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THE EFFECTS OF LOCAL ESTROGEN WITH OR WITHOUT LOCAL TESTOSTERONE ON VULVOVAGINAL AND SEXUAL DYSFUNCTION IN POSTMENOPAUSAL WOMEN: A COMPARATIVE STUDY

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ABSTRACT

Background: The purpose/ aim of this research was to examine the effects of topical estrogen alone or in combination with topical testosterone on urogenital and sexual health in postmenopausal women who are suffering distressing symptoms due to urogenital atrophy caused by decreasing levels of estrogen.

Methodology: this study was conducted in Hayatabad Medical Complex, for a 12-week trial, 81 postmenopausal women with urogenital atrophy and sexual dysfunction were randomly assigned to one of three groups. One group received local estrogen cream, another received a mixture of local estrogen and testosterone cream, while a control group was given nonhormonal lubricant.

The study focused on examining changes in "urogenital and sexuality scores", as well as health of vaginal h indicators such as the vaginal health index and vaginal maturation index (VMI), both at the commencement of therapy and after week 12. This study aims to assess the effectiveness of various treatments in relieving symptoms and improving overall vaginal health in postmenopausal women.

Results: In all four research measures, following 12 weeks of treatment, significant improvements were found, which were strongly connected to reductions in urogenital atrophy and sexual dysfunction complaints in both study groups when compared to the control group. The group two receiving combination estrogen and testosterone therapy exhibited the greatest improvement in sexuality scores. Importantly, no side effects were there.

Conclusion: In conclusion, usage of topical Estrogen, whether used alone or in combination with androgens, proves highly effective in alleviating symptoms of urogenital atrophy and enhancing sexual function in symptomatic postmenopausal women.

Keywords: Local Estrogen Sexual Dysfunction, Postmenopausal, Urogenital atrophy

INTRODUCTION:

Menopause is a critical era in a woman's life marked by the permanent end of menstruation as ovarian activity declines. This hormonal shift causes urogenital aging, a complicated process that affects the, genital tract, pelvic floor, and lower urinary system in women with postmenopausal due to reduced estrogen levels. Symptoms include "urine frequency, dysuria, urgency, vaginal dryness, urinary tract infections, recurrent, burning, itching, discharge, and dyspareunia". Affected women also experience a reduction in "libido, sexual desire, and receptivity, the frequency of sexual thoughts and fantasies, and sexual responsiveness" (1).

According to research, between 50 and 60 percent of postmenopausal women report urogenital and sexual dysfunction symptoms (2).

Exogenous estrogen replacement therapy can typically ease these symptoms. Estrogen therapy has been reported to improve "vaginal maturation index (VMI), lower vaginal pH levels, and reverse vaginal atrophy by stimulating vaginal epithelial revascularization" Given current debate over the of systemic hormone long-term use replacement therapy, for short-term was increasing demand, side-effect-free ways to treating "vulvovaginal atrophy and sexual dysfunction" (3).

Intravaginally administered local estrogen has been shown to be successful in postmenopausal women "as a short-term therapy in lowering urogenital atrophy symptoms and enhancing sexual performance" Furthermore, adding "testosterone to estrogen therapy has been reported to increase sexual function" even more, i-e increasing strength levels, improving general sexuality , and augmenting libido (4, 5).

Thus, the purpose was to explore effect of local Estrogen, either alone/ combined with local Testosterone, on "urogenital and sexual health outcomes in postmenopausal women".

