Zero	0	0	
One	11	12	
Two	9	8	
Three and more	12	12	

*Independent Samples Test. **ANOVA Tests

the severity of urge and stress incontinence in patients treated with vitamin D and E combination cream did not significantly improve compared to that of the first visit ($P > 0.05$) [Table 2].

The results related to the study four weeks after the treatment compared to that of the first visit of patients showed that using conjugated estrogen improved the number of sexual intercourse, libido, and orgasm vaginal symptoms including itching, burning, and dryness of the vagina and dyspareunia ($P < 0.05$). However, the severity of urge and stress incontinence did not improve significantly compared to the severity of these symptoms at the first visit ($P > 0.05$) [Table 3].

Based on Chi-square statistical test and comparison of the therapeutic effects of the combined cream and conjugated estrogen cream, both creams used in this study showed significant effects in improving the frequency of sexual intercourses, the severity of libido, orgasm satisfaction, and improved urinary symptoms (severity, burning, itching, and frequency) ($P < 0.05$). In other words, using a combined cream of vitamin D and vitamin E, like the conjugated estrogen cream, can improve vaginal symptoms in postmenopausal women with genitourinary syndrome [Table 4].

In investigating female sexual function index based on the Independent Samples Test, using a combined vitamin D and E cream and estrogen cream [Table 5] improved all micro-factors of this index, including libido ($P < 0.001$), mental arousal (0.001), vaginal lubrication ($P < 0.001$), orgasm ($P < 0.001$), sexual satisfaction ($P < 0.001$), and pain ($P < 0.001$). Moreover, the total score of this index (FSFI) had a statistically significant improvement in users ($P < 0.001$). Comparing the two creams based on female sexual function index, the two drugs had similar effects in all regards [Table 6] and no special preference was seen

between the two groups based on the Independent Samples Test ($P > 0.05$).

Discussion

The results of the present study indicated that regular use of a combined vaginal cream of vitamins D and E and estrogen vaginal cream can improve libido, orgasm, and the frequency of sexual intercourses in postmenopausal women with genitourinary syndrome (GMS). In line with the results of the present study, Golmakani *et al.* (2018)^[33] and Porterfield *et al.* (2022)^[34] in their study stated that using vaginal suppositories of vitamin E and conjugated vaginal estrogen can improve libido, orgasm, and vaginal lubrication. Contrary to the results of the present study, in another study, Herold *et al.*^[35] administered a dose of 1,000 oral units of vitamin E daily over a 28-day period, yet they found no difference in the participants' sexual behavior or arousal. However, this different result may be due to the form of vitamin E.

Investigating vaginal symptoms including dryness, burning, itching, and dyspareunia in postmenopausal women with genitourinary syndrome in the present study showed that using combined vaginal cream of vitamins D and E can improve these symptoms, and it has similar effects as those of conjugated vaginal estrogen that have been for the related treatment. In line with the results of this study, Bygdeman *et al.*^[36] in their study found that using topical products containing vitamin D in these patients can significantly reduce vaginal dryness and burning and dyspareunia compared to the placebo group. Moreover, in the study conducted by Checa *et al.*^[29] it was indicated that using topical vitamin D can reduce vaginal dryness by 26% in these patients. In their study, Rad *et al.*^[37] concluded that regular and continuous use of vitamin D vaginal suppository can reduce symptoms such as vaginal dryness and pain and is effective in improving vaginal atrophy and reducing pH. In another study, McLAREN *et al.*^[38] stated that long-term use of vitamin E can improve dyspareunia and reduce atrophic ulcers in the lower reproductive system of postmenopausal women. Costantino *et al.* (2008)^[39] investigated the safety and efficacy of vaginal suppositories containing hyaluronic acid, vitamin A, and vitamin E in the treatment of vaginal atrophy; they reported a significant reduction in the symptoms of atrophic vaginitis, including vaginal dryness, itching, burning, dyspareunia, and inflammation.

