

## Review Article

# An Overview of Vulvovaginal Atrophy-Related Sexual Dysfunction in Postmenopausal Women

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## ABSTRACT

Menopause and the climacteric period are associated with adverse risk factors for the development of vulvovaginal atrophy-related sexual dysfunction. Sexual dysfunction is a common problem in postmenopausal women, often underdiagnosed, inadequately treated, frequently overlooked, and most often impairing the quality of life of these women. To provide clinicians with current information on vulvovaginal atrophy-related sexual dysfunction in postmenopausal women. This study is a literature review on vulvovaginal atrophy-related sexual dysfunction in postmenopausal women. Relevant publications were identified through a search of PubMed and Medline, selected references, journals, and textbooks on this topic, and were included in the review. The prevalence of female sexual dysfunction increases with age. It is a common multidimensional problem for postmenopausal women that alter the physiological, biochemical, psychological, and sociocultural environment of a woman. Menopause-related sexual dysfunction may not be reversible without therapy. Estrogen therapy is the most effective option and is the current standard of care for vulvovaginal atrophy-related sexual dysfunction in postmenopausal women. Sexual dysfunction is a common multidimensional problem for postmenopausal women and often impairs the quality of life of these women. Estrogen preparations are the most effective treatment. Selective estrogen receptor modulators, vaginal dehydroepiandrosterone, vaginal testosterone, and tissue-selective estrogen complexes are promising therapies, but further studies are required to confirm their role, efficacy, and safety.

**KEY WORDS:** Estrogen, postmenopausal women, sexual dysfunction, vulvo-vaginal

## INTRODUCTION

Sexual dysfunction is the persistent or recurrent inability to attain or maintain adequate genital lubrication or sexual responses, resulting in personal distress. Sexual dysfunction may involve a reduction in sex drive, a strong dislike of sexual activity, difficulty becoming aroused, inability to achieve orgasm, or pain with sexual activity or intercourse. Female sexual dysfunction is classified basically into four kinds of sexual problems such as desire disorders, arousal disorders, orgasmic disorders, and sexual pain disorders. Traditionally, sexual dysfunction in women was thought to be largely due to psychological problems. Recently, researchers are beginning to uncover many physical causes for sexual problems in women. Although many sexual

problems have an underlying psychological component, possible physical causes must be ruled out in the initial examination. Perimenopause and menopause transition is a time when changes inevitably occur, making female sexual dysfunction very common in this age group.

Sexual dysfunction is a known problem for postmenopausal women. Menopause alters the physiological, biochemical, psychological, and sociocultural environment of a woman.<sup>[1]</sup> Thus, the knowledge and perception of its symptomatology is invaluable to enable appropriate adjustment to this natural phenomenon.<sup>[1,2]</sup> These changes, if not adjusted, may have a negative impact on sexual function. The vast majority of women reach menopause and spend one-third of their lives in this state.<sup>[3]</sup> Menopause is recognized with certainty only in retrospect after 12 months of amenorrhea without obvious pathologic or physiological cause.<sup>[4]</sup> An adequate independent biologic marker for this event does not exist.<sup>[4]</sup>

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The prevalence of female sexual dysfunction increases with age, and the majority of women older than 60 years present with sexual inactivity, difficulty with intercourse, or dyspareunia.<sup>[5]</sup> Estrogen deficiency can affect other aspects of sexual function, including reduced vaginal blood flow and a reduced capacity for arousal and orgasm.

In postmenopausal women, genital arousal may be reduced and sexual pain disorders may occur as a result of the hypoestrogenic state.<sup>[6]</sup> There is a common presentation in postmenopausal women of a lack of mental arousal and a decline of sexual desire after a history of sexual pain, which can lead to the reduction of orgasmic capacity and sexual satisfaction.<sup>[2]</sup> These problems may influence sexual desire, activity, and the relationship of the couple negatively. Thus, it may be necessary to avoid such negative events by treating sexual dysfunction during menopause.<sup>[1,2]</sup> The aim of this review was to provide clinicians with current information on vulvovaginal atrophy-related sexual dysfunction in postmenopausal women.

