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Vulvodynia; an under-recognized disease

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Abstract

Vulvodynia is a chronic condition which affects an increasing number of women; it presents currently an incidence that is higher than had previously been estimated. Regarding pathogenesis, several (hormonal, infectious, inflammatory and psychological) factors have been proposed, but vulvodynia etiology remains still unclear. This disorder is a multifactorial condition with a significant impact on the patient's quality of life, yet is difficult to diagnose (an under-estimated/ under-recognized affection). Certain medical investigations are required in order to exclude other diseases (the diagnosis of vulvodynia being one of exclusion), but anamnesis and physical examination are essential steps in the diagnosis.

Although many therapies have been proposed, both pharmacological and non-pharmacological, a standardized therapy has not yet been established/ generally accepted. Accordingly, many therapeutic options have been studied with varying results. Vulvodynia remains a challenging disease and a multidisciplinary approach is needed to achieve satisfactory outcomes. Further studies are needed to completely understand its pathogenesis and to develop a standardized treatment.

Keywords: vulvodynia, vulvar pain, diagnosis, investigations, therapeutic approaches



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Introduction

Vulvodynia (vulvar pain) is a chronic condition affecting 9-12% of women and reported in women aged 16 to 80 (1). Ethnic differences have been observed, vulvodynia being more frequently encountered in Caucasians than blacks (2). Most commonly patients complain of a burning sensation in the vulvar region (3). Vulvodynia represents an important public health issue; in the United States, the cost of treating these patients varies between 31 and 72 billion dollars annually (4).

For a long time vulvodynia was not clearly defined. In 1976 the term “burning vulva syndrome” was used, but in 2003, it was replaced with the term “vulvodynia” by the International Society for the Study of Vulvovaginal Disease- ISSVD (5). According to the definition of the ISSVD, vulvodynia is a chronic pain localized in the vulvar area which lasts more than 3 months without a proven etiology. Several types of vulvodynia are described: provoked vulvodynia (caused by direct touch, inserting a tampon, or sexual touch) localized especially by the vaginal vestibule, unprovoked vulvodynia (occurring without touch or contact) and, mixed vulvodynia. It may be considered „generalized,” as when the symptoms involve the whole area of the vulva, or localized to the clitoral area (clitorodinia) or to the

vestibule (vestibulodynia) (4, 6). Recently, in April 2015 a classification of chronic vulvar pain was completed which indicates that the vulvar pain may have a specific cause (inflammation, trauma, neoplasm) or may be idiopathic, in which case the term of vulvodynia should be used (4, 7).

Discussion

Pathogenesis

The pathogenic mechanism of vulvodynia is not fully understood. Over time, several theories have been postulated, which have attributed roles to hormonal, infectious/ inflammatory, and psychological factors in its pathogenesis (8).

- *Role of infections.* Inflammatory response developed as a consequence of genitourinary infections may be involved in the occurrence of vulvodynia. For instance, in women with vaginal infection due to *Trichomonas*, pro-inflammatory markers such as IL6, IL8 and TNF alpha were identified. In another study, a group of women with vulvodynia was compared with a group of healthy women and it was observed that a significantly higher percentage of those with vulvodynia were infected with strains of human papilloma virus (HPV) (8). Some authors consider that vulvodynia may occur due to hypersensitivity to various species of *Candida* (9). However no study has revealed a link between any infectious agent and the development of vulvodynia.

• *Neuro-inflammatory hypothesis.* In some cases of vulvodynia histopathological examination displayed an inflammatory infiltrate consisting mainly of mast cells; in other cases a reduced number of mast cells was seen or the inflammatory infiltrate was not identified. With respect to the mediators of inflammation, pro-inflammatory cytokines and vulvovaginal neurokinin CGRP were revealed. Thus, the hypothesis of a neuro-inflammatory process involved in the vulvodynia pathogenesis was suggested (10).

