Genitourinary syndrome of menopause: an overview of clinical manifestations, pathophysiology, etiology, evaluation, and management

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Genitourinary syndrome of menopause, a new term for a condition more renowned as atrophic vaginitis, is a hypoestrogenic condition with external genital, urological, and sexual implications that affects >50% of postmenopausal women. Due to sexual embarrassment and the sensitive nature of discussing symptoms, genitourinary syndrome of menopause is greatly underdiagnosed. The most up-to-date literature pertaining to clinical manifestations, pathophysiology, etiology, evaluation, and management of genitourinary syndrome of menopause is comprehensively reviewed. Early detection and individually tailored pharmacologic (eg, estrogen therapy, selective estrogen receptor modulator, synthetic steroid, oxytocin, and dehydroepiandrosterone) and/or nonpharmacologic (eg, laser therapies, moisturizers and lubricants, homeopathic remedies, and lifestyle modifications) treatment is paramount for not only improving quality of life but also for preventing exacerbation of symptoms in women with this condition.

Key words: atrophic vaginitis, dyspareunia, estrogen-progestin therapy, genitourinary syndrome of menopause, hypoestrogenism, menopausal hormone therapy, nonhormonal vaginal therapy, quality of life, urinary incontinence, urogenital atrophy, vaginal maturation index, vulvovaginal atrophy

Introduction

Genitourinary syndrome of menopause (GSM), previously known as vulvovaginal atrophy, atrophic vaginitis, or urogenital atrophy, is a chronic, progressive vulvovaginal, sexual, and lower urinary tract condition characterized by a host of symptoms secondary to a clinical state of hypoestrogenism after onset of menopause. In 2014, the International Society for the Study of Women's Sexual Health and the North American Menopause Society agreed that "genitourinary syndrome of menopause" is a more inclusive and accurate term to describe the conglomeration of external genital, urological, and sexual sequelae caused by hypoestrogenism during menopause.[1] They also agreed the new terminology would carry less social stigma thus making it easier for women to openly talk about it, especially to their care providers. GSM-like symptoms may also be mirrored in hypoestrogenic premenopausal women. The syndrome or its features manifest in some manner in approximately 15% of premenopausal women[2] and 40-54% of postmenopausal women.[3] Because women have a higher life expectancy than men, and approximately >17% of the population will be age >65 years by 2030, the consequences of declined endogenous estrogen levels in menopausal women should be of great interest to clinicians.[4]

GSM is often underdiagnosed due to sexual embarrassment[5] or general disregard due to associating it as a liability of natural aging. In a recent study, only 4% of women were able to attribute vulvovaginal symptoms to GSM.[6] Only around 25% of women with GSM go to a practitioner for consultation.[2] Another European study found that only 54% of women discuss their sexual health with practitioners when asked, and 33% of women do not discuss it at all.[7] Identifying postmenopausal women's profiles (eg, their tendency to be proactive or reserved) may help bypass the social taboo on discussing GSM, thus expediting evaluation and management.[8] In cases of abrupt estrogen deprivation, eg, surgical menopause, patients can experience significant sexual dysfunction and even poorer quality-of-life outcomes. We presently explore the signs, symptoms, and genitourinary manifestations of GSM; the importance of its early detection; as well as the crucial role of proper patient education in avoiding the long-term risks and complications that may severely compromise quality of life. Management of GSM must ideally be tailored to individual patient medical history, potential risks and benefits of exogenously administered estrogen therapy (ET), as well as patient lifestyle.

Clinical manifestations

Clinicians play a major role in recognizing the signs of GSM because many women are reluctant to report their symptoms due to personal reasons. Additionally, 50% of postmenopausal

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TABLE 1
External genital, urological, and sexual manifestations of genitourinary syndrome of menopause

