Nonhormonal therapeutic options for vaginal atrophy

Climacteric medicine deals with a vast range of conditions and diseases connected with hormone deficiency driven by age-related factors, but the two most common ones are climacteric syndrome and urogenital atrophy (UGA).

Terms and documents

UGA is a complex of vaginal and urinary symptoms connected with atrophic and dystrophic processes in the estrogen-dependent tissues and structures of the lower third of the urogenital tract, namely in the urinary bladder, urogenital tract (urethra), vagina, pelvic ligaments and pelvic floor muscles.

In 2014, the Working Group on Women’s Health and Well-Being in Menopause initiated a plea to the U.S. regulatory authorities to modify the labeling of low-dose vaginal estrogen for the treatment of postmenopausal vaginal atrophy. The plea was motivated by concerns of practicing clinicians that the boxed warning on the labels and package inserts for these products (used in systemic hormone therapy) oversate potential risks and thus adversely affect patient care.


The term “atrophic vaginitis” which is frequently used by Russian and international medical practitioners connotes a state of inflammation or infection, neither of which is a frequent occurrence in postmenopausal women. GSM is a medically more accurate, all-encompassing term, and more acceptable for medical practitioners, researchers, educators, patients and the media. The word “atrophy” has a negative connotation of loss and degradation, whereas the word “atrophy” has a term that has yet to be accepted by the media. Furthermore, VVA does not include impaired function, urinary symptoms of urgency, dysuria and recurrent urinary tract infections.

The term “GSM” will be presented and discussed at annual meetings of the two above-mentioned scientific societies. The boards of both societies officially approved the new terminology in 2014. In the Russian language, there is no well-sounding term starting with the word “genital,” and for us, the terms “urogenital atrophy” or “urogenital syndrome” are more acceptable. Let us wait for the new recommendations and see what they have to say on the matter.

Incidence and manifestations

The data on incidence of urogenital atrophic disorders (UAD) do not reflect the reality. For instance, in Barlow et al [1], which studied 2,045 British women aged 55–85+, urogenital symptoms were identified in every second woman, but only 11% of all patients drew their GP’s attention to those symptoms. According to some authors [2, 3], the frequency of UAD ranges from 3% in perimenopausal to 60% in postmenopause lasting longer than 5 years. 70% of all women affected by UAD reported decline in sexual activity, and there was a decreasing prevalence of sexual activity with increasing age. More than 30% of patients complained of dyspareunia and/or vaginal dryness and linked their sexual inactivity with those symptoms. Smoking women had UAD most frequently in a more severe form, as did women who did not seek medical care.

In the clinical presentation of menopausal UAD two aspects are identified: first, symptoms related to vaginal atrophy, and, second, urinary discomforts (cystourethral atrophy). It must be noted that quite often patients with UAD symptoms do not seek professional advice as they consider them normal manifestations of ageing [1].

Symptoms of vaginal atrophy

- Vaginal dryness, genital itching, vaginal burning
- Dyspareunia
- Recurrent vaginal discharge
- Light bleeding after intercourse
- Vaginal vault prolapse
- Discomfort with intercourse

During menopause, estrogen deficiency disrupts proliferation of vaginal epithelium and urothelium. Decreased vaginal epithelium intermediate cells and decreased glycogenated superficial cells lead to changes in vaginal flora (loss of Lactobacilli, increased pH), which might contribute to a secondary infection. Blood supply disturbance leads to vaginal, detrusor and urinary tract ischemia, resulting in reduced vaginal transudation, hyperactive bladder and stress urinary incontinence. Collagen exchange disorder and eventual collagen activity degradation occurs in the pelvic ligaments, collagen is synthesized in decreased quantities, which results in vaginal vault prolapse, disruption of urethral mobility and location, which makes a major contribution to development of stress urinary incontinence [4].