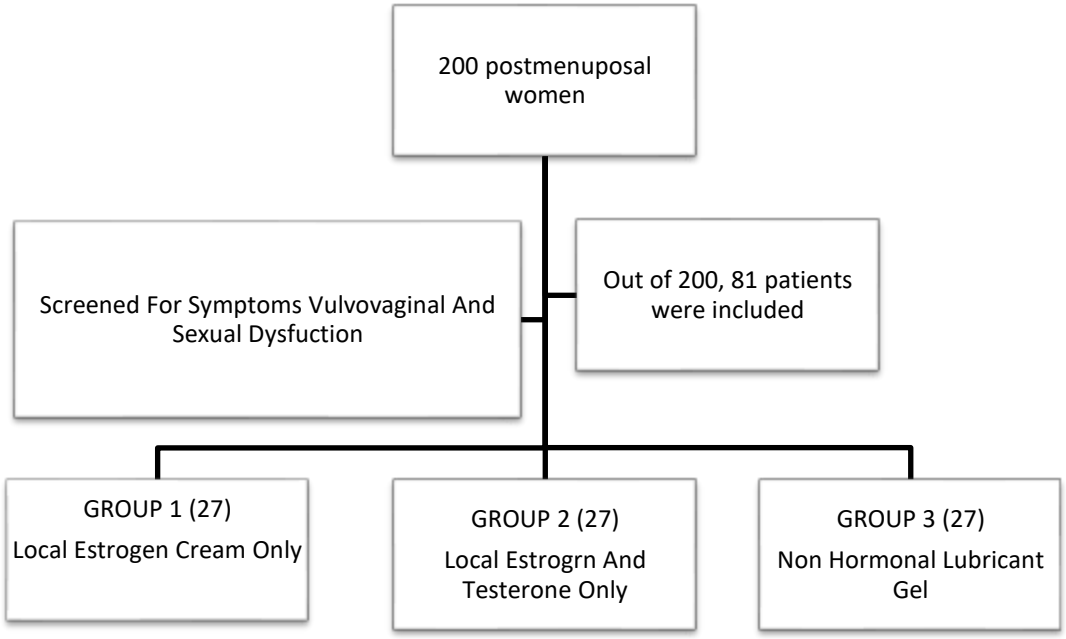
METHODOLOGY:

Study design & setting: The study design was prospective which was placed at Hayatabad Medical Complex, involving 200 "postmenopausal women screened for symptoms of urogenital and sexual dysfunction" Out of which 81 symptomatic women meeting specific inclusion criteria were included after providing written informed consent.

Inclusion and exclusion criteria:

Postmenopausal women aged range from (40-65 years) with signs of "urogenital and sexual dysfunction". They had experienced "spontaneous amenorrhea at least 12 months prior to screening or surgical menopause at least 6 weeks prior" Urogenital symptoms like vaginal atrophy, vulvitis, urethritis, dyspareunia, recurrent urinary tract infections, and urinary incontinence. Sexual dysfunction includes disorders causing distress such as sexual pain disorder, problems with sexual desire, arousal, or orgasm. While the exclusion criteria excluded the women with contraindications to hormone replacement therapy or using any hormonal product within 6 weeks of screening.

Selected patients: The eighty one women be situated randomly distributed into each 27 3 groups:



The "group 1 received local Premarin cream daily for weeks 2" monitored by weekly application twice for 10 week . the Group II received the same Premarin cream regimen as Group 1 plus 2% testosterone cream (1 mg testosterone in petroleum base) twice weekly for 10 weeks. And group 3 or control group given nonhormonal lubricant gel daily for 2 weeks, followed by twice weekly application for 10 weeks. Participants reassessed at weeks 4 and 12, evaluating sexuality scores and urogenital, HEALTH OF VAGINA indices and hormone levels. Side effects were monitored closely. Statistical analysis was performed using SPSS software.

The assessment was done as follow, Urogenital Score, Based on a four-point scale assessing symptoms like vaginal dryness, dyspareunia, and urinary issues. Sexuality Score was evaluated using the Short Personal Experiences Questionnaire, focusing on satisfaction, orgasm, desire intensity, sexual life classification, arousal frequency, sexual activity, and fantasies. "The Vaginal Health Index Scores vaginal moisture, elasticity, pH, and epithelial integrity on a scale of 1 (poor) to 5 (best)" The Vaginal Maturation Index (VMI) indicates estrogenic effects on the vaginal wall, calculated from superficial and intermediate cell percentages. Overall, this study aimed to determine the efficacy of local estrogen alone or combined with testosterone in improving "urogenital and sexual health in postmenopausal women" offering a potential short-term treatment option free from systemic HRT concerns.

