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RESEARCH ARTICLE

EFFECTS OF VAGINAL ESTROGEN THERAPY ON UROGENITAL ATROPHY: COMPARISON OF THREE DOSES

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ABSTRACT

Background and aims: Problems associated with vaginal atrophy affect up to 60% of post-menopausal women. This study aimed to evaluate the effect of vaginally administered estrogen on urogenital atrophy symptoms and compare the outcomes between three different doses of vaginal estrogen to find the optimal dosage without an effect on endometrial thickness.
Material and methods:51 Menopausal women with vaginal atrophy were randomly assigned into three study groups receiving 0.5gr of vaginal estrogen cream, which contains 0.625 mg/gram once a week, twice a week and three times a week for six months. Questionnaires were completed once before the intervention and once at the end of the 6 month follow-up.
Results: Significant relief of dyspareunia was found in all three groups with the highest improvement (69.2%) reported by women in group 2. Frequency of intercourse was significantly increased after the treatment in groups 2 and 3. Respondents in groups 2 and 3 reported a significantly improved couple intimacy and marital relation. Regarding the urinary symptoms, only urine frequency was relived significantly in groups 2 and 3 while urinary incontinency and dysuria did not differ before and after the treatment.
Conclusion: vaginal estrogen therapy is effective in improving dyspareunia and thus sexual function; however its impact on urinary complaints of urogenital needs further investigation. Between the three studied doses, 0.5 gr vaginal estrogen twice a week was shown to be optimal since 0.5 gr once a week was obviously inadequate while 0.5 gr three times a week was unnecessary.

INTRODUCTION

Menopause is a physiologic transition characterized by diminished ovarian function and reduced circulatory estrogen which might lead to significant biological and social alterations in women's life. This estrogen deprived state results in gradual atrophic changes in urogenital mucosa including thinning of the epithelium, reduced collagen content and smooth muscle dysfunction. Such changes can lead to a wide variety of distressing symptoms associated with both vaginal and urinary disorders including vaginal dryness, itching, irritation, dyspareunia, recurrent urinary tract infections, urinary incontinence and urge incontinence (1-7).

Problems associated with vaginal atrophy affect up to 60% of post-menopausal women and might interfere with their normal sexual functioning. With reduced vaginal lubrication and tissue elasticity and structural changes in vagina, many women might experience dyspareunia, decreased sexual arousal and desire, difficulty in achieving orgasm as well as the mentioned urinary and vaginal symptoms (8-10). All these manifestations contribute to sexual dysfunction secondary to vaginal atrophy which is associated with decreased intimacy and frequency of intercourse as well as a general reduction in quality of life (11-15).

As estrogen deficiency is the primary cause of vaginal atrophy, local vaginal estrogen therapy is considered the main treatment particularly in patients with symptoms primarily related to vulvovaginal atrophy. Topical estrogen preparations can improve the atrophic changes by stimulating cell growth and maturation as well as enhancing vaginal blood flow (16, 17). Vaginal estrogen therapy is also known to be able to relive some of the urinary symptoms (18, 19). Since the systemic absorption of local estrogen is very limited, several previous studies have shown few adverse effects with minimal risk of endometrial hyperplasia or cancer (20-25).

A wide variety of local estrogen formulations are available with most of them being comparably effective; however, the optimal dose to achieve maximum effect is still a less addressed clinical issue. Keeping in mind that administering the smallest effective dosage with the lowest frequency is a general recommendation in therapy, in this study we investigated the effects of vaginal estrogen therapy in relieving vaginal and urinary symptoms of vaginal atrophy and sexual

function of menopausal women and compared three dosages to find the optimum therapeutic one with lowest frequency of use and no effect on endometrial thickness.

