The Effect of Moist Exposed Burn Ointment (MEBO) Versus Premarin® (conjugated estrogens) on clinical symptoms and Vaginal Cytology in The Treatment of Postmenopausal Vaginal Atrophy

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ABSTRACT

Vaginal atrophy is a prevalent issue among postmenopausal women who have a variety of symptoms such as discomfort, itching, dyspareunia, increased frequency, urgency, and dysuria. This research compared the results of using the estrogenic vaginal cream Premarin® (conjugated estrogens) to those of using the Chinese herbal ointment MEBO to treat postmenopausal vaginal atrophy. A comparative study was done in a private clinic in Al-Ramadi city in Al-Anbar Governorate/Iraq. From the first of February 2022 to the first of February 2023. One hundred patients were allocated to one of two therapies at random. MEBO was taken three times per week for 14 weeks, while Premarin® was taken daily for two weeks, then twice weekly for the remaining 12 weeks. Following the completion of the treatment, clinical symptoms, as well as the vaginal maturation index and value, were assessed. All symptoms were considerably decreased or eliminated, including itching, discomfort, and painful intercourse, with no difference between the two therapies. Both treatments considerably increased the vaginal maturation index and vaginal maturation value, with Premarin® being marginally superior to MEBO. There were no adverse effects associated with these two medicines. In this study, we found that vaginal application of MEBO three times per week for 14 weeks improved vaginal maturation index and value, alleviating symptoms of vaginal atrophy. MEBO may be an alternative to local estrogen treatment for people with vaginal atrophy.

Keywords: MEBO, Vaginal atrophy, conjugated estrogens.

INTRODUCTION

Menopause is an essential stage in a woman's life, characterized by a loss of reproductive function and expressed clinically as amenorrhea. As population life expectancy increases, women are taking longer and longer to get through menopause, which accounts for a third or more of a woman's total lifespan. Here is where doctors' concerns about women's quality of life come in, even during this delicate time[1].

Topical vaginitis (AV), commonly known as vulvovaginal atrophy (VVA), affects 10%–40% of postmenopausal women[2,3]. Vulvovaginal atrophy can happen in any period of female life but more in menopause. Clinical features are pale, smooth vaginal walls, dry valval, and vaginal mucosa, with a red cervix. PH of the vagina 4.6 and more encourages the diagnosis of vulvovaginal atrophy[4]. A drop in circulating estrogen after menopause causes vaginal, bladder, and urethral tissue to become atrophied and fragile. Usually, the vasomotor symptoms will disappear within months or years, but the other symptoms of the urogenital system will be aggravated as the women age increase[5]. Many other causes of low estrogen state like different breast carcinoma treatments, breastfeeding, and many drugs. In cases not due to menopause, the symptoms of atrophic vaginitis will disappear when the levels of estrogen return to normal[4]. A vaginal swab is a standard for diagnosing vaginal atrophy. Because of the reduction in estrogen, the superficial cell layer thins and shrinks, and parabasal cells multiply. The maturity Index (MI) refers to the number of parabasal, intermediate, and superficial cells per 100 on a smear[6,7].

The developed medical field has many choices to treat it, like using estrogen replacement, whether local or systemic, local dehydroepiandrosterone, selective estrogen receptor modulators, moisturizers, artificial lubricants, and other non-drug modalities. In-time diagnosis and good choice of treatment results in improvement and good health of vaginal mucosa[8]. So, the major target in treating atrophic vaginitis is to improve the patient's symptoms and improve the vaginal mucosa health to return to its premenopausal character[8]. In order to alleviate the discomfort that comes with vaginal atrophy, many women turn to the use of exogenous estrogen (either systemically or topically). The vaginal epithelium develops newly under the influence of estrogen. Exogenous estrogens, on the other hand, have certain adverse effects and may be contraindicated[9]. Despite the effectiveness of estrogen intake in managing the symptoms of perimenopause and the first years of menopause, especially the vasomotor one, the used doses may not be enough to treat the atrophic features that result from long estrogen deprivation[10].

