Local estrogen therapy and the rescue of femininity

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“To pour out your voice, your gentleness
bocal honey and pure wade,
in my terrestrial hands the desire
its roses offers custom fire”.


One of the medium-term effects of hypoestrogenism in the genitalia is vaginal dryness. The lack of estrogenic action at epithelial level produces a thinning of the vaginal wall, the periurethral and bladder epithelium, reducing the lubrication and altering the local bacterial flora. This results in a predisposition to vaginal and urinary infections and symptoms such as burn, genital pruritus and dyspareunia. Estrogens in the patient at reproductive age have a trophic effect at the level of the mucosa of the urogenital, keeping a thickness suitable in the epithelium which allows the production of secretions, promoting a suitable vaginal and bladder environment. For this reason, the treatment of choice to improve vaginal atrophy is the use of local estrogen in the form of rings, creams or vaginal capsules or tablets for long time.

Urogenital atrophy is frequent, not only in menopausal patients, but also in young patients presenting with ovarian failure after oncological treatment, in which case, starts a systemic and/or local estrogen therapy that allows relieving symptoms and preventing infections. However, in patients with ovarian failure after chemotherapy for breast cancer with estrogen receptor positive (ER +), which may or may not be treated with anti-estrogens, there has been resistance to the use of this local estrogen therapy by the eventual systemic effect and the consequential risk of disease recurrence.

In 2012, Le Ray I and col⁴, conducted a study in patients with cancer of breast RE + in order to assess whether the local estrogen therapy increased the risk of recurrence. With a sample of 271 patients with estrogen therapy local, in a group of more than 13,000 patients on hormonal
therapy with tamoxifen or aromatase inhibitors, they found that there was no increase in the recurrence using local estrogen in patients with tamoxifen therapy. However, the results obtained in the group with aromatase inhibitors were inconclusive. Other studies have been reported with a smaller number of patients, who have not found local estrogen therapy effects related to the advance and the relapse of the disease in patients with cancer of breast ER +.

In March 2016, the Committee on Gynecologic Practice of the American College of Obstetrician and Gynecologist, published in the journal Obstetrics and Gynecology, its position on the use of vaginal estrogen in women with a history of estrogen-dependent breast cancer. The recommendations are as follows:

- Local non-hormonal treatment should be indicated as a first option for relief of the symptoms of vaginal atrophy in patient during and after breast cancer treatment.
- The use of local estrogen should be reserved only for patients who do not respond to non-hormonal treatment.
- The decision should be taken in conjunction with the oncologist and the patient should consider the risks and benefits of the use of vaginal estrogens in her condition.
- Data do not show an increase in the recurrence of cancer in patients undergoing vaginal treatment with estrogen.

As the evidence of this last statement is not yet strong and because of the shyness of the conclusions of the Committee, it is important to clarify some aspects of local estrogen therapy. Systemic estrogen levels that can be seen product of vaginal absorption may vary depending on the type of oestrogen involved in the formulation. In addition, it is important to take into account the dosage, in terms of quantity and frequency of administration, which also modifies serum hormone levels. I.e. not all estrogens have the same bioavailability profile after absorption and most likely, by regulating the frequency of administration systemic levels can be decreased, improving vaginal atrophy, which is the goal of treatment, without increasing the risk of recurrence of the malignancy.

There are several types of topical estrogens available, including 17βestradiol, estradiol hemihydrate, conjugated equine estrogens (CEE), mentioned on the suggestions of the Advisory Committee, and estriol, and promestriene, not mentioned but available in many countries. The estrogens to be used must be those designed for local treatment, as there are some presentations with a profile of greater absorption which are used for vaginally replacement therapy and therefore increase systemic estrogen. Generally, low-dose vaginal route has little systemic effects. In a review of the promestriene, a derivative of estradiol, which due to its conformation does not penetrate the basal membrane of the vaginal epithelium, so that systemic levels are virtually non-existent, therefore it is recommended as a local estrogen therapy safe in patients with cancer of breast ER+. When comparing the promestriene with other local estrogenic therapies, its local action was similar and with less systemic effect. On the other hand the estriol, a low potency estrogen but easily absorbed through the mucosa, differs from 17β estradiol,
estradiol hemihydrate and CEE, which are more potent estrogen but with a lower level vaginal absorption profile\(^3\).

Another factor to consider is the capacity of absorption of an atrophic vaginal mucosa compared with a normal mucosa. The absorption of estrogen during atrophy is much higher than in a eutrophic mucosa, is for this reason that it is necessary to start with the minimum dosage and increase gradually, if necessary, when the vaginal epithelium is recovering, avoiding the initial increase of serum estrogen levels.

Although there is not enough evidence, recommended caution with the use of estrogen in patients treated with aromatase inhibitors, as it may reduce their effectiveness. In these cases, if the local non-hormone treatment does not improve symptoms, is recommended to monitor the levels of serum estradiol when using vaginal estrogens to ensure that they remain at low levels.

It should be indicated the use of the local low absorption estrogen only, with the lowest possible dose, which in turn produces relief of symptoms and preferably in combination with local non-hormonal therapies to optimize the effects of both treatments. Improving the well-being of the patient will result in a better quality of life, reducing side effects and procuring a better tolerance that will increase the adherence to adjuvant endocrine therapy, which would avoid relapses by abandonment of therapy. Less radical surgical treatments have fortunately allowed many patients preserve a proper body image and maintaining normal vaginal function would add to the rescue of that femininity that it was falsely believed lost after treatment of breast cancer.


References: