REVIEWS

Vaginal Estrogens for the Treatment of Dyspareunia

Michael L. Krychman, MD

Southern California Center for Sexual Health and Survivorship Medicine, Newport Beach, CA, USA

DOI: 10.1111/j.1743-6109.2010.02114.x

ABSTRACT

Introduction. Vaginal atrophy, which is associated with vaginal itching, burning, dryness, irritation, and pain, is estimated to affect up to 40% of postmenopausal women. Estrogens play a key role in maintaining vaginal health; women with low serum estradiol are more likely to experience vaginal dryness, dyspareunia, and reduced sexual activity compared with women who have higher estradiol levels.

Aims. The purpose of this review is to assess the prevalence and impact of dyspareunia, a symptom of vaginal atrophy, on the health of postmenopausal women and to evaluate treatment options using vaginal estrogens (U.S. Food and Drug Administration [FDA] approved).

Methods. Relevant published literature was identified by searching Index Medicus using the PubMed online database. The search terms *dyspareunia*, *vaginal estrogen*, *vaginal hormone therapy*, *vaginal atrophy*, and *atrophic vaginitis* were the focus of the literature review.

Results. Current treatment guidelines for vaginal atrophy recommend the use of minimally absorbed local vaginal estrogens, along with non-hormonal lubricants or moisturizers, coupled with maintenance of sexual activity. Vaginal estrogen therapy has been shown to provide improvement in the signs and symptoms of vaginal or vulvar atrophy. Vaginal tablets, rings, and creams are indicated for the treatment of vaginal atrophy, and the FDA has recently approved a low-dose regimen of conjugated estrogens cream to treat moderate-to-severe postmenopausal dyspareunia. The use of low-dose vaginal estrogens has been shown to be effective in treating symptoms of vaginal atrophy without causing significant proliferation of the endometrial lining, and no significant differences have been seen among vaginal preparations in terms of endometrial safety.

Conclusion. Women should be informed of the potential benefits and risks of the treatment options available, and with the help of their healthcare provider, choose an intervention that is most suitable to their individual needs and circumstances. **Krychman ML. Vaginal estrogens for the treatment of dyspareunia. J Sex Med 2011;8:666–674.**

Key Words. Dyspareunia; Hormone Therapy; Vaginal Therapy; Estrogen Therapy; Vaginal Atrophy; Postmenopausal Women

Introduction

Vaginal atrophy, which is associated with vaginal itching, burning, dryness, irritation, and pain [1], is estimated to affect up to 40% of postmenopausal women [2–5]. Vulvar changes associated with genital atrophy include thin, pale, smooth, and shiny appearance of the vaginal epithelium; decreased subcutaneous fat and lubrication; inflammation with patchy erythema; and increased friability [2,5]. As women progress through the menopausal transition, vulvar and vaginal atrophic changes become increasingly common [6]. Unlike other menopausal symptoms, the incidence and severity of symptoms associated with vaginal atrophy do not abate over time, but are usually progressive and unlikely to resolve spontaneously [7].

Estrogens play a key role in maintaining vaginal health [8]; postmenopausal decreases in estrogen

Financial support: Editorial support for the writing of this manuscript was provided by Bo Choi, PhD, of MedErgy, and was funded by Wyeth Pharmaceuticals, Collegeville, PA, which was acquired by Pfizer Inc in October 2009.

levels result in changes to the vaginal tissues that directly contribute to the development of vaginal atrophy, as well as reduced expression of sex steroid receptors and, consequently, reduced genital blood flow and lubrication [9]. These changes may include thinning of the vaginal epithelium, loss of vascularity in the vaginal mucosa, loss of vaginal elasticity and distensibility, decreased vaginal secretions and lubrication, and increased vaginal pH (resulting in potential increased risk of infection or tissue trauma) [2,10–12]. In the Yale Midlife Survey, women with low systemic serum estradiol were more likely to report vaginal dryness, dyspareunia, and reduced sexual activity compared with women with higher estradiol levels [13].