A Women's Health Initiative (WHI) study raised concerns about oral hormone replacement therapy for women at high risk of uterine and breast Cancer or in remission. Alternative medicines have been used to address these problems in recent years. Vaginal lubricants and moisturizers are used. Regrettably, many women cannot absorb these products[2]. So local vaginal treatment (rings, creams, tablets) is now more used and advised in treating females suffering atrophic vaginitis of moderate to severe type. Taking into consideration the serious side effects associated with estrogens is an important and suitable use of various estrogens available may offer females with menopausal symptoms considerable improvement of their irritating symptoms and emotional upset that result from atrophic vaginitis[10].

In the early 1990s, the North Central Cancer Treatment Group((NCCTG) Cancer Control Program addressed this clinical question with a clinical protocol in which women were randomly assigned to receive a non-estrogen vaginal lubricant (Replens) versus a placebo lubricant.

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The results of this study provided information that vaginal dryness improved in patients receiving either product. Still, these products are troublesome for many women and seem to need to work better as estrogen. Therefore, there is a need for better non-estrogen treatments for vaginal dryness[3]. MEBO is a type of Chinese patent medication created following Chinese medical theory[11]. It is an effective external medicine used in treating burns. It has antibacterial, anti-inflammatory, and analgesic effects and assistes the start of wound healing[12]. It is a popular dietary supplement in Asia and the Middle East that is manufactured from natural products. Beta-sitosterol and berberine oil are present. This oil relieves pain while soothing wounds and retaining moisture. Epithelialization is improved by β-sitosterol[13]. So, the aims of this study were to: (1) determine how much the vaginal atrophic symptoms of the patients had improved after application of MEBO and Premarin® and (2) examine how MEBO and Premarin® can affect the maturation of the vaginal epithelium.

PATIENTS AND METHODS

One hundred women participated in this comparative research, which was done in a private clinic in Al-Ramadi city in Al-Anbar Governorate/Iraq over one year, from the first of February 2022 to the first of February 2023.

Inclusion criteria:

1. Women who are 49 to 65 years old.
2. Itching, irritation (burning), or dyspareunia are all signs of moderate or severe vaginal atrophy.
3. At least a year has passed since the last menstrual period.
4. Less than 5% of superficial cells must be seen in the baseline vaginal swab.

Exclusion criteria:

1. No high- or low-grade precancerous lesions or cervical or vaginal Cancer.
2. Known or suspected other serious medical condition.
3. Use of hormonal replacement therapy in the last 3 months.
4. Third or fourth-degree vaginal prolapse.
5. Hormonal-dependent tumors.
6. Abnormal vaginal bleeding.
7. History of active thromboembolic disease.
8. Vaginal infection and use of vaginal douches or lubricants.

After obtaining informed consent form all participants, a detailed history was taken from all patients, including age, parity, lasting menstrual period, and gynecological, obstetrical, medical, and surgical history. Physical examination was also done, including sitting blood pressure, heart rate, and respiratory rate. Body mass index was measured for all women. Papanicolaou smears were also done on all women to exclude Cancer of the cervix or vagina or high/low-grade precancerous lesions. A fifty women underwent a 16-week MEBO treatment (Julphar-Gulf Pharmaceutical Industries). During this time, they are instructed to put vaginal MEBO three times a week by vaginal applicator with 10-15 grams of MEBO. The other fifty were instructed to put Premarin® (conjugated estrogens, Pfizer). Vaginal creams come with an applicator that you can use to apply directly to the vaginal tissue. Applicators are designed to help you measure prescription doses cleanly and accurately and should be comfortable and easy to use. Contains 0.625mg of conjugated estrogens per gram of cream. 0.3 mg (one-eighth applicator) daily for two weeks, then twice weekly for 14 weeks.

Before and after 16 weeks of therapy, vaginal swabs were collected. An Ayres spatula is used to get a sample of the vaginal epithelium; as with the Pap smear, the specimen is taken from the center of the lateral vaginal wall. The smears were distributed on glass slides and cured with a fixative spray (70% ethanol) before being transferred to a private laboratory of expert cytotechnologists and cytopathologists. The specimen's maturity was evaluated using traditional manual methods (Epithelial vaginal maturity was assessed manually in a Pap test). Smears were stained by experienced cytotechnologists and cytopathologist). Maturation is an index and fraction (MI and MV) of over 100 cells. Improvement in vaginal maturity at 16 weeks was assessed compared to baseline.

