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Dyspareunia – where and why the pain?

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Dyspareunia is specifically defined as pain during sexual intercourse, or pain with penile penetration of the vagina, with prevalence estimates among midlife women and beyond ranging from 8%–45%. [1] The variation in prevalence is due in part to the population studied, whether individuals are sexually active or not, type of sexual activity (e.g. partnered, type of partner, with or without penetration, vaginal/oral/anal), menopausal status, age, and sexual measures evaluated. The United States (US) National Health and Nutrition Examination survey (NHANES), a survey of the general population, reported an 8% prevalence estimate of dyspareunia among 50–59 year old women. [2] Importantly, it is unknown how many women, at midlife and beyond, stop having sex due to pain and are not included in studies of dyspareunia, but among women 57–64 years of age participating in a later NHANES study only 62% reported at least one "sexual act" in the prior year. [3] Of nearly 9,000 sexually active British women ages 16–74 years, the prevalence of painful sex (vaginal, oral, or anal) was highest in women ages 55–64 at 10.4%, dropping to 5.3% among those 65–74 years of age. [4] Whereas, among women in the Melbourne Women's Midlife Health Study there was a reversal in these trends, with 12% of those average age 50 years, and 17% of those average age of 60 years, reporting dyspareunia. [5] The proportions of individuals with dyspareunia in selected clinical samples, or surveys targeted specifically to midlife women, range from 20%–45% and are higher than general population prevalence estimates of comparable age groups. [1,6] Dyspareunia prevalence estimates from studies including only individuals engaging in sex with penile penetration of the vagina, may represent the tip of an iceberg, and an underestimation of the impact of pain with sex as a major determinant of postmenopausal quality of life. Rather, pain from sex of any kind is most relevant to our patients, regardless of sexual orientation and regardless of whether vaginal penetration occurs. A better understanding of the various psychosocial and etiologic factors impacting sexual activities of any kind, in midlife and beyond, should be a major research goal.

In this issue of *Menopause,* Goetsche et al [7] aim to systematically describe the pain characteristics and anatomic locations of vulvovaginal and pelvic tenderness in a cohort of postmenopausal individuals with moderate to severe dyspareunia, moving the needle forward to address an important aspect of life for all postmenopausal individuals and their partners. This study reports baseline findings from a convenience sample of women recruited for participation in a blinded randomized trial using a topical estrogen intervention. An inclusion criterion was moderate to severe dyspareunia associated with

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genitourinary syndrome of menopause (GSM). Baseline questionnaires included the Vulvar Pain Assessment Questionnaire (VPAQ) [8] and a battery of 13 questions picked from five validated questionnaires for lower urinary tract symptoms (LUTS). [9–13] All participants underwent a systematic vulvovaginal examination that included a visual assessment and cotton swab testing for tenderness that was measured using the Numerical Rating Scale (0–10), vaginal pH and mucosal sensitivity, and palpation of pelvic floor muscles and pelvic viscera for tenderness.

The 55 women recruited over 2 years for this small descriptive study had a mean age of nearly 60 years, reported having been with their present male partner for an average duration of 28 years and had a mean duration of dyspareunia of approximately 6 years. The average intercourse pain score was 7.3 ± 1.8 (scale 0–10). Pain was most often described as “burning” or “raw.” Virtually all had physical findings of vulvovaginal atrophy. Tenderness was most severe and most consistently located at the vulvar vestibule. The median pain scores from swab touch at the vulvar vestibule were between 4–5 (scale 0–10) and topical lidocaine alleviated pain in nearly all participants (91%). Virtually none had vaginal mucosal pain (median vaginal mucosal pain score was 0) and tenderness of the pelvic floor musculature was present in just over one third (35%). LUTS were reported by 82% of participants, including: stress incontinence in 55%, urgency in 44%, and frequency in 44%. Bladder pain not associated with urinary tract infections (UTIs) was reported in 17%, dysuria in 12%, and difficulty voiding, a symptom not listed as a component of GSM [14] was reported in 11%. The authors emphasized the importance of correlating dyspareunia symptoms with genital and pelvic examination findings and the importance of the development of a validated instrument for LUTS associated with GSM.