## METHODOLOGY

We reviewed pertinent literature on vulvovaginal atrophy-related sexual dysfunction in postmenopausal women, and selected references and internet material using the PubMed and Medline databases for relevant publications in journals and textbooks on this topic.

### Pathophysiology

During climacteric, there is cessation of ovarian activity and a fall in the estrogen level with a rebound increase in the secretion of the follicle-stimulating hormone (FSH) by the anterior pituitary gland. The serum estradiol level is 30-300 pg/mL in the reproductive-aged woman depending on the phase of the menstrual cycle.<sup>[2]</sup> In postmenopausal women, this level is decreased by more than 90% to a mean of 6.5 pg/mL.<sup>[7]</sup> The principal estrogen in postmenopausal women is estrone, which also decreases by 70% after menopause.<sup>[8]</sup> Estrone is derived mainly from peripheral aromatization of androstenedione.<sup>[3]</sup> It is the lack of estrogen that causes the majority of the symptoms and pathology of menopause. Estrogen receptors are expressed in the vulvovaginal and urogenital mucosa during the reproductive years of a woman. These receptors are responsible for mediating biochemical and physiologic functions. With the loss of estrogen stimulation, changes occur within the vulvovaginal and urogenital mucosa. There is a characteristic loss of vaginal rugae and shortening and narrowing of the vagina. The thick vaginal epithelium transforms into a pale, dry, thin vaginal epithelium that is more prone to inflammation.<sup>[9]</sup> Vulvovaginal atrophy is characterized by a smooth and shiny appearance of the

vagina and patchy erythema with increased friability. The collagen fibers fuse and undergo hyalinization while the elastin fibers fragment. There is an overall loss of mucosal elasticity.<sup>[9]</sup> During menopause, there is loss of vascular support and reduced vaginal secretions with loss of vaginal transudate. There is an equally reduced cervical mucus and the number of epithelial cells reduce with advancing age.<sup>[10]</sup> The resultant decreased vaginal secretions and the delay in vaginal lubrication during sexual intercourse contributes significantly to dyspareunia in postmenopausal women. Reduced levels of estrogen cause urogenital atrophy and urogenital diaphragm weakness. The atrophic changes in the female lower genital tract lead to symptoms of dysuria, urethral discomfort, and stress incontinence.<sup>[11]</sup>

### Risk factors

The risk factors for menopause-related diseases are premature menopause, surgical menopause, radiation, chemotherapy, especially alkylating agents, smoking, caffeine, alcohol, family history of menopausal diseases, heparin, corticosteroids, and clomiphene given over a prolonged period (over 6 months) leading to estrogen deficiency.<sup>[8]</sup>

### Anatomical changes

The genital organs undergo atrophy and retrogression. The uterus becomes smaller as a result of atrophy of the muscles of the body and fundus. The connective tissues are more conspicuous. The endometrium is represented by only the basal layer with its compact deeply stained stroma and a few simple tubular glands. The lymphoid tissue and functional layer disappear.

The cervix becomes smaller, and its vaginal portion is represented by a small prominence at the vaginal vaults. The vaginal fornices gradually disappear as the cervix shrinks after menopause. Erosions, ectropions, and ulcers are seen more commonly in postmenopausal women.<sup>[12]</sup> Secretion of endocervical glandular mucin is reduced markedly, leading to vaginal dryness. The squamocolumnar junction and transformation zone migrate high into the endocervical canal. This often renders colposcopic assessment difficult.<sup>[12]</sup>

The vagina becomes narrow, and its epithelium becomes pale, thin, and dry and gets easily infected causing senile vaginitis. The vulva atrophies and the vaginal orifice narrows, and this can cause dyspareunia. The skin of the labia minora and vestibule becomes thin, pale, and dry, and there is considerable reduction in the amount of fat contained in the labia majora. Vulvovaginal atrophy often leads to vaginal dryness, itching, irritation, reduced lubrication, dyspareunia, and vaginal bleeding associated with sexual activity.<sup>[11]</sup>

The pubic hair is reduced and becomes grey. The red patches seen around the urethra and introitus are caused by senile vulvitis, and a urethral caruncle may be produced. The pelvic cellular tissue becomes lax and the ligaments that support the uterus and vagina lose their tone and predispose to prolapse of the genital organs.