Statistical analysis: The Statistical Package for Social Sciences (SPSS) version 20 for Windows 2013 was employed to analyze the data. Categorical data are displayed as frequency and percentage tables, as well as bar and bar graphs. Continuous variables are given as mean, standard deviation, median, and range based on the data distribution. To determine the normality of continuous data, the Shapiro-Wilk test was applied. The Student's independent parametric test and the Mann-Whitney nonparametric U test were used to examine differences between continuous variables having a normal distribution.

McNemar's test was used to assess the association of inclusion of women with pre-and post-treatment categorical data. To analyze the variation in continuous variables before and after therapy, the paired t-test was used. The significance level in this study is a p-value less than 0.05.

RESULT

In the present study, the two groups had no significant difference regarding age, body mass index, parity. Body mass index (BMI) as indicated by Table 1.

There was an improvement in all symptoms in both groups following therapy. It was only statistically significant in patients with dyspareunia and statistically highly significant in patients with other symptoms. Some patients had multiple symptoms, i.e., mutually exclusive as demonstrated by Table 2.

As shown from the Figure 1, there was a statistically significant improvement in dyspareunia in both groups (p=0.031, p=0.016 correspondingly), N=100.

Both groups' superficial and intermediate cell counts increased following treatment. However, this rise was statistically insignificant. After treatment, there was a decrease in the quantity of parabasal cells in both groups, although this drop was statistically insignificant as shown in (Table 3) (The mean of vaginal maturation index).

There was a statistically significant rise in maturation value in both groups after treatment (p=0.043 and p=0.023, respectively), although it is more significant in the Premarin® group, N=100 as demonstrated in the (Table 4).

After the completion of treatment, the maturation value increased significantly in all 50 patients treated with MEBO (p= 0.043), N=50 as shown (Figure 2) and There was a significant increase in maturation value in all patients after the treatment by Premarin® (p=0.023), N=50 as demonstrated by (Figure 3).

There was more increase in maturation value in the Premarin® group than MEBO group, but the difference was statistically not significant(p=0.859). Both treatments were effective, but Premarin® was more effective than MEBO, N=100 as demonstrated by (Table 5).

Table 1. Body mass index (BMI)

Characteristic	MEBO group (N=50)	Premarin® group (N=50)	p-value
Maternal age (Years) Mean ± SD	54.7 ± 4.5	55.1 ± 4.9	0.688
BMI (kg/m²) Mean ± SD	22.9 ± 2.2	22.4 ± 2.2	0.224
Parity Median (Range)	8 (2 - 12)	8 (2 - 11)	0.733
Independent t-test, Mann-Whitney U test, NS= not significant at alpha <0.05, SD=standard deviation, N= number.			

Table 2. The clinical characteristics of the women in both groups according to the presence of vaginal atrophic symptoms.

symptoms	MEBO group N=50 Before treatment N (%)	MEBO group N=50 After treatment N (%)	p-value	Premarin® group N=50 Before treatment N (%)	Premarin® group N=50 After treatment N (%)	p-value
Dyspareunia	9 (18.0)	3 (6.0)	0.031*	8 (16.0)	1 (2.0)	0.016*
Burning ,irritation	21 (42.0)	6 (12.0)	<0.001*	20 (40.0)	4 (8.0)	<0.001*
Itching	20 (40.0)	7 (14.0)	0.006*	24 (48.0)	3 (6.0)	<0.001*
McNemar test, * significant at alpha <0.05.						

Table 3. The mean of vaginal maturation index. The table displays that both groups' superficial and intermediate cell counts increased following treatment.

	MEBO group Before treatment Mean±SD	MEBO group After treatment Mean±SD	p-value	Premarin® group Before treatment Mean± SD	Premarin® group After treatment Mean± SD	p-value
Superficial vaginal cells	4.8±2.7	5.9±3.4	0.076 (NS)	4.5±2.9	6.1±4.55	0.052 (NS)
Intermediate vaginal cells	70.5±18.6	75.5±19.2	0.189 (NS)	66.9±15.5	76.0±29.8	0.058 (NS)
Para-basal vaginal cells	20.4±13.5	15.6±10.7	0.052 (NS)	28.6±13.7	15.8±10.5	0.063 (NS)
Paired t-test, NS = not significant at alpha <0.05						

Table 4. The maturation value in both groups before and after therapy.

