2013 Vulvodynia Guideline Update

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■ Abstract: Vulvodynia is a complex disorder that can be difficult to treat. Most patients describe it as burning, stinging, irritation, or rawness. Vulvodynia is a costly disease both economically and on its negative impact on patient quality of life. Although many treatment options are available, no one treatment is effective for all patients, thus the need to individualize management. Measures such as gentle vulvar care, medication, biofeedback training, physical therapy, sexual counseling and surgery, as well as complementary and alternative therapies are available to treat the condition with varying success. ■

Key Words: vulvodynia, vulvar pain, vulvodynia guideline, diagnosis, treatment

Vulvodynia remains a complex disorder that can be difficult to treat. Since the publication of ''The Vulvodynia Guideline'' in 2005, by Haefner et al. [1], and American Congress of Obstetricians and Gynecologists Clinical Opinion on Vulvodynia, in October 2006 [2], there have been a number of reports on the subject but essentially no new breakthroughs in the understanding of the underlying pathophysiology of this disorder or its management. We therefore present here the state of the science about vulvodynia and provide guidance based largely on expert opinion to assist the patient and practitioner in dealing with this complex disorder [1].

Recent reports shed little light on the impact of treatments for the symptoms of vulvodynia. Methodological issues such as small sample size, nonexperimental design, and lack of placebo control compound the problem. Moreover, there is evidence suggesting that the symptoms of vulvodynia fluctuate considerably over time, further blurring interpretation of success or failure of available treatment modalities. This is compounded in studies where long-term follow-up of patient data are not available.

Although vulvodynia is reported by up to 16% of women in the general population, National Institutes of HealthYfunded projects addressing vulvodynia epidemiology, treatment, and outcomes have remained poor [3]. A recent Web based survey was conducted to assess the economic burden and quality of life for women with vulvodynia in the United States and found that the total costs per patient in just 6 months were over $8,800.00 [4]. Thus, the annual national cost burden for vulvodynia was estimated to range from $31 to $72 billion in the United States [4].

Terminology and Classification

The International Society for the Study of Vulvovaginal Disease define vulvodynia as vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder [5]. It is not caused by a commonly identified infection (e.g., candidiasis, human papillomavirus, herpes), inflammation (e.g., lichen planus, immunobullous disorder), neoplasia (e.g., Paget disease, squamous cell carcinoma), or a neurologic disorder (e.g., herpes neuralgia, spinal nerve compression). The classification of vulvodynia is based on the site of the pain; whether it is provoked, unprovoked, or mixed; and subcategorized as generalized or localized. Although it is suggested that features of pain encountered in vulvodynia resemble those of neuropathic pain conditions, a location within the central or peripheral nervous systems has not been identified.

Proposed etiologies include abnormalities that stem from early fetal development, genetic or immune factors, hormonal factors, inflammation, infection, neuropathic changes, and dietary oxalates [1]. However, given the variable presentation and individualized responses to treatment, vulvodynia causation is most likely multifactorial.

Although distinguishing generalized vulvodynia from localized vulvodynia is fairly straightforward (using a

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simple cotton swab test), determining whether they represent different manifestations of the same disease process remains unknown.

Diagnosis and Evaluation

Vulvodynia remains a diagnosis of exclusion. Thus, excluding other treatable causes before assigning this diagnosis is imperative. A thorough history should identify the patient's duration of pain, medical and surgical history, sexual history, allergies, and previous treatments. It is important to ask permission to discuss the patient's sexual history, even if permission seems implied.

