Review

Managing urogenital atrophy

Santiago Palacios

Palacios Institute of Woman’s Health, Antonio Acuña, 9, 28009 Madrid, Spain

ARTICLE INFO

Article history:
Received 16 January 2009
Received in revised form 28 April 2009
Accepted 29 April 2009

Keywords:
Urogenital atrophy
Vagina
Urinary tract
Oestrogen
Vaginal lubricants and moisturizers

ABSTRACT

The objective of this review is to provide a practical guide on the diagnosis and clinical management of urogenital atrophy. A literature search was done in Medline (1969–2008) for original reports, meta-analysis and guidelines in English on urogenital atrophy. This is a common menopausal problem and is caused by oestrogen deficiency. Fifteen per cent of pre-menopausal women and 40–57% of post-menopausal women have symptoms resulting from urogenital atrophy. However, less than 25% of these women receive medical care. Lubricants are temporary measures to relieve vaginal dryness during intercourse and moisturizers give longer symptomatic relief. Oestrogen given systemically or locally in all dosage regimens is effective, but topical vaginal application alone is preferred if systemic treatment is not needed. Treatment is long term and may be required for many years.

© 2009 Elsevier Ireland Ltd. All rights reserved.

Contents

1. Introduction ........................................................................................................................................... 315
2. Pathophysiology ................................................................................................................................. 316
3. Diagnosis ............................................................................................................................................... 316
3.1. Clinical history .................................................................................................................................. 316
3.2. Clinical examination ........................................................................................................................ 316
3.3. Laboratory tests ................................................................................................................................ 316
4. Therapeutic management .................................................................................................................... 316
4.1. Non-hormonal treatments ................................................................................................................ 316
4.1.1. Vaginal lubricants .................................................................................................................... 316
4.1.2. Vaginal moisturizers ................................................................................................................ 316
4.2. Hormonal treatments ....................................................................................................................... 317
5. Conclusions .......................................................................................................................................... 317
Conflict of interest statement .................................................................................................................. 317
References ................................................................................................................................................ 317

1. Introduction

The marked decline in ovarian oestrogen secretion at the menopause gives rise to important changes in the urogenital tract. These may vary considerably from one individual to another.

At one end of the spectrum are women whose urogenital changes are very gradual and hardly perceived, and at the other are those who suffer rapid and severe atrophic changes. In general, women who have sudden oestrogen deprivation, such as that caused by bilateral oophorectomy or pelvic irradiation will suffer more rapid changes and experience more significant symptoms, including vaginal dryness, vaginal/vulvar irritation and soreness, dyspareunia and recurrent urinary tract infections [1]. Furthermore, an increase in pH due to lower lactic acid levels permits the growth of pathogens [2,3].

Fifteen per cent of pre-menopausal women and 40–57% of post-menopausal women have symptoms resulting from urogenital atrophy (UGA) [4,5]. The prevalence of vaginal dryness is 27–55% [6,7], dyspareunia can affect up to 40% of women over 50 [8] and the incidence of lower urinary tract infections ranges between 6% and 8% [9]. Despite the condition being common, less than 25% of these women receive medical care [10].

The high prevalence of UGA and its impact on quality of life shows the importance of this condition. In order to update the management of UGA, a literature search was done in Medline (1969–2008) for original reports, meta-analyses and guidelines in
English. This resulting review is a practical guide to diagnosis and management.

2. Pathophysiology

Oestrogen receptors are present in the vulva, the vagina and the pelvic floor muscles [11,12]. The number of oestrogen receptors in the vaginal mucosa decreases after the menopause. Oestrogen receptors never disappear completely and, in response to exogenous oestrogens, the number of receptors in the vagina can return to pre-menopausal levels [13]. This activation of oestrogen receptors produces an increase in vaginal secretions and epithelial proliferation and vascularisation leading to glycogen deposition and a reduction in vaginal pH due to higher lactic acid production [14].

The bladder and urethra develop from the cloaca. The entry point of the mesonephric ductus divides the cloaca into a cranial portion, from which arises the bladder and the proximal urethra, and a distal portion or urogenital sinus which becomes the distal urethra and vaginal vestibule. It is not surprising, therefore, to find oestrogen receptors in the mucosa of the urethra, vaginal fornix and bladder [15] as well as in the connective tissue surrounding the urethra [16]. After the menopause, the urethral mucosa is atrophic and the collagen content in the connective tissue decreases [17]. There is a reduction in vascular flow in the urethra and the sensitivity of the urethral musculature to adrenergic stimulation diminishes. These effects are reversed when exogenous oestrogens are administered [18].