Maturation value(MV)	MV before treatment Mean±SD	MV after treatment Mean±SD	p-value
MV MEBO group (N=50)	40.05±8.5	43.65±9.04	0.043*
MV Premarin® group (N=50)	37.95±10.65	44.1±15.45	0.023*
Paired t-test, *significant at alpha <0.05			

Table 5. Comparison of the mean maturation value between a group of women treated by MEBO and others treated by Premarin®.

Maturation value	MEBO group (n=50)	Premarin® group (n=50)	p-value
MV after treatment	43.65±9.04	44.1±15.45	0.859 (NS)
Independent t-test, not significant at alpha <0.05			

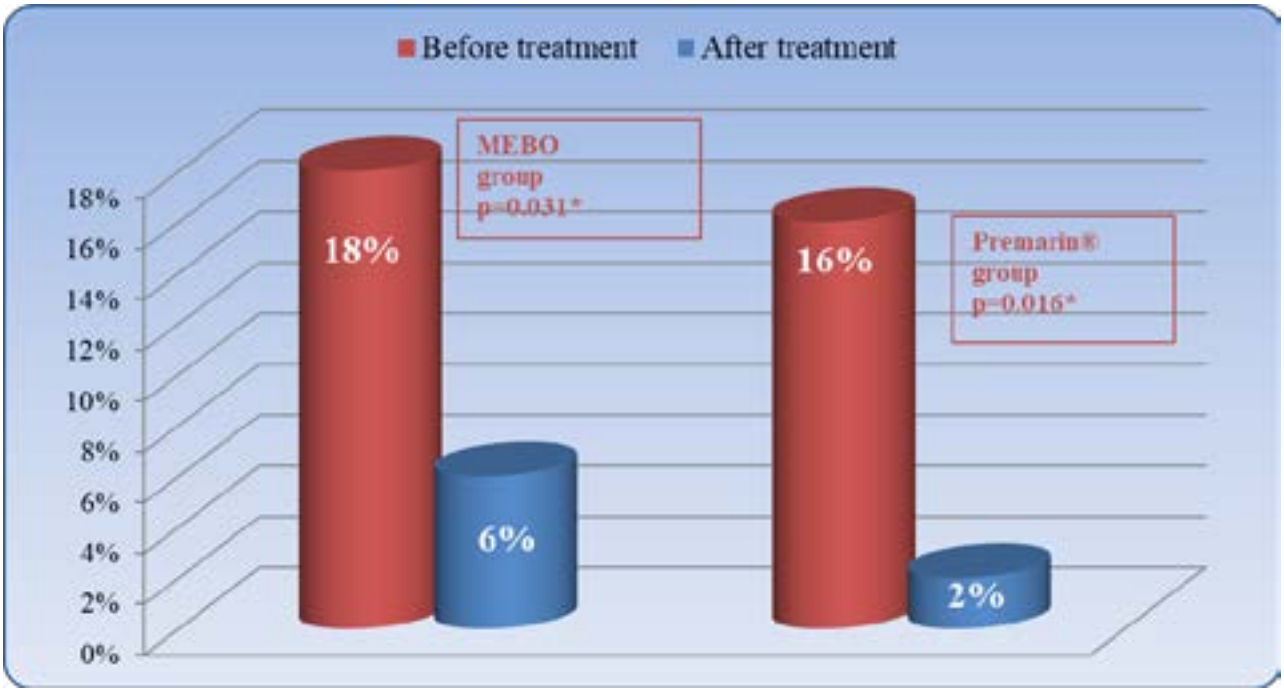

Figure 1. Comparison of the research groups' percentages of patients with dyspareunia before and after the therapy.

