

Vaginal Estrogen Therapy in Postmenopausal Overactive Bladder

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ABSTRACT

Objective: To assess the efficacy of vaginal estrogen therapy in postmenopausal overactive bladder (OAB). **Study design:** It is an OPD (outpatient department) based prospective study. Postmenopausal women attending gynecology OPD with complaint of OAB were enrolled for the study. Women fulfilling the criteria for the study were given estradiol 2 mg vaginal tablet everyday for 2 weeks, then weekly twice for 10 weeks. Patients were assessed by 3-day bladder diary, Patient Global Impression scale, before and after the therapy. **Results:** Ninety-three patients completed the study. Increased frequency of micturition was cured in 92.5% cases; urgency and urge incontinence was cured in 74.2% cases. Patient's subjective feeling of improvement scale revealed only 12.9% women felt either no change or little better; rest all were happy. **Conclusion:** Local estrogen therapy in postmenopausal women with OAB resulted in a good outcome.

Keywords: Overactive bladder, estrogen, vaginal

Menopause causes different types of morbidity in women's lives – urinary incontinence is one of them. Postmenopausal women many a times complain of frequency, urgency, urge incontinence (overactive bladder or OAB). While evaluating them, ruling out infectious etiology (urinary tract infection) is very important. Next to infection, hypoestrogenism is thought to be the major etiological factor. The present study evaluates the efficacy of local estrogen in treating postmenopausal OAB.

MATERIAL AND METHODS

The study was conducted in the Dept. of Obstetrics and Gynecology, College of Medicine and JNM Hospital, Kalyani, Nadia, West Bengal. It was an OPD (outpatient department) based prospective study. Postmenopausal women attending gynecology OPD with complaint of OAB were enrolled for the study.

Inclusion criteria were – 1) Patient should be at least 1 year postmenopausal; 2) increased frequency of micturition and nocturia (normal voiding habits ≤ 8 episodes/day and ≤ 2 episodes/night)¹; 3) urgency of urination \pm urge incontinence. Exclusion criteria were – 1) Undiagnosed vaginal bleeding; 2) endometrial hyperplasia, and other estrogen-dependent disease, especially malignancy; 3) hypertension (blood pressure systolic >160 mmHg, diastolic >100 mmHg); 4) previous thromboembolic episodes; 5) liver disease; 6) estrogen therapy within last 6 months.

Informed consent was obtained from all patients. All patients underwent a detailed history and clinical examination including breast, per abdominal, per vaginal examination, blood pressure measurement, etc. Complete blood count, liver and renal function tests, coagulation profile, Pap smear, pelvic ultrasonography were done for all the cases. Mid-stream urine culture and sensitivity was done routinely before starting estrogen therapy. If infection was present, it was cured with respective sensitive antibiotic. After that also, if OAB symptoms persisted then only vaginal estrogen therapy was started. Urodynamic study could not be done as there is no such facility in our setup. Patients were asked to maintain a 3-day bladder diary before starting therapy and also at the end of the therapy at 12 weeks. Estradiol vaginal tablet 2 mg was inserted in the posterior fornix every night for first 2 weeks; followed by weekly twice for 10 weeks. Total 12 weeks

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therapy was given. The effect of treatment on patients' perception of urgency was evaluated by asking each patient to complete a three-point urgency perception scale at baseline and 12 weeks following treatment.

Patients described their experience when they felt the desire to urinate. The response options included: 1) Unable to hold urine; 2) Usually able to hold urine until I reach the toilet if I go immediately and 3) Usually able to finish my work before going to the toilet². Patient's feelings were also assessed by Patient Global Impression (PGI) scale³. At the starting of the study, PGI of Severity (PGI-S) scale measured the severity of the disease. The woman was asked to check the one number that best described how her urinary tract condition was now – 1) Normal, 2) mild, 3) moderate, and 4) severe. It is a scale which measures the patient's subjective feeling about

the severity of her condition. Result of the treatment is assessed by PGI of Improvement (PGI-I) scale at 12 weeks. This scale measures the patient's feeling of her OAB condition after the treatment – whether improved or not. Again she was asked to check the one number that best described how her urinary tract condition was now, compared with how it was before she began taking medication in this study – 1) Very much better; 2) much better; 3) a little better; 4) no change; 5) a little worse; 6) much worse and 7) very much worse.