• *Hyperinnervation.* Many studies analysed the number of nerve fibers in the vulvar area and the presence of hypersensitivity. A large number of nerve endings acting as nociceptors were observed, which may explain the allodynia experienced by those women. A high sensitivity to different stimuli (tactile, thermic) was revealed especially in the patients with provoked vulvodynia (4). In addition, patients with vulvodynia have lower pain thresholds than healthy women. Somatosensory changes were detected mainly in the vestibular area (10).

• *Muscles dysfunction.* A role in the pathogenesis of vulvodynia has been attributed to pelvic floor muscle dysfunction. Electromyographic studies have shown increased muscle tonus and impaired relaxation in these patients (10).

• *Hormonal factors.* Several authors have described an association between the use of oral contraceptives and vulvodynia, but others have refuted this hypothesis (11). The study of Bazin et al. revealed that women who had used oral contraceptives before age 17 had a higher risk of developing vulvodynia. However the study has as a limitation a low number of women who did not use oral contraceptives (12).

• *Psychological factors.* In terms of psychological factors, vulvodynia is identified more commonly in women with an altered psychological status, those with sleep disorders, with posttraumatic stress or suffering from chronic pain (2). Several studies have highlighted that the women with vulvodynia associate different conditions characterized by chronic pain such as fibromyalgia, irritable bowel syndrome, interstitial cystitis, and temporomandibular joint disorders (13, 14).

Diagnosis

The first symptoms may occur after the first sexual contact or later, and in some cases in childhood. Anamnesis and clinical examination are very important to differentiate between organic chronic pain and vulvodynia. The anamnesis should include information about the patient's sexual behaviour, local hygiene, and clothing. Many times a correct diagnosis is achieved later, after many

visits to different doctors; in some cases it may take several years. Diagnosis of vulvodynia should remain a diagnosis of exclusion. Vulvodynia most commonly occurs in women aged 20 to 40. A higher incidence has been observed in Hispanics. The pain varies in intensity and may be described as a burning sensation or as a pruritus, or it may have an irritative character. Erythema may be noticed especially in the vestibular area and around the Bartholin glands (15-17).

In order to identify the sensitive vulvar area a cotton swab should be used. Commonly the higher sensitive area is identified in the posterior introitus and the posterior hymenal remnants. A thorough genitourinary examination should be performed in order to rule out other conditions such as infections or trauma. In addition, the patients should be referred to a gynaecologist and undergo a colposcopy. An examination of the vaginal secretion to rule out an infection should also be carried out (15, 18).

The most common form is localized provoked vulvodynia. Patients having this form report an intense and long-lasting pain, provoked by a touch, in a certain region, while no pain is felt in other regions. Patients state that the symptoms (pain, burning) may last for several hours. In addition, they present dysuria, difficulty in using tampons

and often interrupt the sexual acts due to dyspareunia (19).

It was observed that remission of the symptoms may occur in 10% of cases, even without treatment and it seems to be related to the onset of the disease. Therefore vulvodynia is primary when the onset is at the time of sexual debut or first tampon insertion, and secondary when the symptoms occur later. The remission occurs most commonly in secondary vulvodynia, a fact that suggests that a different etiopathogenic mechanism may be involved. Analyzing tissue from the involved areas, studies have revealed that in primary vulvodynia the density of nerve fibers is higher and the degree of hyperplasia is greater (20).

The main differential diagnoses are allergic vulvitis, chronic candida vulvovaginitis, lichen planus, lichen sclerosis, vaginismus and vulvar intraepithelial neoplasia (15).

Treatment

The first steps must focus on rules regarding hygiene and diet. The patient should avoid irritating products such as soaps and perfumes or alcohol-based creams and wear cotton clothes and use moisturizing creams. Studies have shown that a diet containing less oxalates and less simple carbohydrates may be useful. In addition, calcium citrate may be administered due to its role in

decreasing the oxalate deposits in the skin (1,21). In many cases vulvodynia is not diagnosed and appropriately treated (22). Since the etiology of the disease is unknown and many mechanisms were supposed to be involved, the treatment is empirical and includes various methods, pharmacological and non-pharmacological. The approach to the patient should be multidisciplinary (3, 23).