Cotton swab testing (see Figure 1 and Figure 1 from The Vulvodynia Guideline [1]) is used to differentiate between generalized and localized pain and to identify areas of localized pain, classifying areas where there is mild, moderate, or severe pain. A diagram of pain locations may be helpful in assessing the pain over time. The vagina should be examined, and tests, including wet mount, vaginal pH, fungal culture, and Gram stain, should be performed as indicated. Fungal culture may identify resistant strains, but sensitivity testing usually is not required. Testing for human papillomavirus infection is unnecessary. Colposcopy, including use of 3% to 5% acetic acid vulvar soak, has been shown to be unnecessary [6]. The role of biopsy remains at the discretion of the individual provider. In a retrospective review, 61% (55 of 90 biopsy specimens) of patients with refractory vulvodynia had clinically relevant dermatoses based on dermatopathologist-analyzed vulvar biopsies [7]. Thus, although there are no specific histopathological features of vulvodynia, practitioners should assess the need for biopsy to exclude other etiologies. Vulvar pain also can be referred pain from other parts of the body, such as the back or hips, so a thorough musculoskeletal evaluation should be performed [1].

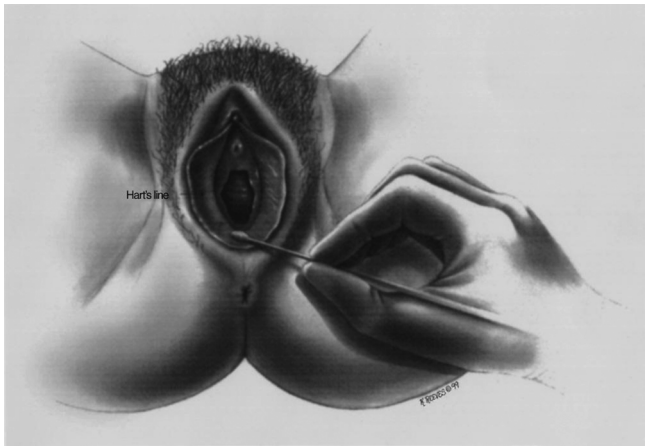

Figure 1. The cotton swab test. The cotton swab is used to test for pain locations on the vulva. Testing starts at the thighs and moves medially to the vestibule. The vestibule is tested at the 2:00, 4:00, 6:00, 8:00, and 10:00 positions. Each time the vestibule is touched if pain is present; the patient is asked to quantify the pain as none, mild, moderate, or severe. Reprinted with permission from *Clinical Obstetrics and Gynecology* (2000;43:689Y700). Copyright 2000, Lippincott Williams & Wilkins.

Guideline Update Methods

A comprehensive search of MEDLINE, PubMed, and Google Scholar was conducted using the key words vulvodynia, vestibulodynia, vulvar pain, dyspareunia, treatment, medication, surgery, vestibulectomy, physical therapy, psychotherapy, alternative therapy, hypnosis, acupuncture, botulinum toxin, nerve stimulation, and electrical nerve stimulation.

The majority of the evidence regarding treatment of vulvodynia published subsequent to The Vulvodynia Guideline continues to be limited by study design (lack of placebo controls, small sample size, and inadequate or unvalidated outcome measures). Thus, The Vulvodynia Guideline remains a practical tool for clinicians. Limited evidence regarding the use of botulinum toxin has emerged, as well as several placebo-controlled trials that underscore the strong placebo effect and the need to include a placebo or comparison group in any treatment studies for vulvodynia.

General Treatment Considerations

Although optimal treatment remains unclear, an individualized, multidisciplinary approach should be considered to address all physical and emotional aspects to which the pain of vulvodynia can be attributed, for example, sexual counselors, clinical psychologists, physical therapists, and pain specialists. Although patients may interpret and perceive this approach to mean that the practitioner does not believe their pain is ''real,'' it is important to begin any treatment approach with a detailed discussion including an explanation of the diagnosis and determination of realistic treatment goals.

Certain comorbidities (e.g., headache, irritable bowel syndrome, interstitial cystitis, fibromyalgia, back pain, and temporomandibular joint disorder) confound establishing a diagnosis of vulvodynia and should be considered when choosing treatment. Often, medications used for one chronic pain syndrome may benefit another chronic pain syndrome. In addition, it is important to

