

Research Article

Efficacy of Intravaginal Estrogen (Estrinol) in Medical Management of Genitourinary Syndrome of Menopause in an Indian Asian Female

Tanudeep Kaur^{1*}, Kumari Anukriti², Jai Bhagwan Sharma³, Kavita Pandey⁴, Rajesh Kumari⁵

¹Department of Urogynecology, AIIMS, New Delhi, India

²Senior Resident, AIIMS, New Delhi, India

³Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India

⁴Gynaecologist and Obstetrician Doctor, New Delhi, India

⁵Department of Obstetrics and Gynecology, Safdarjung Hospital and VMMC, New Delhi, India

***Corresponding Author:** Tanudeep Kaur, Department of Urogynecology, AIIMS, New Delhi, India, E-mail: tanibedi@gmail.com

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Abstract

Background: As high as 60% of postmenopausal women suffer from atrophic urogenital symptoms called as Genitourinary Syndrome of Menopause (GSM), due to declining ovarian function. It causes moderate to severe bothersomeness. Effectiveness of locally applied estrogen over 12 weeks improves their general and sexual quality of life (QOL).

Aims: We aimed to measure the most bothersome of the

various symptoms (MBS), and Female sexual dysfunction (FSD) on a validated Female Sexual Function Index (FSFI) scale and their self reported severity improvement over 12 weeks.

Material and methods: A prospective cohort study of 100 menopausal women with at least one of the various GSM symptoms to assess for the MBS, severity of various GSM symptoms and FSFI scoring; as well as to assess their improvement after 12 weeks of local vaginal

estriol application.

Statistical analysis: SPSS version 19.0.

Results: Most cases were ≤ 60 years, with vaginal symptoms being the most bothersome. Highly significant improvements were seen in all GSM symptoms post treatment including vaginal symptoms, dyspareunia, urgency, frequency, nocturia and stress urinary incontinence (SUI). Also, the improvement in FSFI scoring post treatment was highly significant.

Conclusion: Vaginal symptoms are the most bothersome part of GSM. Local estrogen therapy has a highly significant role in improving all GSM symptoms as well as FSFI scoring leading to a better QOL and sexual health.

Keywords: Genitourinary Syndrome of Menopause (GSM); Menopausal; Urogenital Symptoms; Local Estrogen Therapy; Vaginal Symptoms; Dyspareunia; Urgency; Frequency; Nocturia and Stress Urinary Incontinence (SUI)

1. Introduction

Up to 60% of postmenopausal women suffer from atrophic urogenital symptoms of dryness, itching, burning, irritation of vagina, dyspareunia, dysuria, urgency, frequency and recurrent urinary tract infections (UTIs) due to declining ovarian function. They are together called as the Genitourinary Syndrome of Menopause (GSM) [1, 2]. Most women report these symptoms as being moderate to severe in nature. Vulva, vagina, urethra, bladder and pelvic musculature share estrogen receptors and common embryological origin, hence show conspicuous changes with connective tissue thinning after menopause [1, 3-6]. Effectiveness of locally applied vaginal estrogen over 12 weeks for the same without any need of monitoring or adverse effects

has been established in literature [1, 2]. Thus we aimed to measure the Most Bothersome Symptom (MBS) of the various commonly bothering urogenital symptoms like dryness, itching, burning of vagina, dyspareunia, urgency, frequency, nocturia and stress urinary incontinence (SUI) in these menopausal women. We also measured the subjective self-reported improvement in the severity of these symptoms with intravaginal estrogen over a period of 12 weeks. Since these symptoms also affect the sexual functioning [3-6], we aimed to measure the improvement in FSFI (Female sexual function index) scores, a validated questionnaire used for assessment of female sexual dysfunction (FSD), before and after intravaginal estrogen use over 12 weeks. The improvement in these variables will also improve the quality of life (QOL) and sexual health of postmenopausal women, as there is dearth of data regarding these in Indian women.