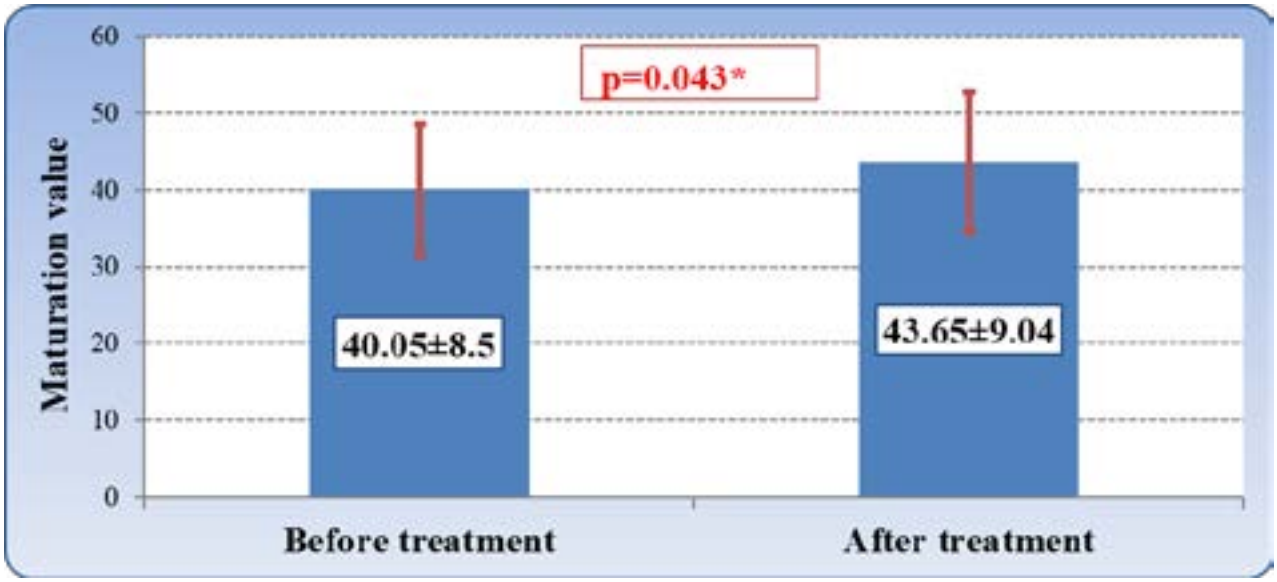

Figure 2. Effect of treatment with MEBO on the maturation value among the participant ladies.