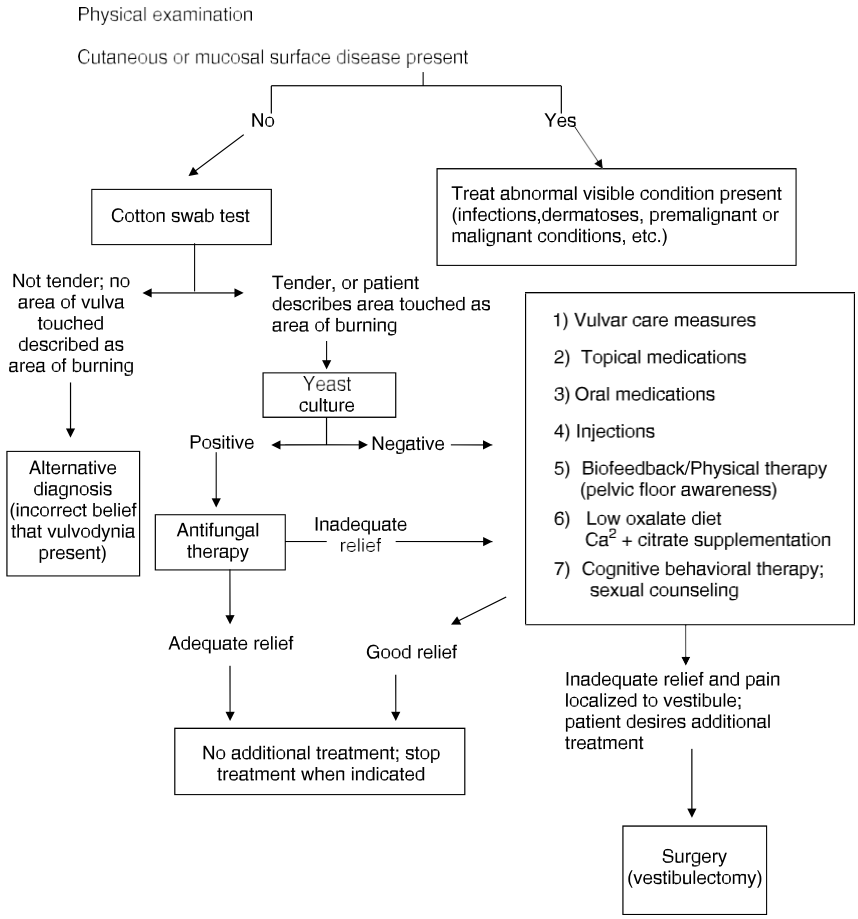

Figure 2. Vulvodynia algorithm. Reprinted with permission from the *Journal of Lower Genital Tract Disease* (2005;9:40Y51)[1]. Copyright 2005, American Society for Colposcopy and Cervical Pathology.

consider potential drug interactions when prescribing a new medication.

Vulvodynia Treatment Overview

As noted in earlier publications, most evidence for treating vulvodynia is based on clinical experience, descriptive/observational studies, or reports of expert committees. Few randomized trials of vulvodynia treatment exist. The previously published vulvodynia treatment algorithm [1] (see Figure 2 and Figure 2 from The Vulvodynia GuidelineVVulvodynia Treatment Algorithm [1]) includes vulvar care measures; topical, oral, and injectable medications; biofeedback training; physical therapy; dietary modifications; cognitive behavioral therapy; sexual counseling; and surgery. Medications used include topical, oral, and intralesional agents as well as pudendal nerve blocks, acupuncture, and hypnotherapy [1]. Newer treatments include the use of stimulators and botulinum toxin. Many medications used are known to interact with other drugs, and many patients with vulvodynia may be taking multiple medications. Clinicians are cautioned to observe for potential drug interactions and prevent this occurrence before prescribing any new medication.

Gentle vulvar care is advised [1]. Common suggestions include wearing cotton underwear during the day and none at night, avoiding vulvar irritants (perfumed substances, dyed toilet articles, shampoos, detergents, douches, and wipes), and use of mild soaps, with none applied to the vulva. The vulva can be cleaned gently with water and patted dry. After cleansing, an emollient without preservatives (vegetable oil or plain petrolatum) helps to hold moisture in the skin and improve the barrier function. If menstrual pads are irritating, cotton pads may be helpful. Adequate lubrication for intercourse is recommended. Cool gel packs may be helpful in some and are preferred over ice packs to avoid irritation from overuse.

