Climacteric. 2012 Oct;15(5):455-9. doi: 10.3109/13697137.2011.644360. Epub 2012 Feb 9.

Endometrial response to concurrent treatment with vaginal progesterone and transdermal estradiol.

Fernández-Murga L, Hermenegildo C, Tarín JJ, García-Pérez MÁ, Cano A.

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Abstract

ABSTRACT Objective To describe the effect of the intermittent administration of vaginal progesterone and a low-dose estradiol patch on endometrial stability, as assessed by the rate of amenorrhea and endometrial stimulation. Methods This was an open study in which 64 moderately symptomatic, postmenopausal women were treated in the outpatient clinic of our University Hospital for different intervals up to 1 year. The treatment consisted of a combination of patches delivering 25 μg/day estradiol and intravaginal pills containing 100 mg of micronized progesterone. Patches and pills were administered concomitantly in a twice-a-week protocol. The endometrial response was assessed by endovaginal ultrasound completed with suction biopsy when required. Results Both cumulative amenorrhea and no-bleeding rates increased progressively and reached 88.9% and 100.0%, respectively, by the 12th month. Isolated or repetitive episodes of bleeding, bleeding and spotting, or only spotting were reported by three, four, and 12 women, respectively. Endometrial thickness remained unaltered. Endometrium was atrophic in the seven women in whom a biopsy was performed. Conclusion The substantially reduced progestogen load determined by this combination achieved an acceptable incidence of spotting or bleeding when associated with a low estrogenic dose. There was no apparent endometrial stimulation. Additional studies are required to confirm this observation.

PMID: 22321028 [PubMed - indexed for MEDLINE]

Minerva Ginecol. 2012 Aug;64(4):321-9.

Role of high molecular weight hyaluronic acid in postmenopausal vaginal discomfort.

Grimaldi EF, Restaino S, Inglese S, Foltran L, Sorz A, Di Lorenzo G, Guaschino S.

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Abstract

AIM: Aim of the present study was to quantify the intensity of vulvovaginal symptoms before and after **treatment** with high molecular weight **hyaluronic acid** (HA), to test the tolerability and safety of the product, to evaluate the effect on the quality of life and the compliance to the **treatment**.

METHODS: This was a double-blind randomized placebo-controlled study. In seven months we enrolled 36 post-menopausal **women**, equally distributed in placebo and active group. The evaluation was based on at least three atrophy-related signs and on the patient reported symptoms. After the written informed consent, the participants were instructed to apply the gel (drug or placebo) daily. Three days after the end of the **treatment** the patients received a final examination to evaluate the progress of symptoms, the presence of any adverse events and their correlation with the **treatment**.

RESULTS: Self-evaluation scales and investigator evaluation showed that the vaginal dryness was significantly reduced both in placebo and in the active group; however, high molecular weight HA was the only active **treatment** in reducing significantly itching and burning ($P<0.02$ and <0.04 respectively). Both treatments significantly reduced vaginal atrophy ($P<0.001$), erythema ($P<0.01$ placebo and $P<0.001$ HA) and vaginal dryness ($P<0.001$), but HA **treatment** was significantly more effective on the first two symptoms. Both treatments were very well tolerated and compliance of the **treatment** was very high.

CONCLUSION: High molecular weight HA could be effective in subjective and objective improvement of **postmenopausal** vaginal atrophy providing a good compliance. No adverse events occurred during the entire period of the study.

PMID: 22728576 [PubMed - indexed for MEDLINE]

Arch Gynecol Obstet. 2011 Mar;283(3):539-43. doi: 10.1007/s00404-010-1382-8. Epub 2010 Feb 5.

The comparison of hyaluronic acid vaginal tablets with estradiol vaginal tablets in the treatment of atrophic vaginitis: a randomized controlled trial.

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Abstract

OBJECTIVE: To compare the effectiveness of the vaginal tablets of **hyaluronic acid** and estrodiol for the **treatment** of atrophic vaginitis.

MATERIALS AND METHODS: Forty-two **postmenopausal women** with symptoms of atrophic vaginitis were randomized to take vaginal tablets of 25 μg estradiol (n = 21) (group I) or 5 mg **hyaluronic acid** sodium salt (n = 21) (group II) for 8 weeks. The symptoms of atrophic vaginitis were evaluated by a self-assessed 4-point scale of composite score and the degree of epithelial atrophy was determined as, none, mild, moderate and severe. Vaginal pH and maturation index were measured and compared in both the groups.