Problems

Therefore, pathogenic importance of hormone replacement therapy in the treatment of UGA is beyond doubt; however, in some cases, topical estrogens might bring about systemic effects (engorged breasts, vaginal bleeding), which causes psychological discomfort and puts acceptability of therapy in question. Furthermore, a special group of patients is comprised of individuals with various oncological problems, especially after a breast cancer surgery. Any mention of hormone replacement therapy, even of topical nature, is unacceptable not so much for the patient as for her doctor, although topical use of oestriol ointments does not cause mammary gland to develop in a systemic way. In that connection, herbal drugs rise to special relevance.

Herbal drugs

In the past few years, herbal drugs have been increasingly used to treat the symptoms of climacteric syndrome. Simultaneously, their impact on the UGA symptoms has also been discussed. Latest Russian studies (V.E. Balan, I.V. Raiaylen) have not discovered any positive impact of red clover or Cimicifuga racemosa extracts on UGA manifestations. All currently known preparations only produce systemic impact, and herbal extracts of topical application have not been used in Russia so far. At the same time, recommendations have been laid down, which suggest nonhormonal lubricants as first-line therapy for women with vaginal atrophy, and prescribe their application on a long-term basis and/or during intercourse (A Level of evidence). If nonhormonal therapy proves to be ineffective, low dosage of topical estrogens is prescribed.

Muvagel®: components and features

One of nonhormonal preparations registered in Russia is Muvagel®, a hormone-like jelly-based vaginal jelly lubricant. Its components (sodium hyaluronate, chamomile andmallow extracts, soybean and red clover vegetable phospholipids, urea, tocopheryl acetate) possess antioxidant and repairation properties, improve blood circulation in the vaginal mucous membrane, enhance the tissue tone and elasticity, and contribute to local resistance to infections of the urogenital tract. The liposomes promote delivery and absorption of the active ingredients. Muvagel® is used for the treatment of conditions accompanied by dryness of the vaginal mucous membrane caused by vaginal atrophy: premenopause, menopause and postmenopause, loss of normal ovarian function for whatever cause (including as a result of an oophorectomy), intake of oral contraceptives or barbiturates, local treatment of vaginitis by antiseptic drugs.

Pragmatic trial

In 2014, the outpatient department of the Moscow Region Scientific and Research Institute of Obstetrics and Gynecology (a public-funded healthcare facility located in the Moscow region) conducted a research to assess the impact of Muvagel®, a hormone-free preparation based on herbal extracts, on the symptoms and clinical presentations of UGA in postmenopausal women.
The purpose of the study was to investigate the impact produced by topical application of Muvagel® on the pH factor of the vaginal contents and the possibility of preventing UGA and its advance.

Research materials and methods

The study included 60 postmenopausal patients. The average age was 57 ± 6.2 years, the postmenopausal period lasting 5.7 ± 3.7 years. All patients had symptoms of mild UGA. Muvagel® was used twice a week during a period of three months.

Research methods:

- Measuring the pH of the vaginal contents with indicator strips;
- Assessing severity of UGA using the evaluations based on the Vaginal Health Index (G. Bachman [4]), Table 1.

We have used D. Barlow’s five-point scale to determine severity of vaginal atrophy symptoms (Table 2).

Results

When the patients were included in the study group, they went through a general check and vaginal examination, and minor atrophic changes of the vaginal vault and labia minora were noticed in all the patients (good elasticity, moderate transudation and lubrication, thinning of the mucosa). The pH ranged from 4.7 to 5.0 (4.9 ± 0.5 on an average).

When the vaginal atrophy symptoms (dryness, itching, dyspareunia) were assessed according to D. Barlow’s scale, those patients scored 2 points (n=86; 95.5%).

New clinical and lab examinations took place one month and three months later. The findings showed that after one month of Muvagel® use positive changes were observed in all the patients, and those changes were recorded during a vaginal exam (better vaginal elasticity and rugosity, sufficient lubrication, dense and normal epithelium).

The pH measure of the vaginal contents of the Group 1 and Group 2 women showed that it had declined to 3.5—4.5 (3.6 ± 0.25, p<0.05). When the vaginal atrophy symptoms were assessed according to D. Barlow’s five-point scale, those patients scored 0–1 points.

The above-mentioned positive dynamics of UGA manifestations remained and was observed again 3 months later, during a new examination.