Investigating the urinary symptoms such as dysuria, frequent urination, and urge and stress incontinence based on clinical history during the four visits in the present study indicated that using both combined vitamin D and E cream and conjugated estrogen cream did not have a significant effect on improving the urinary symptoms of patients with genitourinary syndrome. However, the reason for this can be the low incidence of these symptoms in patients from the very beginning of the study and the qualitative evaluation of symptoms.

The results indicated that the combined vitamin D and E cream used in the present study could be a suitable alternative

Table 2: Frequency distribution of clinical symptoms in postmenopausal women with genitourinary syndrome treated with combined cream of vitamins D and E (based on visit times)

Variable	Before the treatment	Week 4	Week 12	Four weeks after the treatment	P
Number of sexual intercourses					
Zero	18	12	7	7	0.004*
1 time	9	13	9	9	
1-3 times	5	6	15	11	
3-5 times	0	1	1	5	
5-10 times	0	0	0	0	
Severity of libido					
None	18	12	4	4	0.005*
Minor	8	12	14	14	
Mild	4	5	10	7	
Severe	2	3	4	7	
Orgasm satisfaction					
Little	18	13	10	10	0.003*
Minor	11	12	6	6	
Medium	3	5	13	8	
Much	0	2	3	8	
Severity of vaginal itching					
None	12	16	17	25	0.02*
Minor	8	9	12	5	
Mild	10	6	2	1	
Severe	2	1	1	1	
Severity of vaginal burning					
None	4	9	11	17	0.03*
Minor	12	11	12	11	
Mild	10	9	7	4	
Severe	6	3	2	0	
Severity of vaginal dryness					
None	2	8	8	10	0.04*
Minor	11	13	15	17	
Mild	17	9	8	5	
Severe	2	2	1	0	
Severity of dyspareunia					
None	10	15	20	26	0.01*
Minor	14	13	9	4	
Mild	6	2	2	2	
Severe	2	2	1	0	
Severity of dysuria					
None	21	26	26	28	0.38*
Minor	10	5	6	4	
Mild	1	1	0	0	
Severe	0	0	0	0	
Severity of frequent urination					
None	23	25	25	26	0.98*
Minor	6	4	5	4	
Mild	2	2	1	2	
Severe	1	1	1	0	
Severity of stress incontinence					
None	27	27	29	29	0.85*
Minor	1	2	2	2	
Mild	2	2	0	1	
Severe	2	1	1	0	
Severity of urge incontinence					

Contd...

Table 2: Contyd

Variable	Before the treatment	Week 4	Week 12	Four weeks after the treatment	P
None	25	26	27	28	0.29*
Minor	1	1	1	2	
Mild	2	4	4	2	
Severe	4	1	0	0	
Total	32	32	32	32	

*Friedman Test

Table 3: Frequency distribution of clinical symptoms in postmenopausal women with genitourinary syndrome treated with conjugated estrogen cream (based on visit times)

Variable	Before the treatment	Week 4	Week 12	Four weeks after the treatment	P
Number of sexual intercourses					
Zero	29	10	10	7	0.025*
1 time	8	16	10	11	
1-3 times	3	5	10	11	
3-5 times	1	1	2	3	
5-10 times	0	0	0	0	
Severity of libido					
None	13	4	1	1	0.001*
Minor	13	14	7	7	
Mild	6	13	18	11	
Severe	0	1	6	13	
Orgasm satisfaction					
Little	14	10	9	4	0.025*
Minor	12	12	8	7	
Medium	5	8	12	14	
Much	1	2	3	7	
Severity of vaginal itching					
None	9	15	18	20	0.04*
Minor	8	6	8	10	
Mild	8	6	3	2	
Severe	7	5	3	0	
Severity of vaginal burning					
None	8	11	13	21	0.01*
Minor	10	11	15	8	
Mild	12	9	4	3	
Severe	2	1	0	0	
Severity of vaginal dryness					
None	3	9	14	17	0.01*
Minor	13	12	11	12	
Mild	10	7	4	2	
Severe	6	4	3	1	
Severity of dyspareunia					
None	10	15	20	24	0.004*
Minor	12	15	11	8	
Mild	9	5	1	0	
Severe	1	0	0	0	
Severity of dysuria					
None	20	24	25	23	0.80*
Minor	9	5	4	7	
Mild	2	2	3	2	
Severe	1	1	0	0	
Severity of frequent urination					

Contd...

Table 3: Contd...

Variable	Before the treatment	Week 4	Week 12	Four weeks after the treatment	P
None	20	23	25	28	0.57*
Minor	8	5	4	2	
Mild	2	2	2	2	
Severe	2	2	1	0	
Severity of stress incontinence					
None	24	24	25	27	0.35*
Minor	1	2	2	3	
Mild	3	4	5	2	
Severe	4	2	0	0	
Severity of urge incontinence					
None	24	25	25	27	0.89*
Minor	2	3	3	3	
Mild	3	2	3	2	
Severe	3	2	1	0	
Total	32	32	32	32	

*Friedman Test

Table 4: Frequency distribution of clinical symptoms in postmenopausal women with genitourinary syndrome (based on the group)

Variable	Before the treatment			Four weeks after the treatment		
	Study	Control	P	Study	Control	P
Number of sexual intercourses						
Zero	18	20	0.64*	7	7	0.87*
1 time	9	8		9	11	
1-3 times	5	3		11	11	
3-5 times	0	1		5	3	
5-10 times	0	0		0	0	
Severity of libido						
None	18	13	0.22*	4	1	0.078*
Minor	8	13		14	7	
Mild	4	6		7	11	
Severe	2	0		7	13	
Orgasm satisfaction						
Little	18	14	0.56*	10	4	0.22*
Minor	11	12		6	7	
Medium	3	5		8	14	
Much	0	1		8	7	
Severity of vaginal itching						
None	12	9	0.33*	25	20	0.31*
Minor	8	8		5	10	
Mild	10	8		1	2	
Severe	2	7		1	0	
Severity of vaginal burning						
None	4	8	0.24*	17	21	0.17
Minor	12	10		11	8	
Mild	10	12		4	3	
Severe	6	2		0	0	
Severity of vaginal dryness						
None	2	3	0.49*	10	17	0.29*
Minor	11	13		17	12	
Mild	17	10		5	2	
Severe	2	6		0	1	
Severity of dyspareunia						

Contd...

Table 4: Contd...

Variable	Before the treatment			Four weeks after the treatment		
	Study	Control	P	Study	Control	P
None	10	10	0.78*	26	24	0.18*
Minor	14	12		4	8	
Mild	6	9		2	0	
Severe	2	1		0	0	
Severity of dysuria						
None	21	20	0.70	28	23	0.19*
Minor	10	9		4	7	
Mild	1	2		0	2	
Severe	0	1		0	0	
Severity of frequent urination						
None	23	20	0.84*	26	28	0.69*
Minor	6	8		4	2	
Mild	2	2		2	2	
Severe	1	2		0	0	
Severity of stress incontinence						
None	27	24	0.79*	29	27	0.73*
Minor	1	1		2	3	
Mild	2	3		1	2	
Severe	2	4		0	0	
Severity of urge incontinence						
None	25	24	0.87*	28	27	0.89*
Minor	1	2		2	3	
Mild	2	3		2	2	
Severe	4	3		0	0	
Total	32	32		32	32	

*Pearson Chi-Square Test

Table 5: Mean Sexual Function Index of Postmenopausal Women with Genitourinary Syndrome Treated with Combined Vitamin D and E Cream (based on Visit Times)