External genital		Urological		Sexual
Signs and symptoms	**Complications**	**Signs and symptoms**	**Complications**	**Signs and symptoms**
Vaginal/pelvic pain and pressure	Labial atrophy	Frequency	Ischemia of vesical trigone	Loss of libido
Dryness	Vulvar atrophy and lesions	Urgency	Meatal stenosis	Loss of arousal
Irritation/burning	Atrophy of Bartholin glands	Postvoid dribbling	Cystocele and rectocele	Lack of lubrication
Tenderness	Intravaginal retraction of urethra	Nocturia	Urethral prolapse	Dyspareunia
Pruritus vulvae	Alkaline pH (5–7)	Stress/urgency incontinence	Urethral atrophy	Dysorgasmia
Decreased turgor and elasticity	Reduced vaginal and cervical secretions	Dysuria	Retraction of urethral meatus inside vagina associated with vaginal voiding	Pelvic pain
Suprapubic pain	Pelvic organ prolapse	Hematuria	Uterine prolapse	Bleeding or spotting during intercourse
Leukorrhea	Vaginal vault prolapse	Recurrent urinary tract infection	Urethral polyp or caruncle	
Ecchymosis	Vaginal stenosis and shortening			
Erythema	Introital stenosis			
Thinning/graying pubic hair				
Thinning/pallor of vaginal epithelium				
Pale vaginal mucous membrane				
Fusion of labia minora				
Labial shrinking				
Leukoplakic patches on vaginal mucosa				
Presence of petechiae				
Fewer vaginal rugae				
Increased vaginal friability				

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women with mild or moderate GSM are asymptomatic, making diagnosis particularly challenging. Only a weak correlation has been found between symptom score and physical examination of GSM.[9]

Manifestations of GSM are primarily divided into external genital and urological signs and symptoms (Table 1), which can be observed through physical examination.[1] Genitourinary complications experienced secondary to GSM are included in Table 1 to further guide clinicians and health care providers. There may be a linking of certain signs and complications, eg, vaginal vault prolapse and urinary incontinence. Introital stenosis to a width <2 fingers, decreased vaginal depth, and vaginal dryness must be diagnosed before insertion of the speculum, otherwise the pelvic examination will cause considerable pain. Vaginoscopy is an alternative if the practitioner is unable to perform a pelvic/vaginal examination.

GSM is most commonly diagnosed when the patient presents with dyspareunia secondary to vaginal dryness. Common signs and symptoms in order of prevalence and degree of atrophy include vaginal dryness (in 75% postmenopausal women), dyspareunia (38%) and vaginal itching, discharge, and pain (15%).[10,11] When the vulvovaginal epithelium is inadequately lubricated, ulceration and fissures can develop during intercourse, causing dyspareunia. Vaginismus, or painful spasm of vaginal muscles, can also occur as a physiological response when there is anxiety toward expected sexual pain. Sexual manifestations are an extension of those of the external genitalia (Table 1).

Pathophysiology

During female embryologic development, the urogenital sinus, müllerian ducts, and sinovaginal node (ie, Müller tubercle) form the vaginal vestibule and lower fifth of vagina, urinary bladder, trigone, and the entire urethra. Fused müllerian ducts form the uterus and upper four-fifths of the vagina. The genitalia and lower urinary tract share common estrogen receptor function. Due to the common embryological origin, hypoestrogenism has both vulvovaginal and urologic effects; urogenital tissue receptors are dependent on endogenous estrogen levels to maintain normal physiology.[12] During postmenopause, the number of estrogen receptors continue to decrease but never fully disappear. However, in the presence of exogenous administration of estrogen, one can replenish lost estrogen receptors.[2]

In the vulvovaginal tissue, estrogen receptor-α is predominantly present in premenopausal and postmenopausal women, whereas estrogen-β appears to only be expressed in premenopausal women.[13] Estrogen is a vasoactive hormone that increases blood flow.[11] Vaginal lubrication is caused by fluid transudation from blood vessels, and from endocervical and Bartholin glands. Activated estrogen receptors also encourage epithelial proliferation with redundant smooth muscle tissue layer. The formation of rugae aids in expandability, distensibility, and lubrication of the vagina during sexual stimulation. Vaginal secretions, lubrication, and improved blood flow of vaginal walls all help to increase vaginal mechanical

TABLE 2
Causes of estrogen deficiency in premenopausal women or due to factors unrelated to menopause

Type	Cause
Systemic	Hyperprolactinemia (during breast-feeding) Postpartum estrogen deficiency Hypoestrogenism (eg, due to autoimmune disorders affecting ovaries, pituitary tumors)
Pharmacological	Gonadotropin-releasing hormone agonist analogs Leuprolide Nafarelin Selective estrogen receptor modulators Tamoxifen Aromatase inhibitors Danazol Medroxyprogesterone
Iatrogenic	Bilateral oophorectomy (ie, surgical menopause) Ovarian failure secondary to pelvic radiation Chemotherapy Radiation therapy