Topical treatment

Topical lidocaine 5% is the most common drug administered in patients with vulvodynia. Lidocaine through its anesthetic effect decreases hypersensitivity. It is best applied in the evening or before intercourse to relieve pain and discomfort. Haefner et al. have revealed significant improvement of symptoms after 7 weeks of treatment (24).

Some authors have emphasized the efficacy of topical capsaicin. This approach has the disadvantage of causing discomfort on the application area, being discontinued by patients in most cases (11). Estrogen cream may be applied especially in premenopausal women, but studies have shown a variable efficacy (16).

The effectiveness of cromolyn in the treatment of vulvodynia is controversial—in one study results were no better than those of a placebo group (25). Its mechanism of action is based on the

decrease of mast cells degranulation (15). Corticosteroids may be useful if they are administered intralesionally; topical administration did not prove effective (11).

Other topical therapies reported in some studies as effective are nitroglycerin, amitriptyline 2% in combination with baclofen 2% and topical antifungal agents (24).

Systemic treatment

Tricyclic antidepressants, drugs used in neuropathic pain, are often the first-line medication in vulvodynia. Amitriptyline and desipramine are most commonly used (21). However Leo et al. have analysed the available studies on vulvodynia and found no sufficient evidence to support their administration in vulvodynia (26). Tricyclic antidepressants act by blocking the reuptake of noradrenalin and serotonin. Serotonin inhibitors, which are also administered in neuropathic pain, have been suggested as a therapeutic option, but their effectiveness is still questionable, more useful being selective serotonin and norepinephrine reuptake inhibitors (9).

The systemic medication also includes anticonvulsant drugs, gabapentin and carbamazepine, with success rate reported between 50 and 82%. However further studies are needed to demonstrate the efficacy of this drug class (24, 27).

Surgery

In the case of localized pain, surgery may represent a therapeutic option. Studies have revealed that up to 80% of patients who undergo vestibuloectomy report the remission of the disease (21). Nevertheless this method should be reserved for very serious cases (15). The recurrences are common on the remaining vulvar tissue (21).

Other treatments

Psychological and psychosexual therapies play an important role in the management of patients with vulvodynia. Besides basic counseling which may be performed by any physician and consists of reassuring the patient that she has no any underlying disease, cognitive behavioural therapy may be used with significant benefits, according to some studies (3, 28). Psychosexual therapy may be useful in order to improve the sexual contact, requiring several sessions which are best carried out with the patient's partner present (3).

Although physical therapy is not a standardized treatment, it may be effective. Physical therapy includes active exercises for the pelvic girdle and floor, soft tissue mobilization and joint manipulation, electrical stimulation, and bladder and bowel retraining (16, 24). It has been observed that patients with vulvodynia have associated hypertonia of the pelvic floor (11).

Several studies have shown the beneficial role of botulinum toxin in the treatment of vulvodynia. Botulinum toxin inhibits the release of substance P and glutamate from nociceptive neurons (29, 30).

The impact of vulvodynia on the quality of life

Vulvodynia has a significant impact on the patient's quality of life (31). Khandker et al. have shown that patients with vulvodynia often exhibit psychiatric disorders such as anxiety and depression; at the same time vulvodynia represents a risk factor for developing such disorders. (32). It has been observed that the disease has a major social and emotional impact, limiting work-related activities as well as leisure. In addition, these women are sad and frustrated (33).

Patients with vulvodynia report a decrease in sexual desire, in sexual satisfaction and frequency of sexual acts. In addition, patients are more distressed about their body image (4, 34).

Conclusions

Vulvodynia is a disorder difficult to diagnose, with an incidence higher than previously thought. It is a multifactorial condition having a significant impact on the patient's quality of life. The diagnosis is one of exclusion, requiring further investigations. Many therapeutic options have been studied with varying results. Vulvodynia remains a challenging

disease and a multidisciplinary team is needed to achieve satisfactory outcomes. Further studies are needed to completely understand its pathogenesis and to work out a standardized treatment.

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