RESULTS:

At the start of therapy (Table 1), all study parameters in study groups 1 and 2, as well as in the control group, showed comparability. During the study, there was a significant decrease in symptoms of urogenital observed in Group I (60%), Group II (64%), and Group III (27%). The improvement in urogenital symptoms differed significantly between the GROUPS I AND II and GROUP 3. The enhancement observed in group I and II was equal (Table 2).

In the group 1 that was local estrogen, overall 44% "improvement in sexuality scores, the group II local estrogen and Testosterone" there was a substantial 149% improvement. The GroupIII showed improvement a modest 20% in scores of sexuality (Table 2). All three groups showed statistically significant changes, the group III with "local estrogen and testosterone" demonstrated the greatest beneficial effect compared to GROUP I and II.

"The vaginal health index a measure of vaginal epithelial atrophy" showed a significant improvement in research groups one and two, with improvements of 46.5% and 54%, respectively.

Table 2 these improvements were significantly higher than the 21% improvement observed in the GROUP III.

Vaginal maturation index increased by 17%, 18% in Group i and ii, respectively, was higher than the 4.5% increase observed in th group III (Table 2).

Table 1: Initial Comparative Study Parameters in Group I, Group II, and the Control Group

Parameter	**GROUP I (N=27)**	**GROUP II (N=27)**	**GROUP III (N=27)**	**P Value**
Age(YEARS)	54.36 ± 9.64	53.56 ± 6.80	53.80 ± 7.77	0.6
BMI	25.80 ± 2.56	26.06 ± 2.60	25.70 ± 2.52	0.07
Parity	4.98 ± 2.15	5.04 ± 2.16	5.00 ± 2.18	0.6
Time since menopause	9.24 ± 3.47	9.32 ± 3.52	9.18 ± 3.42	0.08
Urogenital score	9.96 ± 3.98	8.68 ± 4.29	8.84 ± 4.05	0.09
Sexuality score	6.44 ± 3.51	6.52 ± 3.41	7.12 ± 3.53	0.06
Vaginal health index	15.32 ± 4.52	15.44 ± 3.61	15.52 ± 4.32	0.7
Vaginal maturation index	48.30 ± 7.26	47.94 ± 8.16	48.98 ± 7.69	0.08

In table 1 Values are presented as mean ± standard deviation. The P value indicates the statistical significance of the differences between groups. A P value suggests no significant difference.

Table 2: Comparative impact of local estrogen, estrogen with testosterone, and non-hormonal gel on vulvovaginal health and sexual dysfunction

Parameter	Group I (n=27)	Group II (n=27)	Group III (n=27)	P
score Urogenital				
week 0	9.87 ± 3.09	8.98 ± 4.65	8.65 ± 3.98	Non-significant
weeks 12	5.31 ± 3.76	4.98 ± 3.88	7.87 ± 3.98	0.02
Mean	60.7	64.3	26.9	
score Sexuality				
weeks 0	6.86 ± 3.87	6.89 ± 3.67	6.98 ± 3.09	Non-significant
weeks 12	8.87 ± 3.36	12.87 ± 4.98	7.45 ± 3.90	0.03
Mean	44.4	149.3	20.6	
VHI				
weeks 0	15.77 ± 4.98	15.89 ± 3.98	15.87 ± 4.45	Non-significant
weeks 12	20.34 ± 4.66	22.45 ± 3.78	17.84 ± 4.59	0.03
Mean	46.5	53.9	20.9	
VMI				
weeks 0	48.15 ± 7.12	47.67 ± 8.45	48.98 ± 7.87	Non-significant
weeks 12	54.56 ± 7.45	55.66 ± 7.32	49.45 ± 7.45	0.01
Mean	17	18.3	4.5	

TABLE II shows values are presented as mean ± standard deviation. "Non-significant" suggests no significant difference. "P value <0.05 indicates a statistically significant difference.*

The study (Table 3) assessed the safety profile of local estrogen and testosterone therapy by examining serum estradiol and testosterone levels, endometrial thickness, and changes in the serum lipid profile. “Serum estradiol levels increased by about 68% in Group 1 and 71% in Group 2 but remained within the postmenopausal range after 12 weeks no significant change in estradiol levels was noted in the local lubricant group”

In Table 3, levels of testosterone were detected in the group i (local estrogen) where levels decreased significantly, reflecting the natural decline in levels of endogenous testosterone over time in postmenopausal women. In contrast, the combination therapy group showed a significant increase

in testosterone levels (approximately 156%), although these values also remained within the range of postmenopausal.
The typical range for serum-free testosterone is 0.4–2.5 pg/mL for people aged 41–60 years and 0.2–2 pg/mL for those aged 61–80 years.

