

Revolutionising genitourinary syndrome of menopause (GSM) treatment (new estriol + lactobacilli)

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Urogenital atrophy is characterised by the changes in the female urogenital tract due to a marked decrease in ovarian oestrogen production. The usual underlying cause of oestrogen deficiency is natural or surgical menopause but can also be triggered by lactation and premature ovarian insufficiency, radiotherapy, tamoxifen therapy or heavy smoking.¹

Oestrogen deficiency results in changes in vaginal physiology, with a decrease in barrier and lubrication functions of the epithelium and lower glycogen content leading to increased penetration by pathogens and symptoms such as a significant increase in vaginal dryness and increased risk of vaginal and urinary tract infections.² Furthermore, a decrease in sexual desire, arousal, orgasm and dyspareunia may affect a woman's quality of life, self-esteem, social life and relationship with their partner.¹

Indications

Estriol + lactobacilli combination vaginal tablets, containing at least 1×10^8 colony-forming units 900 mg viable *Lactobacillus acidophilus* and 0.03mg estriol, are indicated for atrophic vaginitis and symptomatic vaginal atrophy due to oestrogen deficiency during menopause and post-menopause.³

Mechanism of action

Estriol + lactobacilli combination has a dual mechanism of action,³ and the combination of estriol with *Lactobacillus acidophilus* has demonstrated synergistic effects on the vaginal epithelium.¹

- Estriol stimulates the proliferation and maturation of the vaginal epithelium.³ The breakdown of proliferated superficial cells releases glycogen, which serves as a substrate for lactobacilli.¹
- Lactobacilli ferment glycogen to lactic acid, resulting in an acidic environment that is unfavourable for colonisation and growth of pathogenic microorganisms, while also providing optimal conditions for proliferation of lactobacilli.³ The lactobacilli also compete with pathogens for adherence (competitive exclusion)¹, and produce hydrogen peroxide and bacteriocins, which inhibit the growth of pathogenic microorganisms.³

Local treatment with a tablet combining estriol and *Lactobacillus acidophilus*, restores a healthy vaginal epithelium and a more physiological lactobacillary flora, and re-establishes the defence mechanisms against vaginal atrophy and infection.³

Pharmacokinetics

Following vaginal application of estriol, about 20% of the dose reaches the circulation in unchanged form. Vaginal absorption of oestrogen depends on the maturation status of the epithelium – estriol absorption via a well-proliferated vaginal epithelium is markedly lower than that via an atrophic one.¹ Doses of 0.5 mg estriol twice weekly are not associated with a significant increase in serum oestrogen levels after short- (weeks) and long-term (12 months) treatment.¹

Dosing

Due to high affinity of oestrogen for oestrogen receptors in the vaginal epithelium, only a low-dose of hormone is needed to generate sufficient local effect.¹ Ultra-low dose vaginal estriol (0.03 mg), as contained in estriol + Lactobacilli combination, displays similar efficacy to that of 0.5 mg preparations, does not cause endometrial proliferation after 6 months of use and no systemic adverse events are expected due to negligible absorption.¹

Vaginal tablets should be inserted deeply (about the depth of one finger) into the vagina in the evening before retiring. This is best performed in a reclining position with the knees slightly bent towards the chest.³

One vaginal tablet should be inserted daily for at least 12 days. Subsequently, a maintenance dose of 1 vaginal tablet 2 to 3 days per week is recommended.³ For the treatment of postmenopausal symptoms, the smallest effective dose should be used for the shortest period of time.³

Efficacy

In a double blind, placebo-controlled study, 87 postmenopausal women were randomised to once daily treatment with either estriol + lactobacilli combination ($n = 44$) or placebo ($n = 43$). Patients received treatment once daily for 12 days followed by maintenance therapy twice a week for 12 weeks.³ The vaginal maturation index (VMI) increased significantly with estriol + lactobacilli combination (35,2%) compared to placebo (9,9%). The percentage of women with moderate to severe vaginal dryness decreased more with estriol + lactobacilli combination compared to placebo and the lactobacillary grade improved significantly more with estriol + lactobacilli combination when compared to placebo. The maintenance dose of

2 tablets weekly was sufficient to maintain the improved maturation and to prevent relapse of symptomatic vaginal atrophy.³

In a pivotal study cited in Mueck et al.,¹ Jaisamrarn et al. demonstrated superiority of the 0.03 mg estriol and *Lactobacillus* combination over placebo with a significantly higher increase in VMI. During initial treatment, VMI increased considerably from the start of treatment to first follow-up (after two weeks of initial treatment) and remained within the normal oestrogenisation range (>50%) during two months of maintenance therapy.¹

Important prescribing points

- Estriol + Lactobacilli combination vaginal tablets are Schedule 2 and are available in pack sizes of 6, 12 or 36 tablets.
- Store at 2–8°C, storage at room temperature for 1–2 weeks does not affect efficacy.³
- No studies are available on possible interactions between estriol + Lactobacilli combination and latex products such as condoms, diaphragms, etc. As a precaution other methods of birth control

should be used while using estriol + lactobacilli combination and for a few days after stopping treatment.⁵

- Missed doses should be taken as soon as the patient remembers. However, if it is nearly time for the next dose, skip the missed dose. Do not use a double dose to make up for forgotten individual doses.⁵
- Estriol + lactobacilli combination is safe to use in pregnancy and lactation.

References

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