METHODS

After approval of the study protocol by local ethics committee of AJA University of Medical Sciences, this prospective study was carried out on menopausal women referring to gynecology clinic of Imam Reza Hospital in Tehran, Iran during 2010-2011withcomplaints of vaginal dryness, dyspareunia and decreased frequency of intercourse in comparison with premenopause (non-randomized sequential sampling). Diagnosis of urogenital atrophy was established by gynecologic examination and visual inspection of vagina (labial atrophy, thinning and paleness of vulva, narrowing vaginal introitus and loss of rugae) as well as evidences of vaginal atrophy in Pap smear. Patients with breast cancer, history of venous thromboembolism, active urinary tract infection, history of radiotherapy, endometrial thickness more than 5 mm in transvaginal sonography and history of dyspareunia before the menopause were excluded from the study. Informed written consents were obtained from all the participants. Study protocol was approved by Ethic Committee of the Hospital.

Data was collected using questionnaires designed by author and were completed through interview. The questionnaires included questions about the presence of symptoms associated with vaginal atrophy (dyspareunia, dryness) and urinary dysfunction (stress incontinency, urge incontinency, dysuria, frequency and urgency) and their severity and questions regarding sexual function (frequency of intercourse, experience of orgasm and individual's evaluation of couple intimacy).

After recording the demographic data, results from gynecologic examination, pap smear and transvaginal sonography, all patients were prescribed to use 0.5 gr of topical vaginal estrogen once a day for two weeks. Afterwards, the patients were randomly assigned into three study groups: group 1 received 0.5 gr of vaginal estrogen, once a week; group 2, twice a week and group 3, three times a week for six months. Questionnaires were completed once at the beginning of the study and once at the end of the intervention period (6 month follow-up).

A total of 99 patients met the inclusion criteria during the study period and were enrolled to the study; however, only 51completed the required follow up period and the rest were excluded either due to not being available for the follow up visits or non-compliance or misuse of the drug mostly because of concerns about the adverse effects of the hormone therapy.
SPSS version 19 was used for data analysis. Non-parametric tests as well as Kruskal-Wallis test were used to compare data before and after the intervention and between the groups. P-value< 0.05 was considered statistically significant.

Results

A total of 51 menopausal women (mean age: 54; age range: 45-75) completed the study. Age distribution in the three study groups was similar. All of the 51 studied patients were suffering from dyspareunia. Comparing data before and after the intervention showed complete relieve in 11.5% of the patients in group 1, 69.2% of group 2 and 19.2% of group 3. Improvement in group 2 (0.5 gr vaginal estrogen twice a week) was found to be significantly higher than the two others ($P<0.05$) (figure 1).

Regarding sexual function, the frequency of intercourse before and after the treatment was significantly increased in groups 2 and 3; however the difference in group one was not found to be statistically significant. Experiencing orgasm did not show a significant difference when compared with before treatment; however, comparing the intervention groups showed that group 2 reported significantly higher rates of experiencing orgasm than group 1. All study groups reported significantly better intimacy and marital relations (46% in group 1; 90% in group 2 and 75% in group 3). Comparison between groups showed no significant difference.

Analysis of urinary manifestations of urogenital atrophy showed that frequency of stress incontinence, urge incontinence, urgency and dysuria did not differ significantly after treatment with vaginal estrogen, while complaint of urine frequency was significantly decreased in groups 2 and 3.

Comparison of Pap smear results before and after the treatment showed improvement of atrophy in all the study subjects except two who both were from group 1.Repeating vaginal sonography at the end of the study period showed no cases of increased endometrial thickness.

The most commonly observed adverse effect was nausea and vomiting which was most prevalent in group 3 (13.3%).

DISCUSSION

The aim of the present study was to evaluate the effects of vaginal estrogen on vaginal and urinary manifestations of urogenital atrophy and sexual function and comparing three dosages (0.5 gr vaginal estrogen once, twice and three times a week) to determine the optimum dose that can effectively relieve urogenital symptoms and improve sexual relation without causing any change in endometrial thickness. Data analysis form the 51 patients showed that this treatment has a significant impact on dyspareunia, urine frequency, frequency of intercourse and couple intimacy. Comparison of the doses showed 0.5 gr vaginal estrogen applied twice a week as the optimum dosage for symptom relief while once a week dosage was obviously ineffective and three times a week dosage was unnecessary.