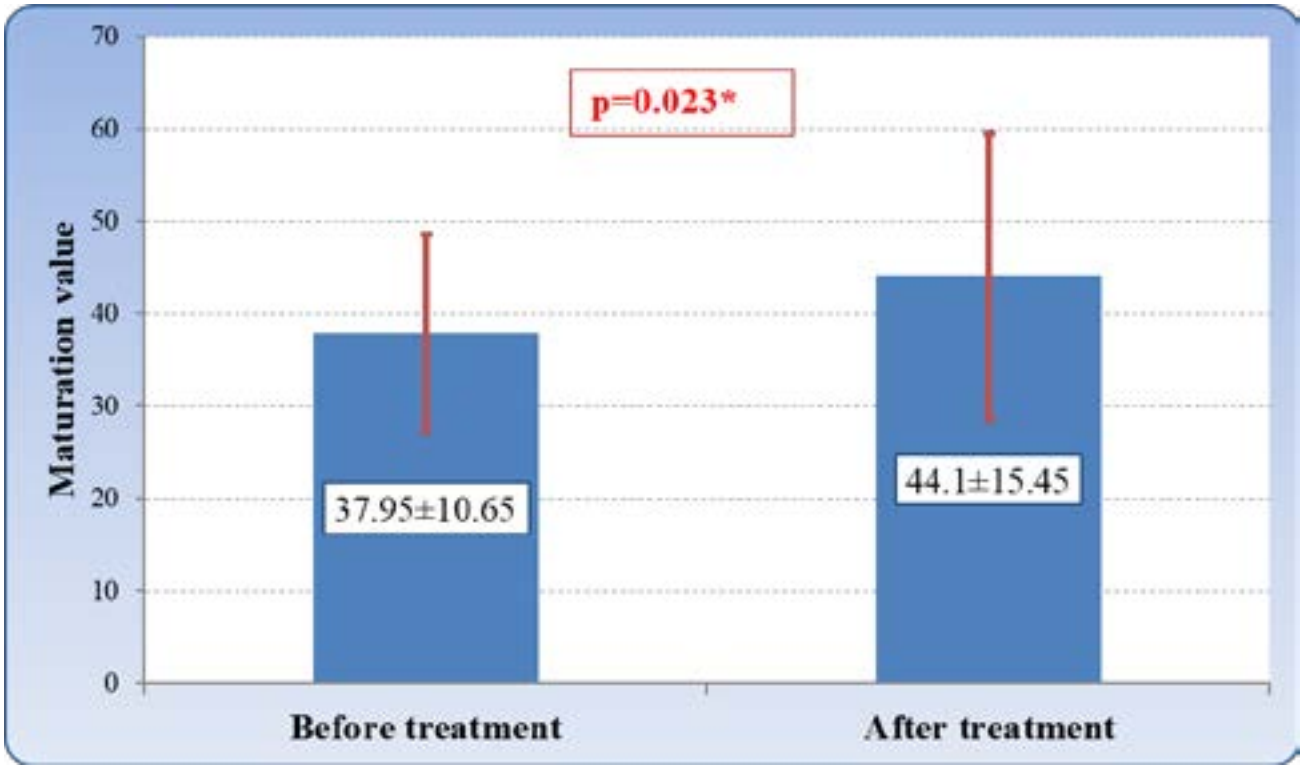

Figure 3. Effect of treatment with Premarin® on the maturation value among the participant ladies.

DISCUSSION

Atrophic vaginitis is a serious problem in gynecology because of its high prevalence and bad effect on females' life. Because of its chronic and continuous spread, finding effective treatment modalities is so important. It is vital to search for new therapies because of the limited effects of known modalities regarding side effects, effectiveness, and patient compliance with treatment[14] Atrophic vaginitis results from a decrease in plasma estrogens level in plasma, which is a feature of menopause. The estrogen receptors are highly concentrated in the lower urinary tract and the vaginal canal. Estrogen levels regulate the mucosa's collagen and mucopolysaccharide content, making the urogenital system thick and humid[15].

The synthesis of estradiol is usually considered an ovarian product. However, many other tissues also can produce estrogen from the androgen and use it in intracrine and paracrine modes. Also, many parts of the human body can produce estrogens, like adipose tissue[16].

In the present study, the body mass index was similar in both groups. As we all know, boosting estrogen levels after menopause by causing adipose tissue androgens to aromatize[17]. So, it may affect the result of the treatment. Therefore, body mass index was not a confounding factor in the present study. In our study, treatment in both groups significantly improves genital symptoms, itching and/or irritation, and dyspareunia. After therapy, all women reported feeling better or much better. An

explanation for this is that MEBO contains some active material, which accelerates blood circulation and removes stasis, dilates micro-vessels, and increases local blood flow so that it can relieve pain and itching. Farther more, it enhances a physiological environment for wound healing[18]. Bachmann and colleagues discovered that using estrogen to restore the health of the vaginal epithelium promotes vaginal compliance, reduces vaginal pH, and increases vaginal blood flow and lubrication.

Modifications in vaginal discharge and electrolytes after one month of therapy and pH and blood flow alterations after 18 to 24 months. Women reported decreased vaginal irritation, soreness, dryness, and burning sensations as they progressed toward a higher quality of life[5]. Reparative alterations were seen in both groups in this investigation. Also, in both groups of treated patients, we saw a non-significant rise in superficial and intermediate cells and a non-significant decrease in parabasal cells. Also a significant improvement in vaginal maturation value in both groups, but it was more notable in group B.

MEBO can facilitate new tissues growth and restore vitality with slough tissues removed, accelerate blood flow and remove blood stasis, enhance epidermis hyperplasia, improve ulcers and micro-circulation of tissues around to accelerate local tissues metabolism, and lead to healing target will be achieved[12]. The vaginal, urethral, bladder and pelvic floor muscles all have estrogen and progesterone receptors. Postmenopausal estrogen levels are extremely low, and atrophy of the mucosal surface occurs, which is associated with vaginitis, dyspareunia, and strictures which can affect the menopausal female quality of life. Urinary symptoms like frequency and dysuria are other symptoms of epithelial atrophy. Therefore, topical treatment with estrogen can help improve these symptoms[19].