Topical

Commonly prescribed topical medications that might cause local irritation include a variety of local anesthetics

(applied immediately before intercourse or in extended use), estrogen cream, and tricyclic antidepressants compounded into topical form. Before prescribing a new course of therapy, clinicians should consider stopping the use of all topical medication to see if symptoms decrease [1].

As previously reported, the most commonly prescribed topical medication remains lidocaine ointment or jelly, applied as required for symptoms and 30 minutes before sexual activity [1]. Lidocaine may cause stinging or sensitization. Male sexual partners may experience penile numbness and partners should avoid oral contact. It is important to use caution in using excessive amounts of lidocaine and other topical anesthetics because of the potential for toxicity and sensitization.

Although nightly application of lidocaine 5% reduced dyspareunia in a prospective cohort, in a randomized, placebo-controlled trial, lidocaine 5% cream was found to be less effective than topical placebo (20% vs 33% response rate, respectively) [8, 9].

Other topical agents found to be no more effective than placebo include cromolyn 4% and nifedipine. Despite a case series demonstrating benefit, the topical application of cromolyn 4% applied locally in a placebo-controlled randomized, double-blind study demonstrated no statistically significant difference in symptom reduction (54% reduction) compared with placebo use (38% reduction) [10]. Likewise, the effectiveness of topical nifedipine 0.2% and 0.4% did not exceed placebo in a double-blind study of 30 women with vulvodynia [11]. Given these previous reports, single-arm and retrospective assessments of other compounded topical agents found to reduce vulvodynia (e.g., gabapentin, 2% amitriptyline and 2% baclofen, nitroglycerine, capsaicin, estrogen) should be interpreted with caution [1]. Several other topical therapies have not been shown to have significant benefit to patients with vulvodynia, including topical corticosteroids, topical testosterone, and topical antifungal medications [1].

Note that a compounding pharmacy may be needed to formulate topical medications. Choosing the proper vehicle for topical medications is important because creams contain more preservatives and stabilizers and often produce burning on application, whereas ointments are usually better tolerated [1].

Emerging Topicals

Vaginal diazepam use has been reported in a few case series and case reports for pelvic floor dysfunction and vulvar pain [12Y14]. However, because diazepam is a benzodiazepine with a central nervous system depressant effect, patients should be cautioned that they may reach systemic therapeutic levels after vaginal administration and that benzodiazepines are addictive [14].

A novel topical cream with a cutaneous fibroblast lysate evaluated in a placebo-controlled crossover study was more effective in reducing focal redness and pain in 30 women with vestibulodynia compared with placebo [15]. Although pain reduction was modest (20%Y30%), the cream was well tolerated. The authors hypothesize that the reason the cutaneous lysate cream might have an effect is that it contains human cytokines that may promote tissue healing.

Oral

A variety of oral medications can be used for vulvodynia pain control. The Vulvodynia Guideline includes tricyclic antidepressants, selective serotonin reuptake inhibitors, venlafaxine, gabapentin, and carbamazepine [1]. With both the antidepressants and anticonvulsants, the dose is gradually titrated to allow tolerance of side effects. Once the desired therapeutic dose is achieved, the full pain response may not be evident for 4 or more weeks.

Antidepressants

Oral tricyclic antidepressants are a common treatment for vulvar pain. Often, amitriptyline is used as a first-line agent. It is started at an oral dose of 5 to 25 mg nightly and increased by 10 to 25 mg weekly, generally not to exceed 150 mg daily [1]. The 5- to 10-mg dose should be used to start treatment in elderly women or those who have side effects [1]. Tricyclic antidepressants should not be stopped suddenly but rather weaned by 10 to 25 mg every few days [1]. Alcohol consumption should be limited to one drink daily. Contraception should be provided to women of reproductive age. Tricyclic antidepressant side effects can be substantial and commonly include sedation, constipation, dry mouth, and cognitive dysfunction.