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compliance.[2] In the advent of hypoestrogenism, these prolubricative and proelastic functions are lost due to diminished collagen, elastin, and hyaluronic acid content; thinned epithelium; impaired smooth muscle proliferation; denser connective tissue arrangement; and loss of vascularity, thus predisposing the woman to irritation and sexual trauma.[14]

The vaginal and urethral epithelium is comprised of nonkeratinized stratified squamous epithelium with superficial, intermediate, and basal cell layers that store glycogen in the presence of physiologic estrogen levels. The epithelium of the vaginal wall is constantly exfoliating and producing glycogen, which is hydrolyzed to glucose. A healthy vaginal flora is composed of a variety of aerobic and anaerobic, gram-positive and gram-negative bacteria. Predominant *Lactobacillus* metabolizes glucose into lactic acid and acetic acid, lowering the vaginal pH to a range of 3.5-4.5. The acidity of the vagina provides natural protection against urinary tract infections (UTI) and vaginitis, discouraging the growth of pathogenic bacteria and infection.[11] Estrogen is vital for modulating innate defenses of the urinary tract. Thus, knowledge of the association between GSM and recurrent UTI can help avoid unnecessary use of antibiotics and prevent antimicrobial resistance.[15]

Atrophy of urogenital tissue is identified with declined endogenous estrogen levels with vaginal epithelium appearing thin, pale, and less rugated. The loss of estrogen is responsible for the reduction of *Lactobacillus*, changing the vaginal fluid to an alkaline pH of $\geq$5.0. The higher pH impairs the viability of healthy vaginal flora[5] and promotes overgrowth of gram-negative rod fecal flora including group B streptococci, staphylococci, coliforms, and diphtheroids, inducing vaginal infection and UTI and inflammation.[16] In decreased levels of circulating estrogen, substantial vascularization is lost in the urogenital tract, making the tissue atrophic. Estrogen deficiency causes loss in dermal collagen in dense connective tissue of the vagina, bladder, and urethra, and then causes the vaginal wall to become thinner and less elastic. In consequence, the vagina becomes shortened and narrowed, which may lead to dyspareunia. The bladder and urethra also become atrophic, causing urinary incontinence and frequency.[2,11] One study reported that 20% of postmenopausal women experienced urge incontinence while roughly 50% experienced stress urinary incontinence.[17] It is thought that estrogen receptors in the bladder trigone and urethra aid in increasing the sensory threshold when the bladder becomes distended. Lack of estrogen decreases the threshold and impairs urethral closure pressure and Valsalva leak-point pressure, contributing to urinary urgency.[17] Research studies have also suggested that in postmenopausal women, the lack of estrogen impairs connective tissue and causes urethral sphincter dysfunction of stress urinary incontinence. In comparison, premenopausal women experience stress incontinence mainly due to anatomical changes.[18] GSM-related incontinence is a key cause of recurrent UTI in postmenopausal women, signifying the importance of GSM evaluation and management to avoid the repercussions of inessential antibiotic therapy.[15]

TABLE 3
Risk factors for genitourinary syndrome of menopause

Menopause
Nonmenopause hypoestrogenism
Bilateral oophorectomy
Cigarette smoking
Alcohol abuse
Decreased frequency and sexual abstinence
Ovarian failure
Lack of exercise
Absence of vaginal childbirth

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Etiology

The etiology of GSM is secondary to decreased levels of endogenous estrogen levels. In the female body, the 3 forms of estrogen produced mainly in the ovaries are estradiol, estrone, and estriol with estradiol being the most abundant in premenopausal women. During the transition between perimenopausal and postmenopausal years, estrone becomes the most prominent and is a less potent form of estrogen.[19]

Table 2 outlines nonmenopause-related causes of estrogen deficiency that may mimic GSM sequelae,[12,16] such as the hormonal therapies and chemotherapy from treating women with breast cancer. Table 3 lists risk factors for developing GSM such as cigarette

smoking, which contributes to decreased circulation and impaired receptor function.[5,12] Table 4 distinguishes between development of superficial and deep dyspareunia.[20,21]

Evaluation

A full history should be performed on patients suspected to have GSM. Lubricants, powders, soaps, spermicides, and panty liners commonly contain irritants that could produce discomfort to the genitourinary region. Antiestrogen medications or a history of oophorectomy, radiation, or chemotherapy increases suspicion of GSM-like symptomology particularly in premenopausal women.