### Menopausal symptoms

Hot flushes  
 Night sweats  
 Palpitations  
 Depression  
 Insomnia  
 Headaches  
 Anxiety  
 Loss of libido  
 Skin atrophy  
 Joint pains  
 Cancer phobia  
 Pseudocyesis  
 Irritability  
 Lack of concentration  
 Dysuria  
 Stress incontinence and urge incontinence  
 Dry vagina

### Classical changes in an atrophic vulvo-vaginal tissue

These are:

- Loss of labial and vulvar fullness
- Narrowing of the introitus and inflamed mucosal surfaces
- Loss of vaginal rugations and occasional vaginal stenosis<sup>[13]</sup>
- Dyspareunia and vaginal bleeding from fragile atrophic skin<sup>[13]</sup>
- Possibility of the prepuce of the clitoris becoming atrophic<sup>[10]</sup>
- Atrophic pattern of predominance of parabasal cells in vaginal maturation index

### Diagnosis

- The first step in the diagnosis is a thorough history taking, general examination including recording of blood pressure, breast palpation, weight, hirsutism, and gynecologic examination
- Pelvic examination: External genitalia for signs of vulval atrophy and vulval lesions
- Pap smear and a vaginal swab for microscopy, culture, and sensitivity
- Vaginal scraping for vaginal maturation index (this index consists of the percentages of the parabasal, intermediate, and superficial squamous cells noted on a cytologic smear of cells from the upper one-third of

the vagina and provides a means of evaluating chronic hormonal influence on the vaginal vault). An atrophic pattern shows the predominance of parabasal cells, whereas estrogen stimulates the development of superficial squamous cells<sup>[14]</sup>

- Measurement of vaginal pH: Hormonal influence can also be effectively measured by moistening a pH test strip to measure vaginal pH<sup>[15]</sup>
- Blood sugar
- Lipid profile
- Mammography
- Ultrasound
- Bone density study
- Bone density test (courtesy of Mayo Clinic products and services): This is used to identify decreases in density, determine the risk of fractures, confirm a diagnosis of osteoporosis, and finally monitor treatment for osteoporosis. A bone density test uses X-rays to measure the quantity (g) of calcium and other bone minerals that are packed into a segment of bone. The bones that are most commonly tested are located in the spine, hip, and forearm. Bone density test results are reported in two measures: T-score and Z-score.

T-score is your bone density compared with what is normally expected in a healthy young adult of your sex. Your T-score is the number of units called standard deviations that your bone density is above or below the average.

Normal bone density is indicated by a score of  $-1$  and above. A score between  $-1$  and  $-2.5$  is a sign of osteopenia (bone density is below normal and may lead to osteoporosis). A score of  $-2.5$  and below density indicates osteoporosis.

Z-score is the number of standard deviations above or below what is normally expected for someone of your age, sex, and ethnic or racial origin. If your Z-score is  $-2$  or lower, it may suggest that something other than aging is causing abnormal bone loss.

### Associations of medical conditions with sexual dysfunction

Some medical conditions are associated with sexual dysfunction and must be evaluated before treatment with medications. These medical conditions are diabetes mellitus, hypercholesterolemia, hypertension, cardiovascular disease, neurologic disease, psychiatric disorders, and genitourinary disease. Certain non-neoplastic conditions such as squamous hyperplasia, contact dermatitis, and lichen sclerosis present with symptoms as seen in atrophic vulvovaginitis. These conditions require tissue biopsies to make a definitive diagnosis.