In 2012, Leo and Dewani [16] conducted a systematic review of antidepressant therapy for vulvodynia. Although descriptive analyses showed some benefit from antidepressants, there were a number of methodological limitations. No reports directly compared pain relieving effects of antidepressants or anticonvulsants of different classes, prohibiting detection of any appreciable benefit to any one agent group when compared with another.

There were two other recent studies using tricyclic antidepressants that failed to show improvement in vulvodynia; in both, the dosage may have been inadequate, and the studies might have been underpowered. A double-blind randomized placebo controlled trial that included

133 women suggested that desipramine as monotherapy or in combination with topical lidocaine was ineffective in treating localized vulvodynia [9]. A randomized, prospective study of 53 women using low-dose amitriptyline (10Y20 mg) in generalized vulvodynia similarly failed to show significant differences in pain-mitigating effectiveness relative to comparator groups including tricyclic antidepressant plus local steroid application and self-management [17].

Anticonvulsants

Although many anticonvulsants are used to manage neuropathic pain disorders, gabapentin has been the most studied and used anticonvulsant for vulvodynia. Gabapentin is typically started at a dose of 300 mg orally for 3 days and gradually increased to a maximum of 3,600-mg total daily dosage [1]. Monitoring and dosage adjustment are required for side effects, but in most cases, the drug does not need to be discontinued. Gabapentin may cause or exacerbate gait and balance problems as well as cognitive impairment in the elderly. Dosage adjustment is necessary in patients with renal insufficiency.

As with tricyclic antidepressants, 3 to 8 weeks of gabapentin dose titration is needed to allow tolerance to adverse effects (including sedation, constipation, dry mouth, and cognitive dysfunction). When the maximum tolerated dosage is reached, 1 to 2 weeks is needed to determine the final pain response. Carbamazepine, another anticonvulsant, may be used for resistant cases [1].

Although observational studies and case reports suggest that anticonvulsants reduce pain for some women, no randomized controlled trials studying the use of anticonvulsants to treat vulvodynia were identified for this update. Cohort studies included the anticonvulsants gabapentin, pregabalin, lamotrigine, and carbamazepine [18Y22]. No comparisons between individual anticonvulsant agents or dosages were reported, and the duration of treatment was variable. The investigation by Harris et al. [18] suggested a response required sustained treatment.

Injections

Intralesional Injections. Although topical steroids generally do not help patients with vulvodynia, The Vulvodynia Guideline notes that the use of trigger point steroid and bupivacaine injections benefitted some patients with localized vulvodynia, whereas the use of interferon > was found to have variable results [1].

Botulinum toxin use has been reported with increasing frequency for disorders involving hypertonicity and neuropathy. Theoretically, botulinum toxin reduces hypertonicity of the pelvic floor muscles and peripheral neuropathy through both peripheral and central nervous mechanisms, leading to less pain. Several small case series and reports identified beneficial results for localized pain at doses of 20 to 100 IU botulinum toxin A, typically divided and injected in multiple sites on one or more occasions [22Y24]. However, the only randomized, placebo-controlled, double-blinded study comparing 20-U botulinum toxin A with placebo resulted in significant pain reduction of equal value in both groups after 6 months of follow-up [23], highlighting the placebo effect issue in many of these studies.

Other injections. In a recent placebo-controlled study conducted to estimate the effectiveness of enoxaparin in treating 40 women with vestibulodynia, 15 of 20 enoxaparin-treated women reported more than 20% pain reduction compared with 5 of 18 women in the placebo group [25]. The authors note the increased presence of heparanase in the vestibule of women with vulvodynia, which raises the possibility of exploring treatment of vulvodynia by blocking its enzyme activity [25].

Vestibulectomy. Although surgery seems to be effective, the lack of randomized studies and insufficient data on complication rates precludes recommendation as the initial treatment for localized pain. The success rate for vestibulectomy ranges between 60% and 90% compared with 40% to 80% for nonsurgical interventions. However, there is no consensus or standardized definition of ''successful'' treatment and methods for evaluation of outcomes between studies [26]. As noted previously, surgical management frequently becomes a treatment option of last resort for patients with vestibulodynia [1]. Sexual counseling may enhance postoperative improvement by reducing vaginismus and poor sexual arousal, which can develop after long-standing dyspareunia [1].

