NAMS Practice Pearl

Genitourinary Syndrome of Menopause: The Unmet Need

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Genitourinary syndrome of menopause (GSM) is a highly prevalent and progressive condition of postmenopausal women that has significant negative effects on vulvovaginal health, sexual health, and overall quality of life. Despite many available safe and effective therapies, GSM often goes undiagnosed and untreated. This* Practice Pearl *addresses the pathophysiology of GSM and reviews available treatment options.

The genitourinary syndrome of menopause (GSM) affects the female genitourinary tract and is associated with estrogen deficiency at menopause. Genitourinary syndrome of menopause is highly prevalent, affecting 27% to 84% of postmenopausal women[1] and is a common cause of dyspareunia. Unlike vasomotor symptoms (VMS), which are most severe in the years around the final menstrual period, the symptoms of GSM begin months to years later, suggesting that development of GSM may be related to both estrogen-dependent and independent factors, making its association with menopause unclear for many women.[2]

Data suggest that GSM negatively affects a woman's sexual health, relationships, and quality of life, whether she is sexually active or not.[3] Despite its prevalence and widely available therapies, only a minority of women are treated for GSM. Barriers to treatment include patient and provider discomfort discussing genitourinary and sexual complaints and lack of knowledge about therapies and cost.[4]

Causes. Natural menopause is the most common cause of GSM, but it can develop in any hypoestrogenic state, including primary ovarian insufficiency, surgical menopause, lactation, and after-cancer treatments. Lower estrogen levels result in decreased expression of ER-β, an increase in vaginal parabasal cells, a decrease in vaginal superficial cells, an increase in vaginal pH, and a diminished lactobacillus-dominant microbiome. Bilateral oophorectomy and use of aromatase inhibitors in survivors of breast cancer are associated with extremely low levels of circulating estradiol and the most severe GSM symptoms.[2]

Diagnosis. The diagnosis of GSM requires the presence of both bothersome symptoms and physical examination findings. The predominant symptoms of GSM include vulvovaginal dryness, burning, vaginal discharge; dysuria; and dyspareunia.[3] Signs of GSM include atrophy of the labia and the clitoris, phimosis of the prepuce, narrowing of the introitus, and dryness and thinning of the vaginal mucosa. Vaginal elasticity is decreased because of reduced elastin and collagen. Other physical findings include diminished vaginal rugae, friable and hypopigmented

tissue, vulvar ulcerations and tears, urethral caruncles, erythema, and prolapse.[1] Although GSM can be diagnosed on the basis of clinical history, a comprehensive pelvic examination is necessary to rule out other disorders, including vaginal or urinary infections, vestibulodynia, vulvar dermatoses, pelvic floor dysfunction, or malignancy.

Treatment. The goal of GSM treatment is to alleviate symptoms and restore lower genital function. Patient education is important and should include information about pathophysiology, vulvovaginal anatomy, and hygiene. First-line therapies include over-the-counter nonhormone vaginal moisturizers and lubricants. Lubricants temporarily alleviate symptoms by reducing friction during sexual activity and can be either water or silicone based. When recommending water-based lubricants, clinicians should consider the osmolality of the products because hyperosmolar options can disrupt the vaginal epithelium.[2] Vaginal moisturizers comprised of ingredients such as polycarbophil or hyaluronic acid used several times per week, irrespective of the timing of sexual activity, supply long-lasting moisture to the vagina. A recent trial of women with GSM that compared an estradiol vaginal tablet (plus placebo gel), a vaginal moisturizer (plus placebo tablet), and dual placebo found similar improvement in pain scores with sexual activity.[5]

For symptomatic women who do not respond to nonprescription therapies, treatment with FDA-approved prescription therapies should be considered. Low-dose vaginal estrogen therapy (ET), including vaginal estrogen creams, inserts, tablets, and ring, have proven efficacy for GSM in randomized, controlled trials (RCTs). Local ET improves subjective and objective measures of GSM, enhances thickness and elasticity of genital tissues, improves vaginal blood flow, lowers vaginal pH, and increases vaginal lactobacilli, with minimal systemic absorption. A 2016 Cochrane review of 30 RCTs reported the efficacy of FDA-approved local ET formulations in terms of relieving symptoms without increased risk of endometrial hyperplasia at 52 weeks. Based on limited data, use of a progestogen in low-risk women with a uterus using FDA-approved local ET is not required.[6] Women should be informed, however, to seek medical attention for any vaginal bleeding.