The proverbial elephant in the room in our understanding of the etiologies of sexual pain associated with menopause, including dyspareunia, continues to be that physical findings do not necessarily correlate well with severity of symptoms, nor is there always a response to treatments chosen specifically to address the presenting symptom complex and targeted examination. The authors point out that successful reversal of vaginal atrophy as judged by mucosal maturation and pH does not fully alleviate symptoms in many women, and that atrophy is not the only etiologic factor underlying postmenopausal dyspareunia. Our studies would support this conclusion.[15] Vaginal estrogen cannot be the only therapeutic answer. While some studies have evaluated anatomic and physiologic changes associated with estrogen deficiency — thinning of the mucosa, decreased blood supply, tightening or prolapse of the genital tract — few have assessed the effects of estrogen on the nerves of the human genital tract, much less linked these findings with a rigorous evaluation of sensory pain of vulvovaginal tissues plus detailed physical evaluation. Further, randomized controlled trials that examine the correlations between pelvic floor musculature pain detected by a thorough standardized examination as used in this study, with subsequent reports of improvements in dyspareunia following targeted pelvic floor physical study, are somewhat lacking. Most studies have been retrospective or observational.[16]

The authors should be applauded for including questions regarding LUTS, as urinary symptoms are an often under-studied aspect of GSM. They point out that there are no single validated instruments for the urinary symptoms of GSM and that the 2020 NAMS

position statement includes “urinary symptoms and conditions of dysuria, urgency, and recurrent UTIs but there is no evidence to support the rationale for including these three symptoms.”[14,7] Rather the authors suggest that the full complement of LUTS known to be influenced by hormonal status should be included in the definition of GSM. A summary of the take-home discussion points from this paper should be noted by clinicians and researchers alike. 1) The detailed physical examination as described in the methods and in Figure 1 is of tremendous value, and is an important aspect of understanding treatment failures; this standardized approach is critical for clinician’s choice of therapy and for comparing research findings. 2) Further assessment of the patient reported outcome measures (PROMS) for LUTS associated with menopause are needed (Table 3) in order to create a validated measure for a better understanding of GSM. 3) While many studies have addressed the gross and histologic structural changes associated with estrogen deficiency — thinning of the mucosa, decreased blood supply, and shrinkage of the genital tract — further research is needed to assess the effects of estrogen deficiency on the sensory neurons, and I might add motor neurons, of the human genital tract.

Not withstanding, some limitations of the study should be considered when interpreting the findings. This was a small, purely descriptive study with no comparison groups; it was not population-based. Results are generalizable only to heterosexual White women having sex with vaginal penetration with moderate to severe dyspareunia who are willing to be randomized to placebo or topical estrogen. Participants were from a single geographic location, Exclusion for acute vaginitis was made based on symptoms and vaginal discharge; no laboratory assessments to diagnose acute vaginitis were described. The examinations of the 55 participants were performed by any one of three unblinded clinicians who interpreted the study findings; training of the clinicians and fidelity of data collection is not described. The modifications of the VPAQ limits comparisons to other populations. The VPAQ only measures vulvar pain and does not measure all aspects of dyspareunia; no fully validated measures were used. Nearly 55% of participants had stopped intercourse for “lengthy periods” due to pain but “lengthy” was not described. Lastly, a high proportion of participants had SUI (55%) and LUTS (82%); these proportions appear higher than in other populations with GSM, but as the authors argue, these associations have not been fully or properly studied. They rightly conclude, “Larger, similarly detailed studies will need to establish what proportion of the GSM population shares these physical examination findings,” and I might add, establish the proportion of the population with GSM who also have contributing LUTS.

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