Variable	Before the treatment	Week 4	Week 12	Four weeks after the treatments	P
Combined vitamin D and E cream					
Desire	2.55±1.38	3.33±1.13	3.67±0.97	4.44±0.97	<0.001*
Arousal	1.57±1.37	1.75±1.36	2.28±1.43	3.21±1.57	<0.001*
Lubrication	1.87±1.49	2.09±1.45	2.74±1.39	3.38±1.52	<0.001*
Orgasm	1.82±1.44	2.16±1.38	2.87±1.37	4.06±1.38	<0.001*
Satisfaction	2.46±1.17	2.78±1.05	3.32±1.19	4.50±1.31	<0.001*
Sexual pain	1.96±1.30	2.24±1.21	2.78±1.35	3.79±1.49	<0.001*
FSFI (Female sexual function index)	12.25±3.82	14.37±3.51	17.69±3.61	23.40±3.58	<0.001*
Estrogen cream					
Desire	2.47±1.10	3.26±1.02	3.60±0.93	4.42±1.08	<0.001*
Arousal	1.44±1.42	1.66±1.39	2.20±1.38	3.20±1.43	<0.001*
Lubrication	2.12±1.50	2.35±1.44	2.81±1.42	3.66±1.39	<0.001*
Orgasm	2.42±1.72	2.70±1.55	3.41±1.33	4.26±1.04	<0.001*
Satisfaction	2.47±1.19	2.73±1.03	3.32±1.02	4.45±0.91	<0.001*
Sexual pain	2.34±1.38	2.48±1.28	2.95±1.36	3.62±1.67	0.002*
FSFI (Female sexual function index)	13.29±3.48	15.20±3.03	18.30±2.73	23.63±2.29	<0.001*

to conjugated estrogen in postmenopausal women with genitourinary syndrome. The findings of the present study also indicated that using a combined vaginal cream of vitamins D and E increased the indicators of desire, orgasm, and satisfaction, and reduced pain to a level higher than the cutoff point; this indicates the proper performance of this cream in these fields. In line with this study, in their study based on

improved ASFQ (Abbreviated Sexual Function Questionnaire) scores after the 12th week of treatment, Golmakani *et al.*^[33] concluded that vitamin E may be an alternative for vaginal estrogen in relieving the symptoms of vaginal atrophy in postmenopausal women, especially those who are unable to use the hormone therapy or have little compatibility with this therapy.

Table 6: Mean sexual function index of postmenopausal women with genitourinary syndrome (based on each group)

Variable	Before the treatment			Four weeks after the treatment		
	Study	Control	P	Study	Control	P
Sexual function index						
Desire	2.55±1.38	2.47±1.10	0.81	4.44±0.97	4.42±1.08	0.94
Arousal	1.57±1.37	1.44±1.42	0.70	3.21±1.57	3.20±1.43	0.98
Lubrication	1.87±1.49	2.12±1.50	0.50	3.38±1.52	3.66±1.39	0.44
Orgasm	1.82±1.44	2.42±1.72	0.13	4.06±1.38	4.26±1.04	0.51
Satisfaction	2.46±1.17	2.47±1.19	0.96	4.50±1.31	4.45±0.91	0.86
Sexual pain	1.96±1.30	2.34±1.38	0.27	3.80±1.49	3.62±1.67	0.67
FSFI	12.25±3.82	13.29±3.48	0.26	23.40±3.58	23.63±2.29	0.75

*Independent Samples Test

One of the limitations of this study was the diversity in the safety and physiology of the participants as well as their mental state; this can undoubtedly affect the sexual symptoms and response to treatment. In addition, due to poor patient compliance, we were unable to obtain biopsies to confirm our clinical diagnosis. Another limitation of the study was our failure to investigate the effects of vitamin D and E combined creams in people who are prohibited from using estrogen (such as people with endometrial or breast cancers and people with abnormal vaginal bleeding).

Conclusion

Based on the results, it can be concluded that the combined vaginal cream of vitamins D and E is a suitable alternative to vaginal estrogen in relieving the symptoms of genitourinary syndrome in postmenopausal women, especially those who are unable to use hormone therapy or have little adaptation with this therapy.

Key points

The combined vaginal cream of vitamins D and E is a suitable alternative to vaginal estrogens in relieving the symptoms of genitourinary syndrome in postmenopausal women, especially those who are unable to use hormone therapy or have little compatibility with this therapy

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given his consent for his clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity.

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Conflicts of interest

There are no conflicts of interest.

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