RESULTS: The symptoms were relieved significantly in both the groups ($P < 0.001$). The relief of symptoms was significantly superior in group I compared with group II ($P < 0.05$). A significant decrease in epithelial atrophy and vaginal pH were detected in both the groups ($P < 0.01$) after **treatment**. The vaginal maturation values were also significantly improved at both study groups ($P < 0.001$). The mean maturation value was significantly higher in group I when compared with group II ($P < 0.001$).

CONCLUSION: Both treatments provided relief of vaginal symptoms, improved epithelial atrophy, decreased vaginal pH, and increased maturation of the vaginal epithelium. Those improvements were greater in group I. **Hyaluronic acid** vaginal tablets can be used in patients with atrophic vaginitis who do not want to or can not take local estrogen **treatment**.

Comment in

The comparison of **hyaluronic acid** vaginal tablets in the **treatment** of atrophic vaginitis. [Arch Gynecol Obstet. 2012]

PMID: 20135132 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

Eur Rev Med Pharmacol Sci. 2008 Nov-Dec;12(6):411-6.

Effectiveness and safety of vaginal suppositories for the treatment of the vaginal atrophy in postmenopausal women: an open, non-controlled clinical trial.

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Abstract

Menopause, due to the physiological decrease in the estrogens levels, is often associated with many symptoms related to **vaginal atrophy** such **vaginal** dryness, dyspareunia, burning, itching, decreasing in libido and therefore a worsening of the quality of life and in particular of the sexual activity. There are many pharmacological remedies to solve these events, first of all hormone replacement therapy (HRT) that up to the 90s was the therapy of choice for the care of the menopause symptoms. This hormonal therapy, however, has been re-considered due to its side effects. As alternative, a clinical trial has been performed to investigate the efficacy and **safety**, in postmenopausal women with urogenital **atrophy**, of the use of **suppositories** for **vaginal** use, containing hyaluronic acid, vitamin E and vitamin A. The trial, according to a open, non-controlled design, was performed on 150 postmenopausal women, 1 **vaginal** suppository per day, for the first 14 days and then a **vaginal** suppository, day in and day out, for other 14 days. The primary endpoint was the evaluation of **vaginal** dryness assessed by a Visual Analogue Scale (VAS) both by the investigator and the patient. The secondary endpoints were the evaluation of all the other symptoms and signs associated with the **vaginal atrophy** (itching, burning, dyspareunia, **vaginal** inflammation or swelling, irritation, assessed by a 4-point scale, presence of **vaginal** abrasions and irritation), and the recording of the adverse events occurring during the trial. The patients have not reported adverse effects during the **treatment**, and the results in terms of **effectiveness** on the **vaginal atrophy** symptoms were markedly positive. A high level of compliance was registered. The product tested can therefore be considered a safe and effective alternative for the **treatment** of **vaginal atrophy** symptoms in postmenopausal women, especially when HRT is not recommended.

PMID: 19146203 [PubMed - indexed for MEDLINE]

Menopause. 2004 Jan-Feb;11(1):49-56.

Efficacy of low-dose intravaginal estriol on urogenital aging in postmenopausal women.

Dessole S, Rubattu G, Ambrosini G, Gallo O, Capobianco G, Cherchi PL, Marci R, Cosmi E.

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Abstract

OBJECTIVE: To assess the **efficacy** and safety of **intravaginal estriol** administration on urinary incontinence, **urogenital** atrophy, and recurrent urinary tract infections in **postmenopausal women**.

DESIGN: Eighty-eight **postmenopausal women** with **urogenital aging** symptoms were enrolled in this prospective, randomized, placebo-controlled study. Participants were randomly divided into two groups, with each group consisting of 44 **women**. **Women** in the treatment group received **intravaginal estriol** ovules: 1 ovule (1 mg) once daily for 2 weeks and then 2 ovules once weekly for a total of 6 months as maintenance therapy. **Women** in the control group received inert placebo vaginal suppositories in a similar regimen. We evaluated **urogenital** symptomatology, urine cultures, colposcopic findings, urethral cytologic findings, urethral pressure profiles, and urethrocystometry before as well as after 6 months of treatment.

RESULTS: After therapy, the symptoms and signs of **urogenital** atrophy significantly improved in the treatment group in comparison with the control group. Thirty (68%) of the treated participants, and only seven (16%) of the control participants registered a subjective improvement of their incontinence. In the treated participants, we observed significant improvements of colposcopic findings, and there were statistically significant increases in mean maximum urethral pressure, in mean urethral closure pressure as well as in the abdominal pressure transmission ratio to the proximal urethra. Urethrocystometry showed positive but not statistically significant modifications.