Our findings showed that topical vaginal estrogen therapy can significantly relive dyspareunia in menopausal women in all of the three experimental dosages; although the highest improvement rate (69.2%) was observed with 0.5 gr estrogen twice a week. It has been shown that high efficacy of local estrogen therapy on dyspareunia due to vaginal atrophy has success rates as high as 80 to 100% (26). Topical estrogen improves vaginal dryness, vaginal vascularity and elasticity and therefore relieves dyspareunia which leads to better sexual function (9,10).

Sexual dysfunction in menopausal women is due to several etiologies such as reduced vaginal lubrication and elasticity as well as diminished sensory responses (9,11,12). Topical estrogen therapy can improve sexual function in menopausal women according to several studies (9-18). Accordingly respondents in our study reported a significantly increased frequency of intercourse after the treatment period with vaginal estrogen. Moreover, improved couple intimacy and marital satisfaction was reported by significantly higher number of respondents after treatment with vaginal estrogen.

Certain urinary disorders associated with estrogen-deprived state in menopause have been reported. Local vaginal estrogen therapy has been shown effective in improving some of them due to the presence of estrogen receptors in urethral mucosa and smooth muscle. Amongst the urinary complaints, vaginal estrogen has been demonstrated to effectively reduce the incidence of recurrent urinary infection; however, its effect on urinary incontinence is controversial (9,17,18,19). In our study, estrogen therapy was not found effective in reliving urinary incontinence; however, complaints of urinary frequency were significantly reduced after treatment.

Among the three doses of vaginal estrogen used in our study, 0.5 gr vaginal estrogen twice a week was found to be optimum since it had the best outcome and the lowest side effects while once a week administration of the drug was inadequate and three times a week was unnecessary. However, it must be considered that outcomes largely depend on the severity of the vaginal atrophy at the beginning of the treatment. In addition, several studies have suggested that despite the fact that no significant adverse effects have been reported with vaginal estrogen therapy, individualization of therapy seems like the best option since the optimal dose to achieve symptom relief varies from woman to woman (24). Our findings are partially limited by the high amount of patient loss during follow up. Most common reasons for leaving the study included stopping application of the vaginal estrogen immediately after observing some symptom relief mostly due to concerns about adverse effects of hormone therapy or the inconvenience of vaginal application.

On the other hand, we aimed to find the lowest effective frequency of vaginal estrogen application, since according to our clinical experience, frequent use of vaginal creams is upsetting for many patients as it was mentioned as one of the leading causes of stopping the application of the cream by many of our respondents. It seems that applying the vaginal estrogen only twice a week not only is effective in symptom relief without any adverse effects, but also is convenient for the patients and therefore increases their compliance. Further more comprehensive randomized clinical trials are needed to study the effect of topical estrogen therapy on urinary symptoms as well as determine the optimal dose of vaginal estrogen for relieving urinary and vaginal complaints.

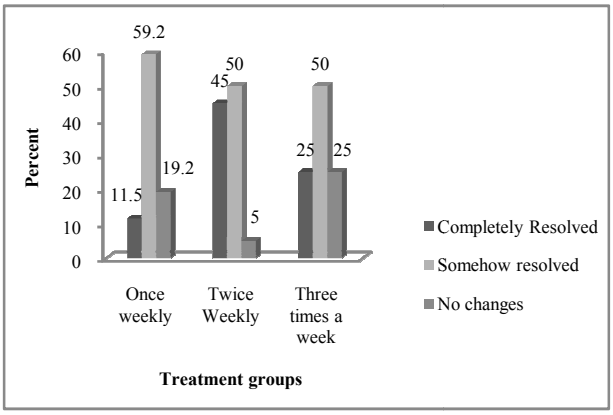

Figure 1 comparing the frequency of dyspareunia after treatment in the three study groups

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