SEXUAL DYSFUNCTION

An expanding armamentarium may aid in the treatment of dyspareunia

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Since the last installment of this Update on Sexual Dysfunction, three new drugs have been added to the armamentarium for menopausal symptoms and dyspareunia:

- paroxetine 7.5 mg (Brisdelle)
- conjugated estrogens and bazedoxifene (Duavee)
- ospemifene (Osphena).

In this article, I present a case-based approach to incorporating these drugs into practice and restoring sexual function in the setting of vulvovaginal atrophy and dyspareunia. As is often the case, decision-making requires sifting through multiple layers of information.

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How to "tease out" the problem and help the patient regain sexual function

Simon JA, Portman DJ, Kazempour K, Mekonnen H, Bhaskar S, Lippman J. Safety profile of paroxetine 7.5 mg in women with moderate-to-severe vasomotor symptoms. Obstet Gynecol. 2014;123(suppl 1):132S–133S.

Conjugated estrogens/bazedoxifene (Duavee) for menopausal symptoms and prevention of osteoporosis. Med Lett Drugs Ther. 2014;56(1441):33–34.

DeGregorio MW, Zerbe RL, Wurz GT. Ospemifene: a first-in-class, non-hormonal selective estrogen receptor modulator approved for the treatment of dyspareunia associated with vulvar and vaginal atrophy [published online ahead of print August 1, 2014]. Steroids. doi:10.1016/j.steroids.2014.07.012.

Goldstein SR, Archer DF, Simon JA, Constantine G. Endometrial safety of ospemifene and the ability of transvaginal ultrasonography to detect small changes in endometrial thickness. Obstet Gynecol. 2014;123(suppl 1):96S–97S.

CASE **Low desire and discomfort during intercourse**

Your 58-year-old patient, G2P2, mentions during her annual visit that she's not that interested in sex anymore. Her children are grown, she's been happily married for 28 years, and she enjoys her job and denies any symptoms of depression. She says her relationship with her husband is good and, aside from her low desire, she has no worries about the marriage.

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Her only medication is paroxetine 7.5 mg/day (Brisdelle) for management of her moderate hot flashes, which she initiated at her last annual visit. She reports improvement in her sleep and menopausal symptoms as a result. She has an intact uterus.

You perform a pelvic exam and find atrophic vulva and vagina with mild erythema, and thinned epithelium. When you ask if she has experienced any discomfort, she reports that she needs to use lubrication for intercourse and that, even with lubrication, she has pain upon penetration and a burning sensation that continues throughout intercourse. She also reports that it seems to take her much longer to achieve arousal than in the past, and she often fails to reach orgasm.

How would you manage this patient?

As always, begin with the history

The transition to menopause creates multiple layers of potential symptoms and problems for our patients, and sometimes medical therapy can generate additional ones.

In a patient reporting the onset of low desire and dyspareunia, you would want to first consider her medication history, despite the clear evidence of vaginal atrophy. Begin by asking whether she is taking any new medications prescribed by another provider. In some cases, antihypertensive drugs, psychotropic agents, and other medications can affect sexual function.

This patient has been taking Brisdelle for 1 year and is happy with its effect on her sleep and hot flashes. Simon and colleagues found this nonhormonal agent for moderate to severe vasomotor symptoms to produce no notable effects in weight, libido, or sleep, compared with placebo.

Nevertheless, in this case, because selective serotonin reuptake inhibitors (SSRIs) such as paroxetine can affect arousal and orgasm, it is unclear whether the ultra-low dose of paroxetine she is taking is contributing to her problems. If you were to discontinue the drug to find out, her vasomotor symptoms and sleep disruption would likely recur.

Your decision-making is important here and should involve the patient in an extensive discussion. If there is not enough time for this discussion at the current visit, schedule a follow-up to address her issues fully.

FAST TRACK

Among menopausal women who continue to have intercourse on a regular basis, vulvovaginal atrophy often is much less troublesome than it is for women who have sex more rarely

Vulvovaginal atrophy has its own timeline

In many cases, vasomotor symptoms such as hot flashes occur years before the skin begins to atrophy in the vulva and vagina, particularly in women who enter menopause naturally. Among menopausal women who continue to have intercourse on a regular basis, however, these skin changes often are much less troublesome than they are for women who have sex more rarely.

In this patient, one possible scenario is that paroxetine caused a slight reduction in sexual interest, and the frequency of intercourse went down as a result. In women who have little or no intercourse, the vagina begins to shrink and the tissues lose elasticity. This patient may have been undergoing the natural process of menopause, and that process may have been compounded by a decrease in the frequency of sex.