CONCLUSIONS: Our results show that **intravaginal** administration of **estriol** may represent a satisfactory therapeutic choice for those **postmenopausal women** with **urogenital** tract disturbances who have contraindications or refuse to undergo standard hormone therapy.

Comment in

Are all estrogens created equal? [Menopause. 2004]

PMID: 14716182 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

PubMed efficacy of vaginal use of topical estriol in postmenopausal women

Display Settings: Abstract

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Clin Exp Obstet Gynecol. 2011;38(2):143-5.

Efficacy of vaginal use of topical estriol in postmenopausal women with urogenital atrophy.

Chuery AC, Speck NM, de Moura KF, Belfort PN, Sakano C, Ribalta JC.

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Abstract

OBJECTIVE: This study evaluates the effect of intravaginal **estriol** on **urogenital atrophy**, Pap smear parameters, colposcopy parameters and discomfort during gynecological examination.

METHODS: 31 **postmenopausal women** who had not used hormone therapy in the previous six months were studied. All **women** used intravaginal **estriol**, 1 mg/day for 21 days. The following variables were analyzed before and after treatment: complaints of **urogenital atrophy**; cytological parameters, colposcopic parameters, and subjective evaluation of discomfort during gynecologic examination.

RESULTS: All **urogenital atrophy** complaints improved after treatment. At the first visit, 45.2% of **women** presented a predominance of profound cells, 51.6% with predominance of intermediate cells, and 3.2% with predominance of superficial cells. At the second visit, these rates were 35.5%, 64.5%, and 0%, respectively. Evaluation of the maturation index showed that 83.9% of **women** had atrophic Pap smears, and 16.1% showed good estrogenic level before treatment. At the second visit, atrophic smears occurred in 12.9%, and 87.1% of **women** exhibited good estrogenic level (chi2 = 20.045; p = 0.000). Colposcopy showed that 71% of **women** had atrophic colpitis and/or petequiae before treatment, while **atrophy** after therapy was present in only 6.4%. The evaluation of other colposcopic parameters also improved after treatment. Great discomfort was reported by 19.4% before and by 0% after treatment.

CONCLUSION: Intravaginal **estriol** 1 mg/day for a period of 21 days was efficient in improving **urogenital atrophy**, Pap smear parameters and colposcopic evaluation in **postmenopausal women**.

PMID: 21793275 [PubMed - indexed for MEDLINE]

MeSH Terms, Substances

LinkOut - more resources

Maturitas. 2012 Apr;71(4):360-8. doi: 10.1016/j.maturitas.2011.12.022. Epub 2012 Jan 28.

Low dose estriol pessaries for the treatment of vaginal atrophy: a double-blind placebo-controlled trial investigating the efficacy of pessaries containing 0.2mg and 0.03mg estriol.

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Abstract

OBJECTIVE: The aim of the study was to confirm the superior efficacy of **estriol** containing **pessaries** compared to placebo in the **treatment** of **vaginal atrophy**.

STUDY DESIGN: In a prospective, multicenter, randomized, placebo-controlled, double-blind study, 436 postmenopausal women with **vaginal atrophy** (**vaginal** maturation index, VMI<40%; **vaginal** pH>5; most bothersome symptom, MBS≥65 on visual analogue scale, VAS) were treated with **pessaries** containing either 0.2mg **estriol** (N=142) or 0.03mg **estriol** (N=147) or with a matching placebo (N=147) for 12 weeks.

MAIN OUTCOME MEASURES: Primary efficacy endpoints included increase in VMI, decrease of the **vaginal** pH value and decrease in intensity of MBS after 12 weeks of **treatment**.

RESULTS: The increase in VMI was significantly greater under 0.2mg **estriol** and 0.03mg **estriol** (46.3±17.0 and 38.4±19.4, respectively) compared to placebo (23.9±21.5; p values<0.001), **vaginal** pH decreased significantly more (-1.6±0.8 and -1.4±0.9, respectively) compared to placebo (-0.6±0.8; p values<0.001) and MBS intensity (VAS) declined significantly more (-52.2±23.7 and -47.1±23.4, respectively) compared to placebo (-31.8±26.3; p values<0.001). Adverse events were rare and occurred at similar rates in all three groups.