2. Material and Methods

A cross-sectional study involving a cohort of 100 postmenopausal sexually active women bothered by at least one of the following urogenital symptoms dryness, itching or burning in the vagina, dyspareunia (pain and discomfort while intercourse), urgency (inevitable desire to pass urine), frequency (urinary episodes ≥ 8 times/day), nocturia (urinary episodes ≥ 2 times/night), SUI (leaking of urine on laughing, coughing, running etc.) was done in the department of obstetrics and gynecology, urogynecology division over a period of 3 months, after obtaining ethical clearance from the institution ethics committee. We included women with naturally acquired menopause, who were sexually active in the last 4 weeks, with a normal urine routine and culture report. Exclusion criteria were women with history of pelvic/ incontinence surgery, on medical treatment for urinary incontinence (UI), history of any postmenopausal bleeding/ unexplained vaginal bleeding, any breast/ uterine/ vulvovaginal/ urethral

pre-malignant or malignant lesions, history of estrogen dependent tumors/ family history of estrogen sensitive tumors in mother, sister or grandmother, history of radiotherapy for any pelvic malignancies, history of SLE, migraine, severe headache, hypertension, heart attack, stroke, angina, liver disease, porphyrias, gall stones, diabetes mellitus, epilepsy, asthma, any bleeding disorder or otosclerosis.

A detailed history as regards their demographic characteristics, name, age, marital status, current medical complaints, medical and surgical history, gynecological history, urological history, obstetric history, menopausal status, sexual history and current medications was taken. It was followed by a detailed general physical, systemic, abdominal, per speculum and per vaginal examination. Subjects were asked about their MBS and to the rate the severity of each of the various GSM symptoms on a subjective four grade scale as none (0), mild (1), moderate (2) and severe (3). This was followed by answering a FSFI questionnaire for sexual dysfunction with a score of ≤ 26.55 being taken as cut-off for FSD [7]. The data so collected was kept confidential. They were then prescribed estriol cream (0.5 mg estriol in 0.5 gm cream base) loaded up to the ring mark of the applicator provided along with the cream for vaginal use every night before going to bed for 2 weeks followed by twice a week for a total duration of 12 weeks. On follow up visit, the improvement in their symptoms was reassessed on the same subjective four grade scale followed by tabulation, interpretation and analysis using statistics, SPSS version 19.0. Wilcoxon signed rank tests were applied to assess the various correlations in the data.

3. Results

Most of our cases were ≤ 60 years (65%) with duration of menopause being 6-10 years (44%). Seventy percent of them were overweight having a body mass index

(BMI) of 25-29.9 Kg/m² with majority of them belonging to the lower middle class (40%) and having only primary level of education (76%) (Table 1). MBS reported by our patients in order of decreasing frequency were the vaginal symptoms namely vaginal dryness, irritation and itching (45%), followed by dyspareunia (14%), urgency & frequency (14%), nocturia (15%), and SUI (12%) (Table 2).

Pre-treatment, 76% patients graded their vaginal symptomatology as severe, 20% as moderate and 4% as mild versus 0%, 11% and 89% respectively after treatment showing a highly significant improvement with local estrogen therapy ($p=0.000$) (Table 3). Dyspareunia was graded in a similar fashion with 76% patients grading it as severe, 20% as moderate and 4% as mild pretreatment versus 0%, 11% and 89% respectively after treatment showing a highly significant improvement with local estrogen therapy ($p=0.000$) (Table 4).

When urinary urgency and frequency were assessed pretreatment, 76% reported them as severe, 20% as moderate, 4% as mild and 0% as none versus 0%, 17%, 81% and 2% respectively post treatment again showing a remarkably significant positive response ($p = 0.000$) (Table 5). Significant improvement ($p = 0.000$) in nocturia is also worth mentioning with 38% reporting grade as severe, 54% as moderate, 8% as mild, and 0% as none prior to treatment versus 1%, 1%, 75% and 23% respectively after treatment (Table 6).

