Primary and Secondary Provoked Vestibulodynia: A Review of Overlapping and Distinct Factors

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ABSTRACT

Introduction: A common subtype of vulvodynia is provoked vestibulodynia (PVD), characterized by severe pain upon contact to the vaginal entrance. Some researchers have further delineated the PVD group based on pain onset (primary vs secondary PVD, referred to as PVD1 and PVD2, respectively).

Aim: This study aims to review available evidence regarding sociodemographic variables, pain characteristics, medical history and examination findings, quantitative sensory testing, genetic markers, psychosocial/sexual/relationship function, treatment outcome, and brain imaging in women with PVD1 and PVD2.

Methods: All available data related to PVD1 and PVD2 were reviewed.

Main Outcome Measures: There is mixed evidence supporting the assumption that women with PVD1 fare worse on all variables investigated.

Results: The review indicated that although women with PVD1 seem to fare worse on many variables examined (eg, pain severity, genetic markers), many studies also indicated no significant group differences or—less commonly—that women with PVD2 fare worse on some variables (eg, sexual function).

Conclusion: Although it has been suggested that different pathophysiologic processes are involved in the development and maintenance of PVD1 and PVD2, the data reviewed were mixed. While most studies indicated that women with PVD1 have higher pain intensity, higher sensitivity, more genetic influence, more evidence of inflammation, lower successful treatment outcomes, and different neural activation patterns and structural findings, these results were not consistently reported. In addition, the data for subgroup differences in psychosocial, sexual, and relationship variables were not convincing. A more precise definition of primary and secondary PVD is needed, and importantly, prospective, longitudinal studies are essential for clarifying any differences within these PVD subgroups.

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Key Words: Vulvodynia; Vestibulodynia; Primary; Secondary; Pain Onset; Pain Characteristics

INTRODUCTION

Vulvodynia (ie, chronic vulvar pain) is a neglected women's health problem. It is poorly understood and often misdiagnosed or ignored; it also entails a substantial personal cost to patients and a significant financial cost to society in terms of direct health-care costs (eg, insurance payments, out of pocket expenses), direct non-health-care costs (eg, parking), and indirect costs (eg, financial loss due to sick leave, employer payments to patients for medically related work loss).[1] Vulvodynia affects approximately 16% of women in the general population[2] and is associated with significant interference in many life domains, such as psychologic adjustment, quality of life, and reproductive potential.[3,4] Difficult to diagnose and treat, many women suffer for long periods of time. One study found that only 60% of affected women sought treatment; 30% consulted three or more physicians to obtain a diagnosis, and the condition remained undiagnosed in 40%.[5] Unfortunately, little is known about the etiology of vulvodynia,[6–12] and its diagnosis is one of exclusion.[13]

The International Society for the Study of Vulvovaginal Disease (ISSVD) currently defines vulvodynia as "vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings".[13] Vulvodynia is divided into two categories based on pain location: *Localized vulvodynia* refers to pain in a particular part of the vulva, such as the vestibule (ie, vaginal entrance); *generalized vulvodynia* refers to pain affecting the entire vulvar region. Each category is further divided based on *when* the pain occurs: provoked (the pain occurs in response to external stimulation, eg, pressure), unprovoked (spontaneous pain which occurs independently of stimulation), and mixed (the pain occurs in both situations). Provoked pain can result