CONCLUSION

In this study there is substantial influence of vaginal swabs on vaginal maturation in MEBO-treated individuals with symptoms of vaginal atrophy and Vaginal application of MEBO 3 times a week has a good therapeutic effect on vaginal atrophy and topical estrogen symptoms. No serious adverse events were associated with it. MEBO may be a topical estrogen replacement therapy and adjunct to systemic hormone replacement therapy in patients with vaginal atrophy.

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Potential Conflicts of Interest: None

Competing Interest: None

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REFERENCE

1. Manea MĂ, Popescu CF, Mitrut P. Correlations between gonadotropins level, vaginal cytology and menopause vessel-active phenomena. Rom J Morphol Embryol 2009;50(4):631-7.
2. Cahill K. The treatment of postmenopausal atrophic vaginitis and dyspareunia with acupuncture and Chinese herbs: a case study. J Chin Med 2012;99:1-6.
3. Loprinzi CL, Balcueva EP, Liu H, et al. A phase III randomized, double-blind, placebo-controlled study of pilocarpine for vaginal dryness: NCCTG study N04CA. J Support Oncol 2011;9(3):105.
4. Mac Bride MB, Rhodes DJ, Shuster LT. Vulvovaginal atrophy. Mayo Clin Proc 2010;85(1):87-94.
5. Krause M, Wheeler TL, Snyder TE, et al. Local effects of vaginally administered estrogen therapy: a review. Int Urogynecol J 2009;15(3):105-14.
6. Jirapinyo M, Titivanichpiwong A. Effects of non-vaginal route hormonal replacement therapy on vaginal maturation index in postmenopausal women. Siriraj Med J 2008;60:20-2.
7. Reiter S. Barriers to effective treatment of vaginal atrophy with local estrogen therapy. Int J Gen Med 2013;6:153-8.
8. Naumova I, Castelo-Branco C. Current treatment options for postmenopausal vaginal atrophy. Int J Womens Health 2018;10:387-95.
9. Van der Laak JA, de Bie LM, de Leeuw H, et al. The effect of Replens® on vaginal cytology in the treatment of postmenopausal atrophy: cytomorphology versus computerised cytometry. J Clin Pathol 2002;55(6):446-51.
10. Lynch C. Vaginal estrogen therapy for the treatment of atrophic vaginitis. J Womens Health (Larchmt) 2009;18(10):1595-606.
11. Zhan HB, Sun QQ, Yan L, et al. Clinical study of MEBO combined with jinhuang powder for diabetic foot with infection. Evid Based Complement Alternat Med 2021;2021:5531988.
12. Junying W, Chuanping H, Yuling J. MEBO for treating skin injury and phlebitis caused by extravasation of chemotherapeutic drugs. Chin J Burns Wounds Surf Ulcers 2000;4:57-9.
13. Jewo PI, Fadeyibi IO, Babalola OS, et al. A comparative study of the wound healing properties of moist exposed burn ointment (MEBO) and silver sulphadiazine. Ann Burns Fire Disasters 2009;22(2):79-83.
14. Benini V, Ruffolo AF, Casiraghi A, et al. New innovations for the treatment of vulvovaginal atrophy: an up-to-date review. Medicina (Kaunas) 2022;58(6):770.
15. Palacios S, Nappi RE, Bruyniks N, et al. The European Vulvovaginal Epidemiological Survey (EVES): prevalence, symptoms and impact of vulvovaginal atrophy of menopause. Climacteric 2018;21(3):286-91.
16. Nelson LR, Bulun SE. Estrogen production and action. J Am Acad Dermatol 2001;45(3 Suppl):S116-24.
17. Kaaks R, Lukanova A, Kurzer MS. Obesity, endogenous hormones, and endometrial cancer risk: a synthetic review. Cancer Epidemiol Biomarkers Prev 2002;11(12):1531-43.
18. Zhi XL, Lin LL. Clinical experience with MEBO in treating 76 cases of chronic cheilitis. Chin J Burns Wounds Surf Ulcers 2000;4:296-7.
19. Palacios S, Castelo-Branco C, Cancelo MJ, et al. Low-dose, vaginally administered estrogens may enhance local benefits of systemic therapy in the treatment of urogenital atrophy in postmenopausal women on hormone therapy. Maturitas 2005;50(2):98-104.