The cornerstone of evaluating menopausal women with sexual health symptoms is the pelvic examination. Atrophic vaginal epithelium appears pale and shiny, and patches of erythema may be present. One should check for any signs of lacerations or lesions, labial fusion, introital stenosis, and friable epithelium. Table 5 catalogs findings of cystoscopic and laparoscopic procedures.

Differential diagnoses that should be evaluated when a woman is thought to present with GSM include bacterial vaginosis, trichomoniasis, candidiasis, contact irritants, foreign bodies, and sexual trauma. Other diagnoses to consider include neoplasia and precancerous neoplasia of external or internal female genitalia, endocrine disorders, infections from body piercing, vaginal stenosis secondary to radiation, lichen sclerosus, and lichen planus.[12]

To aid in the diagnosis of GSM, several laboratory tests are useful. Cytology of the vaginal epithelium shows an increase in parabasal cells and a decrease in superficial cells. Ultrasound examination of the uterus is especially useful as a thin endometrial thickness of $\leq$5 mm indicates decreased estrogen stimulation. Vaginal pH, Pap test, and vaginal culture are also useful in assessing for genitourinary infection. Table 6 lists the diagnostic tests to perform after the initial clinical assessment.

Management

Management of GSM varies according to symptom severity. For moderate to severe symptoms, ET is reported to be the most successful treatment option in terms of increasing the vaginal maturation index (VMI). For milder symptoms, though nonhormonal therapies are subjectively effective, they are suitable for women at risk for estrogen-responsive neoplasia, and do not require prescriptions.[22,23] To assess the effectiveness of treatment, a pH test and cytologic analysis may be utilized. Since GSM is a chronic condition, life-long management is essential to prevent recurrence of symptoms.

Estrogen therapy

ET is the standard treatment for GSM. It has proven to be successful in rapidly restoring vaginal epithelium and associated vasculature, improving vaginal secretions, lowering vaginal pH to restore healthy vaginal flora, and alleviating overall vulvovaginal symptoms.[24] Both systemically (eg, oral or patch) and vaginally administered forms are effective in improving GSM. However, hormonal therapy is only considered after all risk factors and benefits have been thoroughly reviewed with the patient. The lowest effective dosage of systemic ET is always advisable, as the stimulatory effect of high estrogen levels on the endometrium can lead to proliferation, hyperplasia, or carcinoma. Local ET is the most accepted form of therapy for GSM; it also offers the fastest and most effective symptomatic relief. Although local ET does not reduce the risk of osteoporosis or effectively manage vasomotor symptoms, up to

TABLE 4
Classifications, etiologies, and risk factors for superficial and deep dyspareunia

	Subtype	
	Superficial	**Deep**
Prevalence	More common	Less common
Location	Vulvar region, vaginal opening	Pelvic region, internal genitalia
Etiologies	Genitourinary syndrome of menopause, vulvitis, vulvovaginitis, vulvovestibulitis, genital herpes, urethritis, atrophic vulvitis, lack of lubrication, vaginal dryness, vaginal infection, episiotomy, radiotherapy, sexual trauma, and topical irritants	Pelvic inflammatory disease; gynecological, pelvic, or abdominal surgery; postoperative adhesions; endometriosis; genital or pelvic tumors; irritable bowel syndrome; urinary tract infections; and ovarian cysts
Risk factors	Age, menopause, hypoestrogenism, vaginal atrophy, lack of arousal and lubrication, and pelvis floor abnormalities	
Type of pain	Sharp, burning, itching	

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TABLE 5
Physical findings of urogenital instrumentation in genitourinary syndrome of menopause

Cystoscopy	Laparoscopy
Squamous metaplasia of trigone	Atrophic uterus, fallopian tubes, and ovaries
Shortening of urethra	Supporting lax ligaments
Pale urethral mucous membrane	
Urinary sphincter dysfunction (eg, decreased contractility)	
Compliance	
Pale trigone	