## Treatment of vulvovaginal atrophy-related sexual dysfunction in postmenopausal women

The aim of treating vulvovaginal atrophy is to relieve symptoms and to reverse anatomical changes that may have effects on other dimensions of sexual function that result from decreased estrogen levels.<sup>[11]</sup> Estrogen therapy is the most effective option and is the current standard of care for vulvovaginal atrophy. Estrogen therapy is good and a logical treatment option in this population for atrophy-related symptoms like dryness, irritation, pruritus, urinary urgency, and dyspareunia by restoring normal vaginal pH levels and thickening and revascularizing the epithelium.<sup>[11,16]</sup> Intravaginal estrogen therapy in postmenopausal women is effective in relieving symptoms of urogenital atrophy and in improving sexual functions and urinary incontinence.<sup>[17]</sup> Local estrogens for the treatment of vaginal atrophy are estradiol and conjugated estrogens and in a variety of formulations for vaginal use such as creams, tablets, and hormone-releasing rings.<sup>[18,19]</sup> Local estrogen has been shown to decrease vulvovaginal atrophy-related dyspareunia in postmenopausal women.<sup>[19]</sup> Local estrogen therapy may improve sexual desire, arousal, and orgasmic function by increasing blood flow to the urogenital region and by increasing vaginal lubrication and oxygen levels.<sup>[20]</sup> Therapy for atrophic vaginitis requires the use of low-dose estrogen therapy.

### Risks associated with vaginal estrogen therapy

Vaginal estrogen preparations yield low levels of circulating estrogens, but there is risk of endometrial hyperplasia in users who have not had a hysterectomy.<sup>[21]</sup>

### Selective estrogen receptor modulators

Both raloxifene and tamoxifen do not have a beneficial or detrimental effect on vaginal tissue and on symptoms of vulvovaginal atrophy.<sup>[22]</sup> They are commonly used in the treatment of osteoporosis and chemoprophylaxis/treatment of breast cancer, respectively. Lasofoxifene and ospemifene have a positive impact on vaginal tissue in postmenopausal women but have not been approved by the Food and Drug Administration (FDA).

Other promising new therapies are vaginal dehydroepiandrosterone (DHEA),<sup>[23,24]</sup> vaginal testosterone, and tissue-selective estrogen complexes (TSECs), but further studies are required to confirm their efficiency and safety.<sup>[21,24,25]</sup>

### Nonhormonal treatment

Vaginal lubricants and moisturizers are alternative choices to vaginal estrogens for the treatment of vulvovaginal atrophy-related sexual dysfunction.<sup>[26]</sup> They can be safely used by women who do not want to use hormonal therapy.

Moisturizers are used to replace normal vaginal secretions, whereas lubricants are designed to reduce friction associated with sexual activity.<sup>[27]</sup> There are two basic lubricant formulations, water-based and silicone-based products. Water-based lubricants are commoner; water-based lubricants include K-Y jelly, Astroglide, and Slippery Stuff Gel. They are applied to the vaginal introitus before intercourse. Vaginal moisturizers include Replens, K-Y Liquibeads, RepHresh, and Emerita. The commonly used vaginal moisturizer is Replens. Replens is an effective therapy for improving vaginal moisture, vaginal fluid volume, pH, and vaginal elasticity, and for reducing symptoms of itching, irritation, and dyspareunia.<sup>[28]</sup>

### Alternative therapies

Alternative therapies such as acupuncture, plant estrogens, herbal supplements, soy, chasteberry, and ginseng are popular among postmenopausal women; however, data are limited, and they have not been adequately studied for the treatment of vulvovaginal atrophy.<sup>[29]</sup> These agents cannot be recommended as treatment of vulvovaginal atrophy-related symptoms as their sources, doses, and efficiency are poorly documented.<sup>[30]</sup> Vitamin D and dietary supplementation with a soy-based product (a source of phytoestrogen) are used by postmenopausal women, but they have not been studied sufficiently for the treatment of vulvovaginal atrophy.<sup>[31]</sup>