Oestrogens are vasoactive hormones, which increase blood flow by stimulating the release of endothelial mediators such as nitric oxide, prostaglandins and endothelium-derived hyperpolarizing factor [19]. Acute oestrogen deprivation causes a fall in blood flow in the lower urogenital tract. Studies conducted on blood flow in the vulva, as measured by laser-doppler, have found that blood flow velocity increases after administration of exogenous oestrogens with concurrent increases in vaginal secretion and improvement in sexual function [20].

The vagina, the bladder and urethra are surrounded by dense connective tissue of which the most important component is collagen. It has been shown that dermal collagen decreases after the menopause and that this process can be halted with oestrogen therapy [21,22]. Likewise, the collagen surrounding the urogenital tract can diminish after the menopause and increase after oestrogen administration [23,24].

3. Diagnosis

Clinically oestrogen deficiency produces a series of changes in the urogenital tract including predisposition to vaginal infections by a variety of pathogens (streptococci, staphylococci, coliform and diphtheroid bacteria) [25], fissures, petechial haemorrhages and ulceration [25].

Diagnosis requires a clinical history, gynaecological examination and laboratory tests.

3.1. Clinical history

The physician needs to be aware that women may be reluctant to seek help and will need to initiate the dialogue about vaginal dryness, sexual activity and dyspareunia [26,27]. During the conversation, it is important to be made aware of the use of substances which could produce symptoms similar to those of UGA or worsen existing ones, such as perfumes, soap, deodorant, lubricants and spermicides.

Symptoms include vaginal dryness, burning, dyspareunia, pruritus and abnormal discharge. They can have a direct impact on sexuality and are strongly associated with sexual dysfunction and reduced quality of life in post-menopausal women [27,28].

3.2. Clinical examination

As the vulva is an oestrogen target organ, atrophic changes in the external genitalia of post-menopausal women result from not only ageing but also oestrogen deficiency. There is a loss of elastic tissue, subcutaneous fat and pubic hair with reduced secretions from the Bartholin's glands [29].

The labia become atrophied especially the majora. Histological examination shows atrophy of the skin and dermal, papillary and reticular tissue [30]. The vaginal mucosa of post-menopausal women is pale, with reduced vascularisation and epithelial thickness. The rugae may disappear. All these changes result in atrophy leading to inflammation, petechial haemorrhages and ulceration [25].

3.3. Laboratory tests

At the menopause, the ratio of the three vaginal epithelial cell types (parabasal, intermediate, and superficial) changes due to oestrogen deficiency. The proportion of these cell types can be assessed with various scoring systems used to evaluate vaginal smears: the maturation index, the maturation value or the karyopyknosis index [31,32]. The vaginal health index attempts to assess urogenital ageing more accurately [33]. This method indicates vaginal health by scoring vaginal moistness, vaginal fluid volume, vaginal elasticity, vaginal mucosa and vaginal pH on a scale of 1 (poorest) to 5 (best). Vaginal moistness is an assessment of the appearance and spread of the secretions which coat the vagina. Healthy amounts of secretions are scored as 3, with no secretions scored as 1. Vaginal elasticity is a measure of the ability of the vaginal tissue to stretch, judged on pressure from the examiner’s finger. Vaginal epithelial integrity is a measure of the vaginal surface. It takes into account colour, thickness, and ability of the tissue to resist breaking secondary to touch. Vaginal pH can be measured with a pH strip and in atrophic vaginitis is greater than 5.

4. Therapeutic management

Therapeutic strategies are divided into non-hormonal and hormonal.

4.1. Non-hormonal treatments

4.1.1. Vaginal lubricants

These are usually used as temporary measures to relieve vaginal dryness during intercourse. There are different types which may be water, oil or silicone based. Lubricants containing hyaluronic acid [34] have recently been evaluated. Vaginal lubricants can occasionally cause irritation related to the product’s osmolarity; the greater the osmolarity, the greater the risk of irritation [35].

