Vulvodynia: New Concepts and Review of the Literature

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KEYWORDS

• Vulvodynia • Genital tract • Vulvar discomfort
• Multifactorial disorder

Vulvodynia is defined by the International Society for Study of Vulvovaginal Disease (ISSVD) as "vulvar discomfort, most often described as burning pain without relevant visible findings or a specific, clinically identifiable, neurologic disorder."[1] Patients with vulvodynia often describe it as chronic vulvar burning, stinging, irritation, rawness, and, rarely, pruritis.[2] It may be felt only during sexual intercourse, experienced continually, or triggered by nonsexual activities such as walking.[3–6] Although believed in the past to be an uncommon condition, vulvodynia is a major contributing cause for patient referral. Data from a population-based study funded by the National Institutes of Health found that 15.7% of women reported lower genital tract discomfort persisting 3 months or longer.[7] Recent population-based studies show estimates as high as 28%, with 1 study showing that 39% of women who suffer from chronic vulvar pain fail to seek treatment.[7] Frequency of vulvodynia is underestimated partially because of the belief of the medical community that this problem is psychological and thus is not in their realm, and also because affected women are reluctant to discuss their symptoms because of fear of neglect. Vulval pain has been highlighted as a highly prevalent condition that is associated with substantial disability.[8] Although vulvodynia is a multifactorial pain syndrome in which psychological, social, and sexual function interact, it is a diagnosis of exclusion, in which treatable causes such as dermatoses, infection, neoplasia, and neurologic disorder must be ruled out; patients must be properly classified and also appropriate education and psychological support/counseling must be administered. As vulvodynia receives increased attention by both the medical profession and the media, more women are seeking care, information, and guidance.

CAUSES

Infection and Vulvodynia

The causes of vulvodynia are unknown; however, several hypothesis have been proposed to identify causative factors. One of the most consistently reported clinical findings associated with the onset of vulvodynia is a history of frequent yeast infections. A chronic subclinical yeast infection was believed to play a role in the development of symptoms, but the use of antifungal medications has been shown to be inadequate for patients with undocumented yeast infection.[9–11] It is not clear whether the culprit is the yeast itself, the treatments undertaken that can sensitize the tissue, an underlying sensitivity present in the tissue, or simply the most common diagnosis made for unexplained symptoms. A recent study suggested that diverse urogenital infections such as yeast infection, urinary tract infection, trichomonas, and human papilloma virus (HPV) may precede the onset of vulvodynia, with multiple assaults significantly compounding risk.[12,13] However, this has not been a consistent finding within other studies, and prospective studies documenting

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urogenital infections in association with vulvodynia are warranted.

Although HPV was initially reported as a frequent cause of vulvodynia, testing for HPV has shown that this virus is absent in most women with vulvar pain.[14–17] One recent study observed that the low rate of observed infection in women with vulvodynia, and the diversity of HPV types detected in the patient population studied, suggest incidental virus carriage rather than direct cause and effect.[18,19]

Genetic Factors

Gerber and colleagues[20] conducted studies on genetic predisposition and the onset of vulvodynia. They found that more affected women were homozygous for allele 2 in the interleukin-1β receptor antagonist and for allele 2 interleukin-1β gene than nonaffected women. Each of these alleles has been associated with prolonged inflammatory response. Susceptibility to vulvodynia might be influenced by carriage of this polymorphism. They concluded that these findings strongly imply that women with vulvodynia may be at increased risk for a proinflammatory immune response to be triggered by a variety of stimuli and may have difficulty in terminating an inflammatory event that involves interleukin-1β production. A similar deficit in interleukin-1receptor antagonist production has been shown to contribute to chronic inflammation in individuals with inflammatory bowel disease. The investigators also stated that some women have a genetic predisposition to develop a chronic inflammatory response after an inciting event, such as a yeast infection. The prolonged inflammation could trigger other events such as increased sensitivity in both genital and nongenital areas of the body. It has been reported that affected women have more somatic pain disorders and show increases in sensitivity to nongenital touch, pain, and temperature.[21–23]

Vulvodynia as a Neuropathic Disorder

Vulvodynia has features that are characteristic of other chronic neuropathic pain conditions. These features include the persistent and burning quality of the pain, the allodynia and hyperpathia, the absence of physical findings on examination, lack of associated pathologic condition of the tissues, and strong association with depression, and are all reminiscent of other neuropathic syndromes such as regional pain syndrome (formerly reflex sympathetic dystrophy), and pudendal neuralgia.[8,24–29] The transition from the nociceptive to neuropathic pain is key in vulvodynia because it underlies the shift from a pain disorder in which sexual intercourse elicits pain to a pain disorder that is progressive and ongoing even with the avoidance of any further intercourse.[8,28] The role of neuropathic pain in vulvodynia is supported by a documented response to agents used to treat neuropathic pain. Immunohistochemistry has shown altered density of nerve endings such as the vanilloid receptor VR1 (TRPV1), which is expressed by nociceptors, and is triggered by capsaicin, noxious heat, protons, and chemicals produced during inflammation; as well as increased number of intraepithelial free nerve endings, calcitonin-related gene peptide (peptide found in nerve fibers), lowered tactile and pain thresholds, nociceptor sensitization, and overall peripheral nerve hyperplasia.[30–34] Several studies report successful treatment of localized vulvodynia with botulin toxin A.[35–38] Moreover, increased blood flow and erythema in the posterior vestibular mucosa have been shown in vulvodynia via laser Doppler perfusion imaging of the superficial blood flow in the vestibular mucosa. Researchers postulated that such observation is the result of both neovascularization and angiogenesis along with the release of neuropeptides from C fibers in the skin, which produces an axon reflex causing vasodilatation and increased blood flow.[39]

Pelvic Floor Abnormalities and Vulvodynia

Most women with vulvodynia exhibit pelvic floor abnormalities. Pelvic floor performance is significantly lower in affected patients in terms of contractile and resting ability and stability and efficiency of contraction.[40–44] Pelvic floor abnormality may serve as causative or aggravating factors in the development of vulvodynia. Rehabilitation of pelvic floor muscles via surface electromyography has been successful in reducing pain and increasing sexual interest, pleasure, and activity.[8]

Hormonal Influence

Hormones have a role in the genesis and continuance of many pain syndromes. Some clinic-based studies support an association between hormonal contraception and vulvodynia. The effect of oral contraceptives (OCs) on vulvar epithelium is largely unknown, however they may "alter the vaginal epithelium by promoting loss of a cyclic pattern, low karyopyknotic index and the appearance of navicular cells with marked curling and folding."[45,46] The presence of estrogen from OCs and the increased number of parabasal cells (a marker of atrophy), is unexpected. According to a recent study, women taking OCs have lower mechanical pain thresholds in the vestibular region compared with controls.[45] Other studies suggest