Serum estradiol levels in menopausal women using low-dose vaginal ET (2 mg vaginal ring, 10 µg vaginal tablets, or 4 and 10 µg vaginal gel cap) remain within the postmenopause range. Neither the Women's Health Initiative Observational Study of 45,000 women nor the Nurses' Health Study of 54,000 postmenopausal women found any increased risk of cardiovascular disease, breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, or death in women using vaginal ET.[4,7] When prescribing local vaginal ET, women should be educated about the safety of these products and informed about the FDA mandated "black box warning" (not supported by data on local ET). Local ET continues to be an underused treatment option for women with GSM.[3]

Another treatment for dyspareunia associated with GSM is ospemifene, an oral selective estrogen-receptor modulator with agonistic vaginal effects. Although ospemifene has shown antiestrogenic activity in preclinical models, ospemifene should not be used in women with known or suspected breast cancer because data are lacking in humans at this time. Another option, dehydroepiandrosterone, a steroid precursor to androgens and estrogens, is available as a daily vaginal insert (prasterone) and is not contraindicated in survivors of breast cancer. Shared decision making is critical when choosing and initiating any GSM therapy.[4]

Survivors of breast cancer. Management of GSM in survivors of breast cancer is complicated for many reasons. When nonhormone options fail, several professional societies, including the American Congress of Obstetricians and Gynecologists[8] and The North American Menopause Society,[9] have endorsed the recommendation to use low-dose ET in survivors of breast cancer in conjunction with the patients' oncologists.[8,9] Current data show no increased risk of breast cancer recurrence in survivors of breast cancer who use vaginal ET.

Other therapies. Energy-based therapies, including laser (fractional CO_2, Erbium, YAG) and radiofrequency are emerging therapies being used for treatment of GSM. Fractional CO_2 laser therapy uses fractionated energy to create small wounds in the mucosal epithelium that stimulates collagen and elastin formation. A multicenter, randomized, single-blinded trial of vaginal laser therapy versus estrogen cream for the treatment of GSM found that laser therapy and ET produced similar effects in terms of patient global impression of improvement, in incidence of adverse effects (minimal in each group), and in sustained efficacy at 6 months.[10] Although laser GSM treatment holds promise, especially for survivors of breast cancer,[9] larger, blinded, long-term, randomized, sham-controlled studies are needed to evaluate the safety and efficacy before widespread adoption. The out-of-pocket costs also should be considered.[1]

Vaginal dilators and pelvic floor physical therapy are adjuvant strategies for GSM-associated dyspareunia. Graduated dilators, including rigid plastic, flexible silicone, and patient-controlled expandable dilators have been shown to improve dyspareunia.[2] Women should be instructed to use vaginal dilators for 10 to 20 minutes, three to five times per week. Increased pelvic floor muscle tone, spasm, and the presence of myofascial trigger points also can contribute to persistent dyspareunia in women with GSM. Referral for pelvic floor physical therapy can be integral in reestablishing pelvic floor muscle relaxation and comfort.

Pearls. Many postmenopausal women suffer unnecessarily with painful symptoms of GSM. It is imperative that clinicians do more to meet the unmet needs of these women. All clinicians should routinely ask about GSM symptoms and, when present, provide education on the physiologic basis for symptoms as well as the efficacy and safety of available treatment options including pelvic floor physical therapy, nonhormone and local hormone therapies, and laser therapy. With this approach and with shared decision making, an individualized treatment plan can be developed. We must not allow women to continue to suffer when safe and effective therapies are available.

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Disclosures

Dr. Kellogg Spadt reports Consultant for Materna and Speaker for Amag and Duchesnay.
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