4.1.2. Vaginal moisturizers

These may contain a bioadhesive polycarbophil-based polymer, which attaches to mucin and epithelial cells on the vaginal wall and retains water. Moisturizers can provide more long-term relief of vaginal dryness and need to be applied less frequently than lubricants. Comparative studies of a vaginal polycarbophil moisturizer (Replens®) and oestrogens have shown the same degree of efficacy in reducing symptoms such as itching, irritation and dyspareunia [36,37]. Replens® also has a positive effect on the maturity of the vaginal epithelium [38]. Another vaginal moisturizer, based on pectin (Summer’s Eve®), has the same beneficial effect on vaginal
Low dose topical oestrogens: advantages and disadvantages.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid enterohepatic circulation</td>
<td>No systemic benefits</td>
</tr>
<tr>
<td>Lowest possible dose</td>
<td>Mode of administration unacceptable for some women</td>
</tr>
<tr>
<td>No/minimal endometrial stimulation</td>
<td></td>
</tr>
<tr>
<td>Progestogens not required</td>
<td></td>
</tr>
<tr>
<td>Minimal side effects</td>
<td></td>
</tr>
<tr>
<td>Exerts mainly local effect</td>
<td></td>
</tr>
</tbody>
</table>

dryness as Replens® [39]. We can conclude that vaginal moisturizers are an alternative choice treatment to HRT for the symptoms of UGA [40].

4.2. Hormonal treatments

All the clinical guidelines on atrophic vaginitis conclude that both systemic and local hormone replacement therapy are first choice treatments, with high efficacy rates, as they rapidly improve the maturation index and the thickness of the vaginal mucosa, reduce vaginal pH and improve the symptoms of vulvovaginal atrophy [40–43].

The 2006 Cochrane systematic review [41] identified 19 good quality trials in which 4162 post-menopausal women were randomised to different vaginal oestrogen preparations, and the endpoints were efficacy, safety and acceptability. The conclusions show that oestradiol vaginal tablets are slightly more effective than the vaginal ring and that they are both clearly superior to the placebo in improving dyspareunia, dryness and pruritus. Conjugated equine oestrogen (CEE) vaginal cream is superior to moisturizers for dryness, elasticity and vaginal flow volume and there are no differences between the three analysed preparations (CEE cream, oestradiol tablets and oestradiol-releasing ring) with regards to the proportion of responders, decrease of parabasal cells, karyopyknosis index, maturation index and vaginal health index.

The Cochrane review [41] reported no significant differences between vaginal rings, creams or tablets for endometrial thickness, hyperplasia and the proportion of women presenting adverse events. However, the risk of vaginal bleeding has been described with all local oestrogen therapies [44,45], together with a possible increase in the risk of candidiasis [46]. Most of the studies conducted with local estrogen preparations were undertaken over 3–6 months, so there is limited long term safety information [47,48].

The result of the meta-analysis conducted by Cardozo et al. [10] showed that oestrogens are more effective than a placebo and that the vaginal route is linked to a better outcome for most symptoms, concluding that all of the tested doses of oestrogens, administered both orally and vaginally, are effective in treating urogenital atrophy. Furthermore low dose local oestrogens, both oestradiol and oestril, are as effective as systemic administration. A transdermal patch releasing 14 μg of oestradiol has recently been shown to have a similar effect on the pH and vaginal maturity index, similar to that of a vaginal ring releasing 7.5 μg of oestradiol per day [49]. The advantages of low dose topical oestrogens are detailed in Table 1.

From a practical perspective, and due to the similar efficacy and safety of all local oestrogen preparations, the patient should be able to choose the preparation which she finds the most suitable. She needs to be informed that the greatest effect will be found after one to three months of treatment [10] and that the use of an additional progestogen is not necessary when using local oestrogens [43]. Duration of treatment is long term as symptoms return when treatment is stopped and annual review is recommended.

Systemic hormone replacement therapy should therefore be used when, in addition to UGA, there are other symptoms related to oestrogen deficiency such as hot flushes. However, the benefits and risks of its administration should always be discussed.

5. Conclusions

The symptoms of UGA are due to oestrogen deficiency. While not life threatening, UGA can cause discomfort and dyspareunia and result in reduced sexual activity and quality of life. Vaginal lubricants and moisturizers are all helpful but tend to provide short term relief. Oestrogen therapy is the first choice of treatment. All the available products are effective but low dose vaginal preparations are preferred in the absence of other menopausal symptoms.

Conflict of interest statement

The author declares that he has no conflict of interest.

References
