

## EDITORIAL

# Sexual pain in the menopausal patient: individualizing treatment still best

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When one reads the protocol of well-designed, placebo-controlled clinical trials, the conclusions can often be accurately surmised before the results are read. This was, however, not the case regarding the results of the clinical trial published in this issue of *Menopause* that examined three different interventions (vaginal estrogen, vaginal bioadhesive moisturizer, and vaginal placebo) on amelioration of pain with sexual activity and sexual frequency.<sup>1</sup> What the researchers found was that postmenopausal women using a vaginal moisturizer or a low-dose vaginal estrogen did not report greater increases in sexual activity or improvement in pain with sexual activity as compared to placebo. What was most surprising were the data that noted the placebo performed as well as the vaginal estrogen and the vaginal moisturizer in treatment efficacy.

What was not unexpected was the outcome that the estrogen intervention was similar in treatment efficacy to the vaginal bioadhesive moisturizer. As noted in research studies by Bygdeman and Swahn<sup>2</sup> and Nachtigall<sup>3</sup> who initially looked at this question, they also reported that the bioadhesive vaginal moisturizer, the same one that was used in the trial in this publication, was similar in terms of patient-reported relief of genitourinary syndrome of menopause (GSM) symptoms as compared to vaginal estrogen. Data from Bygdeman and Swahn's open-label, 3-month duration study noted that of the 11 sexually active women in the vaginal estrogen group and the 11 sexually active women in the vaginal moisturizer group, none reported pain with sexual activity at the conclusion of the study. In fact, most women in both groups reported no sexual pain after only 2 weeks of intervention.<sup>2</sup> Nachtigall studied a group of 30 women (15 in the estrogen arm and 15 in the bioadhesive moisturizer arm) and also noted comparable results. She reported that both interventions significantly increased vaginal moisture, vaginal fluid volume, and vaginal elasticity and decreased pH to premenopausal acidic values in women with GSM.<sup>3</sup>

The effectiveness of this bioadhesive moisturizer has not only been studied in humans, but also in baboons. I was the examining gynecologist for two of these nonhuman primate trials.<sup>4</sup> The purpose of these studies was to study vaginal health before and after vaginal application of this bioadhesive moisturizer in a nonhuman primate (the baboon) with declining estrogen levels. The research tested the effects this intervention had on vaginal atrophic changes in this animal model. Baboons were chosen because the literature suggests that they go through a menopause that is similar to humans. In fact, female baboons and macaques appear to be the most similar to women in terms of menstrual cycle, pregnancy, and menopause. The menopause in baboons, however, occurs at a younger age than that in humans. In captive and noncaptive baboons, cessation of menstruation tends to occur at approximately 26 years which is accompanied by loss of fertility versus women in whom an average menopausal age is around 51 years. In the research I was involved in, this bioadhesive moisturizer was tested in eight "menopausal" baboons. Although there was not a comparator intervention and no "patient" report of symptom relief, the results also mirrored the human results. With this intervention in baboons, there was marked improvement in their vaginal pliability, elasticity, and secretions, with decreased pH and increased thickness of the vaginal epithelium.<sup>4</sup>

What was not expected regarding outcomes was that the placebo was reported to be as efficacious as the other two interventions. But perhaps these results are not unexpected when one considers that the placebo was a hydroxyethylcellulose gel, one of the main ingredients in the marketed lubricant, K-Y Jelly. This lubricant (K-Y Jelly) contains both glycerin and hydroxyethyl cellulose as the lubricant components as well as other ingredients. Although, as the authors note, this hydroxyethylcellulose gel, when evaluated in vaginal microbicide studies, has a minimal effect on vaginal microbiota and inflammation, it may, in itself, have had some lubricating properties, despite not having the glycerin component. Therefore, although considered a placebo, perhaps it may have had a desirable physical effect in the vaginal area when used by the women in the study.

Of most importance, this study reinforces the fact that human sexual activity is affected by many factors, and not solely dependent on vaginal health and one specific intervention. Unfortunately, one of the major contributors to sexual

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health and wellness that is not included in most studies is the sexual health and expectations of the woman's partner and the overall wellness of their relationship. As the authors note, at enrollment in this study, the women noted "that their partners wanted more sex, or that they wished they wanted more sex." Perhaps future studies should include data from sexual partners, especially for participants who are engaging in sexual activity, because partners have an important role in sexual frequency and satisfaction. It's also important for the health care providers to ask about sexual activity and provide management strategies to those women who, although reporting GSM symptoms, would like to continue sexual activity. As has been shown by one of the early studies by Leiblum et al,<sup>5</sup> continued sexual activity in itself is beneficial for vaginal health. Therefore, asking about a sexual partner and whether there are sexual health issues in the relationship is important as well as offering management strategies. For those women who report no sexual partner, encouraging nonpartnered sex also appears to be beneficial for overall vaginal health.<sup>5</sup>

Clearly, the take-home message from this clinical trial is worth repeating. That, as the investigators noted, "providers and women should choose treatments for postmenopausal vaginal discomfort based on individual preference regarding cost and formulation." However, I would add one other consideration. That is, guidelines from professional societies,

such as The North American Menopause Society and task forces should always be taken into account when recommending management strategies, as these guidelines are an excellent resource for best practice templates. Not only will these professional guidelines advise practitioners on best practice for over-the-counter and prescription GSM interventions, but also for procedure-based ones. Perhaps one day in the future in the field of menopause and specifically for GSM, we will be able to practice precision medicine and offer individualized preventive and intervention strategies based on the genetic understanding of how each individual responds to a specific intervention.

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