The SUI symptomatology also had significantly improved after treatment ($p = 0.000$) with pretreatment grading showing 35% as severe, 40% as moderate, 25% as mild and 0% as none versus 1%, 22%, 42% and 35% post treatment (Table 7). The FSFI scoring pretreatment showed 100% of cases having a FSFI score of ≤ 26.55 , i.e., were sexually dysfunctional versus 8% post

treatment with a highly significant improvement (p = 0.000) (Table 8). Therefore, our GSM parameters and FSFI scoring had highly significant improvement (p=0.000) after 12 weeks of local estriol therapy.

Demographic variable	Cases
Age	
<=60 years	65 (65%)
>60 years	35 (35%)
Years since menopause	
</=5 years	13 (13%)
6-10 years	44 (44%)
>10 years	43 (43%)
Socio-economic class	
Upper	6 (6%)
Upper middle	32 (32%)
Lower middle	40 (40%)
Upper lower	22 (22%)
Level of education	
College graduate	7 (7%)
Partial college	17 (17%)
High school graduate only	76 (76%)
BMI	
18.5-24.9 (Normal weight)	6 (6%)
25-29.9 (Over weight)	70 (70%)
30-34.9 (Obese Type I)	24 (24%)
40.1-50 (Obese Type II)	0 (0%)

Table 1: Demographic data

Symptom	Percentage (%)
Vaginal symptoms	45
Dyspareunia	14
Urgency and Frequency	14
Nocturia	15
Stress Urinary Incontinence (SUI)	12

Table 2: Most Bothersome Symptom (MBS) before treatment.

Grades	Before Treatment %	After Treatment%	p value
None (0)	0	0	P = 0.000
Mild (1)	4	89	
Moderate (2)	20	11	
Severe (3)	76	0	
Total	100	100	

p=0.000, highly significant

Table 3: Vaginal symptom grading before and after treatment.

Grades	Before Treatment %	After Treatment%	p value
None (0)	0	0	P = 0.000
Mild (1)	4	89	
Moderate (2)	20	11	
Severe (3)	76	0	
Total	100	100	

p=0.000, highly significant

Table 4: Dyspareunia grading before and after treatment.

Grades	Before Treatment %	After Treatment%	p value
None (0)	0	2	P = 0.000
Mild (1)	4	81	
Moderate (2)	20	17	
Severe (3)	76	0	
Total	100	100	

p=0.000, highly significant

Table 5: Urinary urgency and frequency grading before and after treatment.

Grades	Before Treatment %	After Treatment%	p value
None (0)	0	2	P = 0.000
Mild (1)	4	81	
Moderate (2)	20	17	
Severe (3)	76	0	
Total	100	100	

p=0.000, highly significant

Table 6: Nocturia grading before and after treatment.

Grades	Before Treatment %	After Treatment%	p value
None (0)	0	35	P = 0.000
Mild (1)	25	42	
Moderate (2)	40	22	
Severe (3)	35	1	
Total	100	100	

p=0.000, highly significant

Table 7: Stress Urinary Incontinence (SUI) symptomatology grading before and after treatment.

FSFI Scores	Before Treatment %	After Treatment %	p value
≤26.5	100	8	p = 0.000
>26.5	0	92	

p=0.000, highly significant

Table 8: Female Sexual Function Index (FSFI) score before and after treatment.

4. Discussion

Women continue to suffer silently as they take these vulvovaginal symptoms as a normal part of their ageing process. The older term vulvovaginal atrophy (VVA) has now been replaced by GSM since 2014 in consensus with the International society of women’s sexual health and the North American Menopause Society [3]. NICE guidelines of 2015 recommend use of intravaginal estrogen therapy for urogenital atrophy symptoms in menopausal women (including those on systemic hormonal replacement therapy) for as long as needed and even with a higher dose if required because of its effective local action with no side effects, with a review of its efficacy and tolerability every 3 months [2, 4-6]. Literature has proved its statistical supremacy in relieving SUI by increasing the blood supply and hence MUCP (Maximum Urethral Closure Pressure) by urethral coaptation [8]. Also, the frequency of the uninhibited uterine contractions and their amplitude are dampened, instigating the role of estrogen deficiency in overactive bladder (OAB) patients (Cochrane 2007) [9]. Erekson et al, in 183 postmenopausal women reported

dryness of vagina in 35.8% of patients, i.e. 128/183, having a significant impact on their emotional and sexual life with 76.2% reporting sexual dysfunction [10].