CONCLUSIONS: Superiority of **estriol** containing **pessaries** over placebo was shown in the local **treatment** of **vaginal atrophy**. Even a very **low dose** of 0.03mg **estriol** proved sufficient for local **treatment** of **vaginal atrophy** with excellent tolerability.

PMID: 22285095 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

LinkOut - more resources

Maturitas. 2005 Feb 14;50(2):98-104.

Low-dose, vaginally administered estrogens may enhance local benefits of systemic therapy in the treatment of urogenital atrophy in postmenopausal women on hormone therapy.

Palacios S, Castelo-Branco C, Cancelo MJ, Vázquez F.

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Abstract

BACKGROUND: When genital atrophy exists, systemic hormone therapy (HT) has a timing until to induce **vaginal** proliferation and symptomatic relieve. Thus, in order to obtain a prompt improvement, the association of **local** therapy acting on the genital epithelium to the systemic treatment should be considered.

OBJECTIVE: To evaluate the effects of a combined therapy consisting of **vaginal** estriol with transdermal 17-beta-estradiol (50 microg/day) plus medroxyprogesterone acetate (5 mg/day) per os in shortening the period of uro-genital symptoms.

SUBJECTS AND METHODS: In a randomized, double blind, controlled with placebo study, 27 women with climacteric symptoms and atrophic vaginitis were treated for 4 months with HT plus **vaginal** estriol 0.5 mg/day (group E) or placebo (group P). Patients use the **local** medication daily for the first 3 weeks and twice-weekly thereafter. Before entering in the study, patients were asked about HT and selected for inclusion. In the first visit, electible patients after written informed consent were randomized to receive HT plus **local** estriol or placebo. All the subjects had baseline studies, including medical history, physical examination, blood and urine analysis. In order to evaluate the effect of **local** treatment on urinary and genital symptoms, a score for genital, urinary and colposcopic complaints (0 minimum-100 maximum) was developed. This score and Blatt-Kuperman were recorded and performed in every control. Results: There were no differences on climacteric symptoms relief between the two groups. Additionally, the improvement in urinary symptoms at the end of the study was similar for both groups (from 16.5 +/- 6.1 to 8.5 +/ - 2.4 for E group and from 15.8 +/- 7.8 to 8.8 +/- 2.7 for P group; $P < 0.01$ versus basal); however, those women in group E reached significant improvement on urinary complaints since the first month of treatment. Additionally, a significant difference between E and P was observed at months 2 and 3, although no differences were detected at the end of the study. Papanicolaou smear showed reactive or reparative changes and karyopyknotic index exhibited a significant increase in superficial cells in both groups and at the end of the study.

CONCLUSIONS: Adding **vaginal** estriol to HRT may shorten the latency period for urinary symptoms.

Menopause. 2012 Oct;19(10):1130-9.

The therapeutic effect of a new ultra low concentration estriol gel formulation (0.005% estriol vaginal gel) on symptoms and signs of postmenopausal vaginal atrophy: results from a pivotal phase III study.

Cano A, Estévez J, Usandizaga R, Gallo JL, Guinot M, Delgado JL, Castellanos E, Moral E, Nieto C, del Prado JM, Ferrer J.

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Abstract

OBJECTIVE: The aim of this study was to evaluate the efficacy and safety of a **new low-concentration estriol formulation** (0.005% **estriol** vaginal **gel**), providing an **ultra low** dose of **estriol** per application (50 μg), for the local treatment of postmenopausal vaginal atrophy.

METHODS: Postmenopausal women with symptoms and signs of vaginal atrophy were enrolled in a prospective, double-blind, placebo-controlled study. Women received either 1 g of vaginal **gel** containing 50 μg of **estriol** or placebo **gel**, daily for 3 weeks and then twice weekly up to 12 weeks. A cytological vaginal study, evaluation of vaginal pH, and assessment of symptoms and signs of vaginal atrophy were performed, and changes between baseline and weeks 3 and 12 were assessed. Adverse events were recorded.

RESULTS: A total of 167 women were included (114 received **estriol** and 53 received placebo). After 12 weeks of therapy, a superiority of **estriol** compared with placebo **gel** was shown in the change in maturation value and vaginal pH ($P < 0.001$ and $P < 0.001$, respectively). The superiority of **estriol** was well demonstrated in improvement of vaginal dryness ($P = 0.001$) and the Global Symptom Score ($P = 0.018$). **Estriol gel** proved also superior in the improvement of several of the most outstanding vaginal signs of vaginal atrophy evaluated. After 3 weeks, **estriol gel** also showed a superiority over the placebo **gel** in most symptoms and signs evaluated. Treatment-related adverse events were similar among groups.