Table III Comparative impact of local estrogen, estrogen plus testosterone, and non-hormonal gel on serum estradiol levels (pg/ml), serum-free testosterone levels (pg/ml), and endometrial thickness

Parameter	**Group I (n=27)**	**Group II (n=27)**	**Group III (n=27)**
Serum estradiol			
weeks 0	29.23 ± 17.65	36.44 ± 23.65	27.33 ± 11.64
weeks 12	47.66 ± 20.64	60.23 ± 31.65	29.32 ± 8.4
Mean change %	68***	71***	8.4*
Serum free testosterone			
weeks 0	0.675 ± 0.66	0.76 ± 0.12	0.55± 0.23
weeks 12	0.675 ± 0.66	1.76 ± 1.33	0.34 ± 0.56
Mean change %	2.1*	156***	12**
Endometrial thickness			
weeks 0	4.54 ± 2.23	4.34 ± 2.67	4.23 ± 2.24
weeks 12	4.87 ± 2.65	4.32 ± 2.23	4.23 ± 2.65
Mean change	4.54*		

Table III shows values are presented as mean ± standard deviation. "*", "**", "***" indicate levels of statistical significance.*

In this study, endometrial thickness remained unchanged after 12 weeks of therapy in all groups.
Local estrogen therapy did not significantly alter total cholesterol, LDL, or apolipoprotein-a levels ($P > 0.05$) after 3 months. However, it notably decreased serum triglycerides and VLDL levels, while increasing HDL levels significantly ($P < 0.05$). Similar trends were observed in the control group. Total cholesterol and LDL levels showed no significant changes over the 12-week period, but HDL and apolipoprotein-a levels increased significantly (Table 4).
Local hormone therapy had no significant adverse effects. In the local estrogen group, 6 out of 27 women reported increased vaginal discharge. Among those receiving combination therapy (27 women), 5 reported increased vaginal discharge and 3 experienced burning micturition. No adverse effects were reported in the local non-hormonal lubricant gel group. Local testosterone therapy did not induce acne, hirsutism, weight gain, or voice changes. Both local estrogen and combined estrogen plus testosterone therapies were well tolerated by postmenopausal women, with good compliance.

Table 4: Comparative effect of local estrogen, estrogen and testosterone, and non-hormonal lubricant gel on serum lipid profile

Variable	Group	Week 0	Week 12	Mean change	P
Serum cholesterol	1	198.64 ± 36.17	195.24 ± 34.73	3.92	0.01
	2	166.80 ± 24.89	164.80 ± 23.31	3.41	0.03
	3	172.44 ± 33.07	172.84 ± 33.84	2.0	0.04
Serum triglycerides	1	147.80 ± 44.38	136.52 ± 32.30	9.9	0.02
	2	113.36 ± 26.67	105.48 ± 21.46	9.27	0.03
	3	123.52 ± 42.02	109.84 ± 31.52	13.4	0.04
Serum LDL	1	127.80 ± 36.15	122.04 ± 34.41	6.7	0.04
	2	106.00 ± 23.68	| 100.81 ± 25.12	7.1	0.02
	3	111.85 ± 28.59	111.49 ± 31.52	2.5	0.05
Serum VLDL	1	33.11 ± 10.48	30.97 ± 8.08	9.5	0.04

	2	26.30 ± 6.91	24.87 ± 5.84	8.6	0.03
	3	28.30 ± 10.00	25.56 ± 7.91	13.4	0.04
Serum HDL	1	43.08 ± 11.17	48.44 ± 9.99	15.2	0.02
	2	40.48 ± 9.28	45.36 ± 10.05	14.8	0.04
	3	38.24 ± 10.31	43.04 ± 11.11	15.4	0.02
Serum apolipoproteina	1	137.89 ± 16.07	135.50 ± 16.86	3.9	0.01
	2	129.56 ± 15.41	| 138.12 ± 16.48	8.9	0.03
	3	132.72 ± 17.66	135.56 ± 16.02	4.4	0.02

Table 4 shows the values are presented as mean ± standard deviation. It was statistical significance.