Discussion

The results of the research showed that Muvagel® use is effective for patients with mild UDA, which is proven by a number of objective criteria. When Muvagel® is used on women with dyspareunia symptoms, those symptoms disappear in 63.3% of cases after one month of use, and in 80% of cases after three months of use.

In our opinion, prescribing an integrated UGA therapy regimen with multiple components, which targets different pathogenic factors, ensures best performance and helps reduce side effects. No doubt, the treatment of severe forms of UDA should be based on hormone replacement therapy. It has been shown that during climacteric estrogen deficiency disrupts proliferation of vaginal epithelium and urothelium. Emergence of vaginal atrophy symptoms is driven by changes in the vulvovaginal area, which are characterized by thinning of the mucous membranes, disturbed blood circulation and worse secretion. The vagina might contract in length, and urothelium. Emergence of vaginal atrophy symptoms includes use of hormone-based and nonhormonal preparations [5]. The latter group includes lubricants, intimate hygiene products and herbal dietary supplements (Cimicifuga, soybean, etc.), Muvagel® belongs to that group as well [2].

In connection with a review of many aspects of the use of hormone replacement therapy after a well-known study (2002) of the Women’s Health Initiative, or WHI, its effectiveness for the treatment of UGA was redefined. Vaginal atrophy symptoms remain the key indications for hormone therapy. Systemic therapy is indicated for a combination of vaginal atrophy symptoms with other climacteric disorders.

The study showed that use of the hormone-free preparation Muvagel® to treat initial manifestations of UGA in postmenopausal women improves a number of objective indicators and clinical implications, and prevents further advance of the symptoms. Therefore, the drug in question, producing a corrective action on the pH level of the vaginal contents, can be used with success for prevention and treatment of mild UGA, including cases when there are contraindications to any type of menopause hormone therapy.

Table 1. Vaginal health index

<table>
<thead>
<tr>
<th>Score</th>
<th>Index severity</th>
<th>Elasticity</th>
<th>Transudation</th>
<th>pH</th>
<th>Epithelium integrity</th>
<th>Moisture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Severest atrophy</td>
<td>None</td>
<td>None</td>
<td>&gt; 6.1</td>
<td>Petechiae, bleeding</td>
<td>Pronounced dryness, inflamed surface</td>
</tr>
<tr>
<td>2</td>
<td>Pronounced atrophy</td>
<td>Weak</td>
<td>Scanty, superficial, yellow</td>
<td>5.6—6.0</td>
<td>Bleeding after intercourse</td>
<td>Pronounced dryness, surface is not inflamed</td>
</tr>
<tr>
<td>3</td>
<td>Moderate atrophy</td>
<td>Average</td>
<td>Superficial, white</td>
<td>5.1—5.5</td>
<td>Bleeding during scraping</td>
<td>Minimal</td>
</tr>
<tr>
<td>4</td>
<td>Weak atrophy</td>
<td>Good</td>
<td>Moderate, white</td>
<td>4.7—5.0</td>
<td>Dense and thin epithelium</td>
<td>Moderate</td>
</tr>
<tr>
<td>5</td>
<td>Normal</td>
<td>Excellent</td>
<td>Sufficient, white</td>
<td>&lt; 4.6</td>
<td>Normal epithelium</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Table 2. Vaginal atrophy symptom severity score according to the Barlow scale [5]

<table>
<thead>
<tr>
<th>Score</th>
<th>Symptom severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A minor problem that does not affect everyday life</td>
</tr>
<tr>
<td>2</td>
<td>A discomfort that periodically affects everyday life</td>
</tr>
<tr>
<td>3</td>
<td>A pronounced recurrent problem that affects everyday life</td>
</tr>
<tr>
<td>4</td>
<td>A pronounced problem that continuously affects everyday life</td>
</tr>
<tr>
<td>5</td>
<td>A very pronounced problem that interferes with life</td>
</tr>
</tbody>
</table>

The Russian version of this article was published in: Zhenskaya Konsultatsiya (Women’s Health Clinic) magazine. 2015. No. 1. P. 13—14.