Our study also reported vaginal symptoms as the most commonly bothering symptom (45%), with 100% of them suffering from sexual dysfunction, with a highly significant improvement on intravaginal estrogen use over 12 weeks, dropping post therapy to a miniscule 8%. An index pan-European study done by Barlow et al on 3000 menopausal women across six European countries reported dyspareunia in 24.8%, vaginal symptomatology in 10.6% with 40.7% reporting it as moderate and 16.5% as severe, incontinence symptoms in 7.4% with 41.7% reporting it as moderate and 22.1% reporting it as severe, urinary frequency in 12.7% with 39.1% being moderately bothered and 13.5% being severely bothered by it. They used all sorts of vaginal estrogen preparations and documented their efficacy as similar to the most effective systemic therapy [11]. Our study had vaginal symptomatology rates of a whopping

45% and dyspareunia of 14% with 76% of our patients grading their vaginal symptomatology as severe and 20% as moderate. The urgency and frequency rates in our study were around 14% with 76% reporting severe bothersomeness and 20% reporting moderate bothersomeness. SUI was reported in 12% women in our study. Our study was further supported by Lose G et al, who proved the dual efficacy of intravaginal estrogen use on UI as well as vaginal irritative symptoms in postmenopausal women [12].

Our study findings are also consistent with 2006 Cochrane review presented by Suckling J et al as regards the local estrogen use in vaginal atrophy [13]. Long CY et al in his study also demonstrated the use of local/ oral estrogen therapy in diminishing the urinary frequency/ urgency & SUI symptomatology in 60% over 3 months in conformity with our study findings [8]. Our data shows highly significant improvement in SUI symptoms ($p = 0.000$) with pretreatment grading showing 35% as severe, 40% as moderate, 25% as mild and 0% as none versus 1%, 22%, 42% and 35% post treatment. Also, the hormone and urogenital therapy committee did a meta-analysis and showed a subjective improvement in SUI symptomatology of GSM from 64-75% with local intravaginal estrogen use nearing our study findings [9]. David D Rahn et al did an extensive comprehensive analysis searching Medline and Cochrane databases from inception to April 2013, including all randomized controlled trials and prospective comparative studies and found vaginal dryness, itching or burning to be the most bothersome symptom as in our study. He also found that in comparison to placebo all vaginal estrogen preparations are effective and safe without any additional need for monitoring as regards endometrial hyperplasia and adenocarcinoma [14]. Another study by Maria Grazia Matarazzo documented improved urodynamic profile of OAB and GSM patients with vaginal estriol over 12

weeks, though this point was not a part of our study but supported our results as we also witnessed improvement in our vaginal & urinary symptomatology profile. Her study reported pretreatment vaginal dryness to grading to be mild in 5%, moderate in 10% and severe in 85% which improved to none grade in 89.2% and mild grade in 10.8% with significant results [15].

A comparative study of vaginal estrogen, vaginal laser, or combined treatment to find out what works best for GSM & FSD using the FSFI score as used by us was initiated by Cheryl B. Iglesias, reporting all three options effective for vaginal dryness with worsening of vaginal pain on FSFI scoring with laser alone or with laser and vaginal estriol combined while our results were very satisfactory as far as vaginal estriol use was concerned both for GSM as well as FSD [16]. Stephanie S. Faubion et al, Revive Survey (Real Women's Views of Treatment Options for Menopausal Vaginal Changes) and Chae HD et al also gave evidence of vaginal symptoms being the most bothersome ones [17-19]. The sexual dysfunction component in each of these studies is to the tune of 59% which improved significantly over 12 week's use of vaginal estrogen in sync with our study. A small sample size and the bias during subjective reporting of symptoms due to over exaggeration were the limiting factors of our study.

5. Conclusion

Vaginal symptoms are the most bothersome part of GSM. Local estrogen therapy has a highly significant role in improving all GSM symptoms as well as FSFI scoring leading to a better QOL and sexual health.

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