## Induction of menopause with chemotherapy in breast cancer patients

A good number of women with breast cancer have some sexual dysfunction after treatment of the cancer.<sup>[32,33]</sup> Surgical treatment of breast cancer results in deprivation of estrogen and the onset of menopausal symptoms, which affect sexual function negatively.<sup>[17,34]</sup> Women who survive breast cancer after treatment have a high prevalence of severe postmenopausal symptoms because of the induction of a premature menopause with chemotherapy.<sup>[17,34]</sup> This results in a profound deprivation of estrogen.<sup>[35]</sup> Aromatase inhibitors (AIs) have been shown to disrupt sexual function.<sup>[36]</sup> With the increasing use of AIs, the number of women who present with symptomatic atrophic vaginitis after treatment for breast cancer is likely to increase.<sup>[37]</sup> As there is greater incidence of vaginal atrophy in women taking AIs, a safe and effective non-estrogen therapy is necessary. Low-dose vaginal estrogen therapies were effective for relieving urogenital atrophy in survivors of breast cancer, whereas nonhormonal moisturizers only provided transient benefit.<sup>[38]</sup> A patient with a history of breast cancer can use less effective vaginal moisturizers or lubricants if she does not want to use vaginal estrogen preparations.<sup>[17,27,38]</sup>

## Psychosocial issues in postmenopausal women

The association between many psychological factors

and sexual dysfunction may be bidirectional in terms of causation;<sup>[39]</sup> however, studies have demonstrated strong correlations between psychosocial factors and the prevalence of sexual dysfunction in women.<sup>[39]</sup> Furthermore, treatment with certain antidepressants increases the risk of sexual dysfunction. Psychosocial issues result in both positive and negative perceptions of menopause-associated changes. The changes are concerns about body image and increased changes in the body (wrinkles, body shape/weight, loss of muscle tone), loss of sexual self-confidence or performance anxiety, diminished affection for or attraction to partner, affective disorders (depression, anxiety), distress (personal, emotional, occupational, sexual), fulfillment of life goals (or lack of fulfillment). Other psychosocial issues are positive perception of menopause such as an increased sense of freedom from fear of pregnancy, from menstruation, from childcare responsibilities, and freedom to concentrate on one's own needs.<sup>[40]</sup>

Aging and menopause are associated with significant changes in body image that are driven by weight gain, changes in body shape, changes in career, stresses such as reduced attention and care for elderly parents, changes in facial appearance, and low self-esteem with other health issues such as uterovaginal prolapse and incontinence. These may lead to an extended period of grief over lost youth and beauty with an increased risk of anxiety and depression. The partner is undergoing changes of aging equally and may no longer elicit the same degree of sexual attraction from the woman.

Partner issues and relationship dynamics are contributors to sexual dysfunction. The availability of a partner can be a problem for aging women, because of divorce, separation in marriage, death or chronic illness of partner, sexual dysfunction of partner, or extramarital affairs.<sup>[41]</sup> Frequent problems may be a result of poor communication in terms of changes related to aging in both women and their partners. Both partners are likely to undergo decreased sexual responsiveness with aging, which can lead to performance anxiety.<sup>[39,41-43]</sup> Partner relationships of long duration may undergo a gradual diminution of sexual frequency. In case of infidelity on the part of the partner, it can lead to withdrawal, anger, rage, or disaffection and ultimately to 'sexual retirement.'<sup>[39]</sup> Attenuated sexual desire in postmenopausal women is associated with low levels of satisfaction from the relationship, increased distress, and low frequency of sexual activity.<sup>[39,41,44]</sup>

## CONCLUSION

Menopause is associated with various endocrine changes, which bring about female sexual dysfunction. The following complaints are common in postmenopausal women such as vaginal dryness, dyspareunia, decreased libido, and

poor sexual satisfaction. These complaints are prominent in women with premature menopause.<sup>[45]</sup> Low-dose local vaginal estrogen is effective and well tolerated in treating vulvovaginal atrophy-related sexual dysfunction.<sup>[46-48]</sup> Women with a history of breast cancer and severe vaginal atrophy-related dyspareunia and ineffective nonhormonal therapies could be offered vaginal estrogen preparations with the lowest systemic absorption rate.<sup>[49]</sup> Women who wish to avoid the use of hormone therapy could be offered vaginal lubricants and moisturizers applied on a regular basis.<sup>[50]</sup> Data are limited on SERMs,<sup>[51]</sup> TSECs,<sup>[52-54]</sup> vaginal DHEA,<sup>[55]</sup> and vaginal testosterone,<sup>[56]</sup> but they showed a positive impact on vaginal tissue in postmenopausal women; however, further studies are needed to confirm their efficacy and safety.<sup>[23,57]</sup>

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