Compared with other menopausal symptoms, urogenital symptoms are more likely to develop after longer-term estrogen depletion, as relatively lower estrogen levels are required to maintain vaginal health than are required to prevent vasomotor and other symptoms [2,10]. Changes associated with urogenital atrophy may result in painful intercourse (dyspareunia), which can have a negative impact on sexual function [14–16]. The Menopause Epidemiology Study of 1,480 sexually active postmenopausal women [3] aged 40 to 65 years showed a significant association between dyspareunia and vaginal atrophy based on results of the Arizona Sexual Experience Scale questionnaire; women with sexual dysfunction were 3.84 times more likely to suffer from vaginal atrophy compared with women without sexual dysfunction. The effects of vaginal atrophy are far reaching, beyond having an impact on overall sexual functioning and sexual satisfaction. Women may experience frequent urinary tract infections or discomfort in the activities of daily living, such as pain while sitting or crossing their legs [8].

Both orally and vaginally administered estrogen therapies are effective for the relief of vaginal dryness and restoration of vaginal moisture; however, systemic estrogen therapy may not provide the same degree of relief for women suffering from dyspareunia compared with topical treatment. A meta-analysis [17] of data from 10 randomized controlled trials (Stouffer method) showed that vaginal estrogen therapy provided the greatest relief of symptoms and improvement in the signs of vaginal or vulvar atrophy. A recent randomized comparison of 57 postmenopausal women with previous hysterectomy [18] suggested that vaginal estrogen therapy improved some aspects of sexual function to a greater extent than oral treatment. Vaginally applied, minimally absorbed local estrogen therapy may also be more appropriate than systemic therapy for women who are not experiencing severe or debilitating vasomotor symptoms [7]. Current treatment guidelines for vaginal atrophy recommend the use of vaginal estrogens along with nonhormonal lubricants coupled with the maintenance of sexual activity [14,19].

Etiology and Diagnosis of Dyspareunia

As previously noted, declining estrogen levels associated with menopause are an important cause of vaginal atrophy leading to dyspareunia [20]. A recent systematic review [21] of 122 observational studies showed that peri-/postmenopausal status (odds ratio [OR] = 1.52; 99% confidence interval [CI], 1.22–1.89), ethnicity (OR = 1.67; 99% CI, 1.02–2.72), and previous pelvic inflammatory disease (OR = 9.98; 99% CI, 4.69–21.24) were significantly associated with dyspareunia, as were abuse/psychological factors. However, it has been noted that other known medical contributors to dyspareunia, such as vulvodynia and vestibulodynia, were not reported in this systematic review [20].

A careful, comprehensive medical assessment for dyspareunia and its etiology must be completed to exclude any other underlying pathological conditions [22]. Immunologic causes of dyspareunia include autoimmune diseases, such as lichen sclerosus and Sjögren's syndrome [20], while some commonly used over-the-counter medications such as antihistamines can adversely affect the vulvar tissues [23]. In addition, dyspareunia can be caused or impacted by gastrointestinal disorders (e.g., ulcerative colitis, irritable bowel syndrome), gynecological disorders (e.g., pelvic inflammatory disease, fibroids, endometriosis), and neurological issues (e.g., neuropathic pain, fibromyalgia, myalgic pelvic floor), to name a few possibilities [20]. These other less common but treatable entities must be ruled out when local estrogen vaginal therapy fails to eradicate or relieve dyspareunia after a reasonable trial of therapy (i.e., 6–8 weeks).

Dyspareunia has recently been defined at the 2nd International Consultation on Sexual Medicine [24] as "persistent or recurrent pain with attempted or complete vaginal entry and/or penile vaginal intercourse" that is not the result of other abnormalities (e.g., structural or physical). Three key aspects to the clinical diagnosis of dyspareunia have been described [20]: a comprehensive history of the pain, including determination of the exact