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TABLE 6
Diagnostic tests to consider post–initial clinical assessment

Tests	Findings
Pelvic exam with speculum and bimanual palpation (with topical anesthesia); vaginoscopy	Loss of rugae
Rectal exam	Rectal mass; rectocele
Transvaginal ultrasound; hysteroscopy	Endometrial stripe <5 mm indicating loss of estrogenic stimulation; pelvic mass
pH test	Symptomatic pH: 5–7 (normal pH: 3.5–4.5)
Vaginal cytology	Basal epithelial cells predominate and decreased percentage of superficial cells
Wet mount	Presence of leukocytes and paucity of *Lactobacillus*
Pap test	Atrophy of cervix and stenosis of os
MRI/CT scan	Pelvic and adnexal abnormalities

CT, computed tomography; *MRI*, magnetic resonance imaging.

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90% of women report subjective improvement of their symptoms.[25]

As with all hormone replacement therapies, some risks accompany the benefits of treatment. Each woman should discuss her situation with her physician to determine the duration and severity of her series of symptoms. Women may prefer to avoid hormone therapy and approach the option of over-the-counter vaginal creams for symptomatic relief.

Although side effects are uncommon, systemic ET is associated with breast tenderness and/or enlargement, vaginal bleeding or spotting, nausea, and modest weight gain. In cases where the patch is used, some irritation at application sites may occur. The most common side effect of hormone replacement therapy is increased systemic estrogen. Additionally, some women might experience headache, back pain, abdominal pain, and vaginal yeast infections. Breast tenderness most often decreases with time, and taking oral estrogen with food can prevent nausea. Common side effects of intravaginal products include vaginal secretion, vaginal spotting, and genital pruritus. To avoid any harmful long-term side effects of hormone replacement therapy, many physicians advise patients to use the cream or gel for 6 months, discontinue temporarily, and then resume treatment.

Contraindications to the use of ET include known or suspected cases of breast cancer, estrogen-dependent cancers, undiagnosed vaginal bleeding, history of thromboembolism (ie, blood clotting disorders), endometrial hyperplasia or cancer, hypertension, hyperlipidemia, liver disease, hypersensitivity to active compounds in ET, history of stroke, venothrombotic events, coronary heart disease, pregnancy, smoking in those age >35 years, migraines with neurologic symptoms, and acute cholecystitis/cholangitis.

Systemic. Systemic hormone replacement therapy is suggested to patients who seek relief from GSM symptoms in addition to relief from hot flashes and protection from osteoporosis.[26] Due to concomitant use of progestin in women with a uterus, systemic ET is associated with adverse effects such as endometrial bleeding, breast tenderness, increased risk of stroke, venous thromboembolism, and breast cancer. Potential adverse effects of estrogen-progestin therapy may cause the therapy to be contraindicated and unacceptable to some women. Women taking systemic hormone therapy with unresolved symptoms should also take continuous or intermittent topical ET.

Topical. Topical estrogens alone supply sufficient estrogen to reduce symptoms and reverse atrophic vaginal epithelial conditions. The treatment limits systemic absorption by avoidance of hepatic metabolism. Thus, additional progestin is not necessary to prevent endometrial hyperplasia or cancer. Topical treatment is advised to patients who seek relief solely from vaginal atrophy symptoms, as the low dose of estrogen may not be enough to alleviate other menopausal symptoms. In contrast to systemic estrogen, topical estrogens do not solve vasomotor symptoms associated with menopause or reduce the risks of osteoporosis. According to the North American Menopause Society, low-dose vaginal estrogens decrease vaginal pH, increase the number of vaginal lactobacilli, improve vaginal and urethral cytology, and prevent frequent UTI.[11] Vaginal ET trials have also demonstrated relief of urinary symptoms of urgency, frequency, nocturia, and stress/urgency urinary incontinence.[23] Vaginal tablets, creams, and rings are the routes of low-dose local estrogen; the 2006 Cochrane Database of Systematic Reviews stated that all types are equally effective in resolution of dyspareunia, vaginal itching, and dryness.[27]

Women should choose the option of low-dose vaginal ET based on their personal preference and lifestyle. Women may select the tablet over the cream due to reduction in mess. Creams are currently the most common choice of vaginal product for the treatment of GSM and provide flexibility of dosage and frequency of administration. Advantages of estradiol-releasing vaginal rings are that they are long-acting over a period of 3 months and require less sustained effort to use. However, there are reports of occasional vaginal ring expulsion so adequate dexterity is required for insertion and removal. Cystoceles or rectoceles may also cause the ring to become displaced and fall out.