If you were to discontinue the paroxetine, it would still be necessary to treat the vulvovaginal skin and work on manual techniques to gently dilate the introitus.

Option 1: Systemic hormone therapy

Systemic estrogen is the most effective treatment for menopausal vasomotor symptoms, reducing hot flashes by 50% to 100% within 4 weeks of initiation. However, because our patient has an intact uterus, any systemic estrogen she opts to use must be opposed by a progestin for safety reasons.

In terms of estrogen, her options are oral or nonoral formulations. Not only would estrogen manage our patient's hot flashes but, over time, it would improve her sexual problems and atrophy, which might or might not improve her current complaint of low desire. You likely would need to add a short regimen of topical estrogen and perhaps even a dilator to restore her sexual function completely, however.

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Since our patient chose the nonhormonal agent Brisdelle to manage her menopausal symptoms, she may be worried about the increased risk of breast cancer associated with use of a progestin in combination with estrogen. One hormonal option now available that eliminates the need for a progestin is conjugated estrogens and bazedoxefine (Duavee). Bazedoxefine is a third-generation selective estrogen receptor modulator (SERM). This drug has estrogen-like effects on bone and antiestrogen effects on the uterus.

Duavee is indicated for use in women with a uterus for treatment of:

- moderate to severe vasomotor symptoms of menopause
- prevention of postmenopausal osteoporosis.

Among the risks are an increased risk of venous thromboembolism (VTE) and stroke. It is not approved specifically for the treatment of dyspareunia.

Another hormonal option is ospemifene (Osphena), an estrogen agonist/antagonist indicated for the treatment of moderate to severe dyspareunia in menopausal women. Among the drugs in its class, such as tamoxifen and raloxifene, ospemifene is the only agent that maintains a full estrogenic effect on vaginal tissues. Its risks include VTE and stroke.

Although the labeling includes a warning about the risk of endometrial hyperplasia associated with its use, Goldstein and colleagues found no significant difference in the rate of endometrial thickening greater than 5 mm between women taking ospemifene and those taking placebo after 1 year of daily oral treatment. No carcinomas were found in either group.

Option 2: Local estrogen

If our patient declines all systemic hormone therapy, the topical approach should resolve her vulvovaginal symptoms, and she could continue taking Brisdelle for her menopausal symptoms. Vaginal estrogen would address the skin problems, provided the patient applies it correctly. Many women are afraid to use estrogen creams and compensate by applying them only to the vulva, thinking that, by limiting their use to external tissues, they are avoiding any associated risks.

If she opts for the local approach, this patient should be encouraged to use transvaginal estrogen in small doses to increase the elasticity of the vulvovaginal tissue, even though it may require daily use for a week or two to improve her symptoms, after which once- or twice-weekly administration should suffice.

The use of low-dose vaginal cream for a short duration is unlikely to increase her risks in any way.

Local estrogen is available as a tablet, cream, or ring.

Option 3: A nonhormonal approach

If the patient refuses any hormonal agent—even topical estrogen—I would recommend the use of silicone-based lubricants and a dilator and prescribe more frequent penetration to increase elasticity and reduce pain.

Brisdelle could be continued to address her menopausal symptoms.

Don't overlook behavioral techniques

Before this patient leaves your office with the option of her choice, a bit of counseling is necessary to instruct her about methods of restoring full sexual function.

Pain is a powerful aversive stimulus. This patient clearly states that she has had less frequent intercourse as a result of dyspareunia. It is not unusual for patients to develop a "habit" of avoidance in response to the behavior that causes their pain.

One recommendation is to talk to this patient about putting sex back into her life by encouraging her to increase sexual activity *without penetration* until she begins to arouse easily again. Arousal produces physiologic effects, increasing the caliber and length of the vagina as well as lubrication. The use of fingers or dilators may help restore caliber.

The patient can be encouraged to engage in snuggling and cuddling to regain those activities without the fear of pain associated with penetration. Follow-up after 2 weeks of

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this therapy can confirm the restoration of tissue elasticity, and the green light can be given for penetration to begin again. Couples can be encouraged to plan a "honeymoon weekend" and put some fun back into their sex lives so that this phase of healing doesn't become an onerous task.

CASE Resolved

After a discussion of her options, the patient chooses to stick with Brisdelle and use behavioral therapy alone to resolve her dyspareunia. At her follow-up visit 2 weeks later, she reports that she has enjoyed the period of pain-free "sex" and feels ready to add penetration into her activities.

You encourage her to continue sexual intercourse on a regular, relatively frequent basis to prevent a recurrence of dyspareunia. She continues to use silicone-based lubricants.