DISCUSSION:

Estrogen deficiency has a major negative influence on women's quality of life after menopause, resulting in urogenital atrophy and related symptoms such as urinary tract infections and sexual dysfunction (6, 7). The recommended treatment strategy for vulvovaginal atrophy is vaginal estrogen therapy for women who are predominantly suffering urogenital symptoms and do not have additional menopausal symptoms. In addition to reducing urogenital symptoms, local estrogen treatment increases libido, arousal, and sexual desire. In comparison to estrogen alone, adding testosterone to estrogen therapy increases libido, energy, and sexual satisfaction (8).

Intravaginal conjugated equine estrogen cream significantly reduced urogenital symptoms and nearly 100% of patients reported satisfaction in a trial involving Thai women (8). Another randomised double-blind placebo research found that 51.9% of patients found local estrogen to be effective in reducing their subjective vaginal atrophy symptoms, while the placebo group only saw improvements of 15.5% and 41.4% ($P < 0.01$) (9). Nevertheless, nothing is known about the impact of localized testosterone and estrogen cream combination on urogenital symptoms. “Excellent and quick improvement in vaginal dryness” was shown in a double-blind, randomized study with both estrogen-only and estrogen + oral testosterone groups, with no discernible differences between them (10).

In a randomized trial evaluating the effects of estrogen alone versus estrogen with testosterone on symptoms related to sexuality, Davis et al. discovered that both groups had higher scores on measures of sexuality. Statistical significance indicates that the combination therapy group showed more improvements in sexuality than the estrogen alone group (11). Comparably, compared to “the estrogen-only group, the estrogen plus testosterone group saw higher increases in sexual interest, desire frequency, and sexual responsiveness in a study involving 218 postmenopausal women aged 40–65” (12). In a second double-blind randomized trial, libido and sexual activity significantly improved when oral testosterone combined with estrogen was compared to estrogen therapy alone and placebo (13).

Significant advantages of estrogen therapy were demonstrated by another study, which found that the vaginal dryness index improved by 67% with local estrogen compared to 28% with local lubrication gel (14). Nonetheless, there were no appreciable variations in vaginal health metrics between the local estrogen and estrogen plus testosterone groups (15).

In investigations, local estrogen therapy increased blood estradiol levels slightly but significantly; placebo groups did not see similar increases (16). Clinically significant differences in serum biochemistry values “between the estrogen and placebo groups were not observed in studies utilizing low-dose conjugated estrogens for atrophic vaginitis” (17). Although there is a lack of safety information on “topical testosterone cream and its impact on serum lipid profiles, Watts discovered in one trial that combination estrogen and testosterone therapy” reduced HDL levels but had no effect on LDL or blood pressure.

It is safe to utilize local estrogen in this way, as previous research has consistently demonstrated no discernible variations in endometrial thickness.This summary emphasizes how local estrogen

therapy helps postmenopausal women's urogenital health and quality of life; advantages are amplified when paired with testosterone.

CONCLUSION:

Local estrogen administered intravaginally is an effective short-term therapy for relieving urogenital atrophy symptoms and improving sexual function in postmenopausal women. For those experiencing inadequate symptom control with estrogen alone or primarily reporting “decreased sexual drive and satisfaction post-menopause, combined local estrogen and androgen therapy may be considered”It's important to note that testosterone therapy can lead to side effects such as “hirsutism, acne, weight gain, voice changes, and clitoromegaly, which is an irreversible consequence of excessive testosterone therapy” Women with breast or uterine cancer, cardiovascular disease, or liver disease should avoid testosterone therapy. This conclusion highlights the benefits of local estrogen therapy while underscoring the need for cautious consideration of combined therapies and careful monitoring of potential risks.

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