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from sexual activities (leading to dyspareunia, or painful intercourse), non-sexual activities, or both. This definition has allowed for the delineation of several subtypes of vulvodynia. The most common form is provoked vestibulodynia (PVD), which affects 12% of women in the general population.[2] PVD is characterized by severe pain—typically described as burning, searing, sharp, and cutting[14]—that occurs in response to pressure localized to the vestibule during activities involving pressure to the vaginal opening. Most research on samples of women with PVD focuses on differences between women with and without this condition[15–17], with a handful of studies comparing women with PVD to women with other pain conditions, such as chronic pelvic pain.[18] It is, however, becoming clear that women with PVD do not constitute a homogeneous group. Within the PVD group, there appears to be at least two major subgroups based on pain onset: women with primary PVD (PVD1, also called lifelong or early onset PVD) report having experienced vulvar pain since their first attempt at activities involving vaginal penetration (eg, tampon insertion, sexual activities), whereas women with secondary PVD (PVD2, also termed acquired or later onset PVD) report experiencing developing the pain after a period of pain-free penetrative activities. Based on the clinical literature, PVD1 and PVD 2 are believed to affect an equal number of women[19]; however, the specific question of the prevalence of subgroups based on onset has never been confirmed via an epidemiologic study. Based on one study examining remission of vulvar pain in women with primary vulvodynia using a subsample of a random sample of women presenting to health services, prevalence rates suggest that approximately 35% presented with primary vulvodynia and 65% with secondary vulvodynia.[20] In addition, Nguyen, Reese, and Harlow demonstrated that women of Hispanic origin were more likely to report histories consistent with PVD1, as well as a burning type of pain, as compared with non-Hispanic Whites.[21] Studies examining the prevalence of the primary and secondary forms of PVD are needed, given that research (reviewed below) has indicated numerous significant differences between these subgroups. Typically, the pattern of findings suggests that women with PVD1 fare worse on many variables ranging from self-reported pain characteristics to neural correlates of painful sensation, and some have even suggested that PVD1 and PVD2 develop from different etiologic pathways and entail different triggers.[10,22-24] However, most of these studies are cross-sectional; therefore, firm conclusions regarding "cause and effect" (eg, do women with PVD1 fare worse from the beginning, or is it because they, in fact, experience pain more intensely than women with PVD2?) cannot be made.

PRIMARY AND SECONDARY PVD SUBGROUPS

Sociodemographic Variables and Pain Characteristics

Several studies have indicated that women with PVD1 and PVD2 differ on some sociodemographic variables and self-reported pain variables. Compared with women with PVD2, women with PVD1 are more likely to be younger at symptom onset,[22,25,26] single,[22,26] less likely to have had children[19,22,23,26-28] and report experiencing the pain for significantly longer.[27,29,30] In addition, many studies have found that women with PVD1 report more severe pain with first and subsequent intercourse attempts[19,28] (pain ratings during first intercourse data from 27: PVD1 mean = 7.04 and PVD2 mean = 5.12 [$P = .05$], on a scale from 0, *no pain at all*, to 10, *worst pain ever*) and a history of more severe vulvar pain[19] than women with PVD2 (but see Sutton et al[28] for no differences between subgroups in terms of percentage of painful intercourse occasions, intercourse pain ratings, or duration of painful symptoms postvaginal penetration). Furthermore, Heddini et al reported that primary PVD status accounts, in part, for intercourse pain scores.[31] Many of these differences can be explained by the earlier onset of the pain in women with PVD1; for example, it is not surprising that women who have had the pain longer are younger at symptom onset and report lengthier pain symptoms than those who have not had the pain for as long, leading to conflated findings. However, other between-groups differences are not as easily explained as these ones (eg, the higher pain ratings in women with PVD1), suggesting that PVD1 may be a more severe form of PVD than PVD2.

Medical History and Examination Findings

Studies have indicated that women with PVD1 are more likely to report a family history of dyspareunia,[19] a history of childhood enuresis (eg, bedwetting),[32] and dysmenorrhea (ie, painful menstruation)[23,33] than women with PVD2. In addition, women with PVD1 are less likely to have confirmed physical findings of infections or to report having undergone aggravating local treatments before pain onset[19] than women with PVD2.

Although two studies demonstrated that women with PVD1 and PVD2 did not significantly differ on various gynecologic examination findings (eg, pain intensity ratings collected during a randomized cotton-swab palpation of the vulvar vestibule and vulva, as well as during speculum insertion; degree of mucosal atrophy),[28,34] other studies have reported differences in the extent of the painful area involved in pain symptoms. In a clinically based sample of women with PVD, Bornstein et al found evidence of involvement of a larger portion of the vestibule in women with PVD2 (anterior and posterior) compared with those with PVD1 (posterior only).[22] Similarly, in a study involving 132 women with PVD who had sought treatment in a multidisciplinary vulvodynia program, Brotto et al. found that women with PVD2 self-reported more severe pain at the clitoral hood—but not at the labia minora, labia majora, or clitoris—than those with PVD1.[33] Some researchers have suggested that this pattern could indicate different processes of pain development or expression, for example, a higher likelihood of inflammation affecting the vestibule in women with PVD2 as compared with PVD1.[24] In line with this idea, one research team found subgroup differences in protease inhibitors via examination of vaginal secretions.[35] Various proteases and protease