Roughly 80-90% of women on local ET report subjective improvement

and relief from GSM.[12,16,22] Care and monitoring are often customized depending on a woman's medical history and symptoms. Relevant factors include whether a woman is premenopausal or postmenopausal, whether she has a uterus, and whether she has had hormone-dependent cancer (eg, breast or endometrial). In asymptomatic women using topical estrogens, there are currently insufficient data to recommend annual endometrial surveillance.[28]

Selective estrogen receptor modulator

Another oral treatment option for GSM are selective estrogen receptor modulators (SERM). Ospemifene was approved by the Food and Drug Administration in 2013. Ospemifene provides a therapeutic pharmacologic treatment option for patients who are not candidates for ET. The current literature shows that it is both efficacious and safe in treating vulvovaginal atrophy and dyspareunia by improving vaginal structure and pH.[29] Double-blind placebo-controlled studies have shown that it remains efficacious and safe up to 52 weeks while providing greater symptomatic relief than vaginal lubricants. There were no cases of endometrial cancer and <1% of patients experienced endometrial hyperplasia with treatment.[30] Similar to ET, ospemifene increases the incidence of thromboembolism and should be avoided in patients with increased risk of venous thromboembolism.

Lasofoxifene is another SERM that binds to both estrogen receptor types and has high oral bioavailability. Three phase III clinical trials showed that lasofoxifene is effective in increasing bone mineral density.[31-33] Additionally, the drug has been shown to have many other beneficial effects such as decreased coronary disease, stroke, vaginal pH, and vaginal dryness.[34]

A newer therapy, tissue-specific estrogen complex, involves combining a SERM with a conjugated estrogen. Studies show that pairing bazedoxifene, a SERM, with estrogens is associated with higher safety and better tolerability than estrogen-progestin therapy.[35,36]

Laser therapies

Recently, the use of laser treatment has become an innovative treatment option for GSM. In 2014, the Food and Drug Administration approved the use of fractional microablative carbon-dioxide laser therapy for genitourinary surgery. At specific diode parameters, laser therapy stimulates improved vascularity; improved glycogen storage, collagen, and extracellular matrix production; as well as cellular proliferation to increase the thickness of the squamous epithelium with the formation of new papilla, thus enhancing the viability of the vaginal epithelium.[37-39] One study reported that improvement of vaginal dryness, pruritus, dysuria, and dyspareunia was maintained at 12 weeks' follow-up posttherapy.[40] This study included 50 women and reported an 84% satisfaction rate with the laser treatment. In addition, no adverse events were reported during the study period. Additional research has shown that the microablative therapy also significantly improves quality of life and sexual function.[38] In all, 85% of women who were previously not sexually active due to GSM symptoms regained a normal sexual life at 12 weeks following therapy.[41]

Novel nonablative laser therapies are also being studied for use in the treatment vulvovaginal symptoms. Pilot studies have found that vaginal erbium laser treatment significantly improves both vaginal dryness and dyspareunia up to 24 weeks after treatment.[42] Precise impulses are released to raise the temperature of vaginal tissue, stimulating remodeling of collagen in the introitus and vaginal canal. Novel low-energy dynamic quadripolar radiofrequency (DQRF) lasers are now also being used for vulvovaginal treatment. Previous ex vivo and in vivo studies demonstrated that DQRF thermal treatment could produce thickening and rearrangement of collagen and elastin fibers without side effects in the epidermis, nerves, or blood vessels.[43] A study conducted by Vicariotto and Raichi[44] demonstrated that in women with vaginal laxity, DQRF produced subjective improvement in laxity, sexual satisfaction, dysuria, and incontinence. As an attractive novel nonhormonal therapy for GSM, additional studies are needed to explore the long-term safety and efficacy of various laser therapies on genitourinary symptoms.