CONCLUSIONS: 0.005% **Estriol** vaginal **gel**, a **new formulation** providing an **ultra low** dose of **estriol** per application, was shown to be safe and effective in the treatment of postmenopausal vaginal atrophy.

PMID: 22914208 [PubMed - in process]

Publication Types

LinkOut - more resources

Menopause. 2009 Sep-Oct;16(5):978-83. doi: 10.1097/gme.0b013e3181a06c80.

Efficacy and safety of vaginal estriol and progesterone in postmenopausal women with atrophic vaginitis.

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Abstract

OBJECTIVE: The aim of this study was to assess the **efficacy** and **safety** of intravaginal **estriol** and **progesterone** on **atrophic vaginitis** in **postmenopausal women**.

METHODS: Under a physician-sponsored Investigational New Drug application, 19 healthy **postmenopausal women** with **atrophic vaginitis** received **vaginal** suppositories containing **estriol** (1 mg) and **progesterone** (30 mg). The participants were instructed to insert one suppository intravaginally once daily for 2 weeks and thrice weekly for a total of 6 months. **Vaginal** pH, **Vaginal** Maturation Index, urinalysis, self-reported **vaginal** dryness, menopausal quality of life, and serum **estriol** and **progesterone** levels were measured at enrollment and after 3 and 6 months of suppository use. Endometrial biopsies were obtained at enrollment and at 6 months. After 2 weeks of therapy, six participants had serum **estriol** and **progesterone** measured.

RESULTS: The **Vaginal** Maturation Index, **vaginal** pH, and **vaginal** dryness rating improved significantly at 3 and 6 months compared with baseline. Menopausal quality of life scores improved significantly in all domains, with the sexual subscale showing the most improvement. There were no cases of endometrial hyperplasia after 6 months of suppository use. Serum preinsertion **estriol** at week 2 and months 3 and 6 were similar to baseline levels. Serum preinsertion **progesterone** increased but returned to baseline preinsertion levels at month 6, and preinsertion levels were significantly less at month 6 compared with month 3.

CONCLUSIONS: Intravaginal administration of a combination **estriol** and **progesterone** agent to **women** with **atrophic vaginitis** may represent a safe and effective alternative to systemic hormone replacement, although this study was not adequate to provide proof of **efficacy** given that it was uncontrolled.

PMID: 19390463 [PubMed - indexed for MEDLINE]

Gynecol Endocrinol. 2010 Jun;26(6):404-12. doi: 10.3109/09513591003632258.

Low-dose vaginal estrogens or vaginal moisturizer in breast cancer survivors with urogenital atrophy: a preliminary study.

Biglia N, Peano E, Sgandurra P, Moggio G, Panuccio E, Migliardi M, Ravarino N, Ponzone R, Sismondi P.

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Abstract

The study aim is to evaluate the efficacy and safety of two **low-dose vaginal** estrogen treatments (ETs) and of a non-hormonal **vaginal moisturizer** in postmenopausal **breast cancer survivors** with **urogenital atrophy**. Eighteen patients receiving estriol cream 0.25 mg (n = 10) or estradiol tablets 12.5 microg (n = 8) twice/week for 12 weeks were evaluated and compared with eight patients treated with polycarbophil-based **moisturizer** 2.5 g twice/week. Severity of **vaginal atrophy** was assessed using subjective [**Vaginal** Symptoms Score (VSS), Profile of Female Sexual Function (PFSF)] and objective [**Vaginal** Health Index (VHI), Karyopycnotic Index (KI)] evaluations, while safety by measuring endometrial thickness and serum sex hormones levels. After 4 weeks, VSS and VHI were significantly improved by both **vaginal** ETs, with further improvement after 12 weeks. PFSF improved significantly only in estriol group ($p = 0.02$). Safety measurements did not significantly change. **Vaginal moisturizer** improved VSS at week 4 ($p = 0.01$), but score returned to pre-treatment values at week 12; no significant modification of VHI, KI, PFSF was recorded. Both **low-dose vaginal** ET are effective for relieving **urogenital atrophy**, while non-hormonal **moisturizer** only provides transient benefit. The increase of serum **estrogens** levels during treatment with **vaginal** estrogen at these dosages is minimal.

PMID: 20196634 [PubMed - indexed for MEDLINE]