RESULT

Hundred women were enrolled for the study. Four were unfit for estrogen therapy after investigations. Three were lost to follow-up. Total 93 women completed the trial. At the beginning of the study, increased

Table 1. Frequency of Micturition, Nocturia and Nocturnal Enuresis Before and After Therapy

Frequency of micturition	No.	Percentage (%)	Nocturia	No.	Percentage (%)
At starting			At starting		
9-15 times	38	39.6	3-4 times	13	13.5
16-20 times	43	44.8	5-6 times	4	4.2
>20 times	15	15.6	Total	17	17.7
Total	96		After 12 weeks of therapy		
After 12 weeks of therapy			3-4 times	2	11.8 (2/17)
≤8 times	86	92.5	Nocturnal enuresis		
9-15 times	7	7.5	At starting	5	5.2
Total	93		After 12 weeks of therapy	0	0

Table 2. Urgency and Urge Incontinence

	No.	Percentage (%)
At starting		
I am usually not able to hold urine	84	87.5
I am usually able to hold urine until I reach the toilet if I go immediately	12	12.5
I am usually able to finish my work before going to the toilet	0	0
Total	96	100
After 12 weeks of therapy		
I am usually not able to hold urine	23	24.7
I am usually able to hold urine until I reach the toilet if I go immediately	1	1.1
I am usually able to finish my work before going to the toilet	69	74.2
Total	93	100

Table 3. Patient Global Impression Scale

	No.	Percentage (%)
Patient Global Impression of Severity (PGI-S) scale (at the beginning)		
Normal	0	
Mild	19	19.8
Moderate	56	58.3
Severe	21	21.9
Total	96	100
Patient Global Impression of Improvement (PGI-I) scale (after 12 weeks of therapy)		
Very much better	69	74.2
Much better	12	12.9
A little better	7	7.5
No change	5	5.4
A little worse		
Much worse		
Very much worse		
Total	93	100

frequency of micturition >20 times was present in 15.6% cases, nocturia in 17.7% cases and nocturnal enuresis in 5.2% cases. Eighty-four (87.5%) patients had urge incontinence. Patient's subjective feeling revealed that 21.9% had severe problem.

At the end of 12 weeks of vaginal estrogen therapy, 92.5% women had no more increased frequency of micturition. There was no case of nocturnal enuresis. Urgency and urge incontinence was cured in 74.2% cases. Patient's subjective feeling of improvement scale revealed only 12.9% women felt either no change or little better; rest all were happy (Tables 1-3).

DISCUSSION

Local estrogen therapy in postmenopausal women resulted in a good outcome in relation to their improvement in OAB problem.

Hypoestrogenism affects the sensory threshold of the urinary tract, and this reduces the volume and time needed to change the first sensation to void into the feeling of imminent micturition, and in some subjects causes involuntary detrusor contraction⁴. This could be the reason why estrogen therapy helped in reducing the OAB symptoms in postmenopausal women.

Various studies have demonstrated that estrogen replacement can improve, or even cure, urinary stress and urge incontinence. High-dose estrogen can decrease the total number of voids in a 24-hour span, including nocturnal voids⁵. Cochrane database review 2009 also revealed that estrogen therapy can cure or improve urinary incontinence in women, especially urge incontinence⁶.

In evaluation of estradiol absorption from vaginal tablets in postmenopausal women, it was found that absorption of the drug is not so high to cause systemic side effect. Over 12 weeks of therapy also, absorption patterns remained consistent, and there were no accumulations of circulating E2⁷.

Cardozo et al⁸ had performed a systematic review of the effects of estrogen therapy on symptoms suggestive of OAB in postmenopausal women. Eleven randomized trials were identified where total of 430 subjects were included. Estrogen (estriol, estradiol, conjugated estrogens or combination of estradiol and estriol) systemic or local vs. placebo was reviewed. Overall, all of the outcome variables, which included diurnal and nocturnal frequency, urgency, number of incontinence episodes, first sensation to void, and bladder capacity,

were significantly improved in patients given active treatment compared with those taking placebo. When the authors analyzed data separately for systemic and local therapies; however, they found that only numbers of incontinence episodes and first sensation to void were significantly improved in patients taking systemic treatment, whereas local treatments had beneficial effects on all outcomes. Based on these findings, it was concluded that estrogen therapy may be effective in relieving the symptoms suggestive of OAB, but local administration may be the most effective route of administration.

In light of available evidence, it seems preferable to use vaginal estrogens rather than systemic for the management of menopause-related bladder problems⁹.

In our study, though 100 patients were initially recruited, 93 could complete the whole course. Other studies on effect of vaginal estrogen on urinary incontinence in postmenopausal women had sample sizes of 40 (Enzelsberger et al¹⁰, used estriol cream 1 mg/day, 3 mg/day), 59 (Nelken et al¹¹, estradiol vaginal ring vs. oral oxybutynin), 110 (Cardozo et al¹², used 17-beta estradiol tablet) cases.

CONCLUSION

The bladder and its surrounding structures are rich in estrogen receptors and there are demonstrable physiological and anatomical changes that occur around and immediately after menopause. The prevalence of many bladder symptoms, such as frequency, urgency and incontinence (OAB) does seem to increase around menopause. Hence estrogen therapy, especially vaginal therapy which has less systemic side effects than oral form, appears to be helpful in managing such situation.

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