Synthetic steroid

Tibolone, a synthetic steroid, has been found not only to improve the VMI but also increase sex drive through its part-androgenic properties. Moreover, urinary incontinence problems of nocturia and urgency were found to be minimized.[45]

Oxytocin

Oxytocin, the neuropeptide released by the posterior pituitary gland, has also been studied amidst concerns over ET. A randomized double-blind controlled trial conducted in Stockholm reported that application of oxytocin gel produced healthier and more normalized vaginal epithelium. Treated participants reported significant reduction in their most bothersome symptom. Additionally, vaginal pH decreased with use of oxytocin and no increase in endometrial thickness was observed.[46]

Intravaginal dehydroepiandrosterone

Dehydroepiandrosterone (ie, prasterone) is a steroid hormone intermediate in the biosynthesis pathway for androgen and estrogen synthesis. A recent randomized, double-blind, placebo-controlled phase III trial showed that daily intravaginal application of 0.5% dehydroepiandrosterone increased superficial cell percentage and decreased parabasal cell in the vaginal epithelium, decreased vaginal pH, and decreased sexual pain. At gynecological examination, dehydroepiandrosterone application improved vaginal secretions, epithelial thickness, and color in comparison to placebo.[47] As a promising novel therapy, more research is needed to assess the long-term efficacy and safety of dehydroepiandrosterone.

Moisturizers and lubricants

Moisturizers and lubricants are used for temporary relief of vaginal dryness and itching during sexual intercourse. These

therapy options do not reverse most vaginal atrophic effects and have effectiveness length of <24 hours. Hence, they are more useful and recommended to women with mild symptoms, or should be used in conjunction with systemic or topical ET. Moisturizers may contain polycarbophil-based polymers that adhere to the epithelial and mucin cells on the vaginal wall to preserve moisture levels.[24] When selecting a lubricant or moisturizer, it is advised that the product should mimic vaginal secretions in terms of osmolality, pH, and composition.[48]

Homeopathic remedies

It is estimated that 10% of women experiencing vaginal symptoms of GSM are using herbal therapies such as black cohosh, dong quai, phytomedicines, nettle (250 mL infusion/d), comfrey root, motherwort, soy foods, and chaste tree extract. Other alternatives and complementary therapies are chickweed tincture, wild yam, and acidophilus capsules. Although homeopathic remedies show improvement in vaginal tissue flexibility, studies show that there is no proven efficacy on the vaginal epithelium and treatment of GSM.[16] Some vitamins such as vitamin E and D have been used for GSM therapy; vitamin D may help generate keratinocyte proliferation and differentiation in the vaginal epithelium.[24]

Lifestyle modifications

Increased sexual activity is advised for maintaining robust vaginal muscle condition. There is a positive link between sexual activity and maintenance of vaginal elasticity and pliability as well as lubricative response to sexual stimulation. Sexual intercourse improves blood circulation to the vagina and seminal fluid also contains sexual steroids, prostaglandins, and essential fatty acids, which serve to maintain vaginal tissue. Vulvovaginal tissue stretching also helps to promote vaginal elasticity. Masturbation or sex devices are options for patients without a partner.[22] Stress-reduction therapy and psychological counseling may benefit women with nonorganic causes of vaginal dryness. Cessation of smoking can help relieve symptoms. Lastly, wearing looser undergarments and legwear may improve air circulation, discouraging growth of microorganisms.

Conclusion

"Genitourinary syndrome of menopause" is the latest terminology instated to increase awareness and reduce social stigma of the genitourinary sequelae and sexual dysfunction associated with postmenopausal hypoestrogenism. ET is the mainstay of medical treatment but the risks and benefits should be thoroughly discussed with each patient. More importantly the physician and patient should work together to find the optimal combination of lifestyle changes and management options. Global assessment scales for GSM are currently seeing development; a proposed tool rates elasticity, lubrication, and tissue integrity; state and color of individual vulvovaginal and urethral anatomy; as well as pH and VMI.[49] Such assessment tools may help a physician to tailor treatment based on the objective and subjective severity of signs and symptoms. Newer treatments such as laser therapy are promising but require further studies to prove long-term efficacy. ■

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