Regardless of the surgical technique, vestibuloplasty has been noted to be ineffective [26]. There may however be subsets of patients more likely to experience a benefit from vestibulectomy surgery. Patients with secondary dyspareunia have odds of improvement greater than those of patients with primary dyspareunia; those with constant pain in addition to dyspareunia are more likely to fail from improving their pain after surgery [27].

Long-term outcomes were queried at means of 2.8 to 3.4 years after vestibulectomy for provoked vestibulodynia, with 35% to 68% reporting a complete cure or major improvement, and 24% to 56% reporting a partial

response [28Y30]. Women with secondary vestibulodynia were more likely to report a complete cure than those with primary vestibulodynia (56% vs 17% in one study) [29].

Laser

Tommola et al. [26] noted lower success rates with laser ablation than with cold knife excisional procedures. There were only 4 reported studies on laser ablation therapy before 1995. In 2007, a retrospective study noted less pain with sexual intercourse among 24 of 37 women treated with pulsed laser therapy [31].

Parturition After Vestibulectomy

One small cohort study included 44 of 109 women having at least one-term pregnancy after vestibulectomy [32]. Route of delivery included cesarean in 21 cases and vaginal in 23 cases (one of which sustained a fourth-degree perineal laceration). Although the study did not address recurrent vulvar pain after delivery, the authors found that vaginal delivery after vulvar vestibulectomy seems to be a safe option, with no increase in perineal morbidity greater than that reported in the general population [32].

Biofeedback and Physical Therapy

As noted in The Vulvodynia Guideline, women with vulvodynia should be assessed for pelvic floor dysfunction [1]. Biofeedback and physical therapy are used in treating vulvar pain, both for localized and generalized pain. These techniques are particularly helpful if there is concomitant vaginismus. Biofeedback aids in developing self-regulation strategies for confronting and reducing pain. Physical therapy treatment techniques include internal (vaginal and rectal) and external soft tissue mobilization and myofascial release; trigger-point pressure; visceral, urogenital, and joint manipulation; electrical stimulation; therapeutic exercises; active pelvic floor retraining; biofeedback; bladder and bowel retraining; instruction in dietary revisions; therapeutic ultrasound; and home vaginal dilation [1, 33].

Although physical therapy has been shown to be effective in treating vulvodynia, the approach is individualized, and so outcomes cannot be accurately validated or reproduced [34].

An emerging treatment for vulvodynia is transcutaneous electrical nerve stimulation (TENS). The TENS has been effective in other chronic pain conditions. A randomized controlled trial of TENS in 40 women with vestibulodynia demonstrated improved pain and sexual function in the TENS group compared with the control group [35]. Subsequently, TENS was evaluated in 20 women administered either palmitoylethanolamide and transpolydatin or placebo to assess for synergy with no noticeable improvement beyond the use of TENS for vestibulodynia [36].

Complementary and Alternative Therapies

Many women use other types of treatments before, during, and after seeking conventional medical diagnosis and treatment for their vulvar pain symptoms. Behavioral, dietary, homeopathic, and Chinese treatments were noted in The Vulvodynia Guideline [1]. However, for each, the overall success remains unclear given the lack of available evidence to date.

Nerve Blockade/Implants

Uncontrolled case series reported treatment successes of targeting peripheral and central pain components of both generalized and localized vulvodynia with multilevel local anesthetic nerve blockade [37, 38]. As with other interventions, the studies were small, were uncontrolled, and used differing protocols. Enrolled women had tried numerous previous treatments without improvement, and those with more severe baseline pain showed less improvement [38].

There are sporadic reports of successful vulvodynia treatment using peripheral subcutaneous neuromodulation [39, 40]. In addition, there is a report of benefit from transcranial direct current stimulation in a woman with a 4-year history of vulvodynia [41].

Counseling

As noted in The Vulvodynia Guideline, a comprehensive treatment approach is beneficial because sexual pain, no matter what the cause is, involves physical, psychological, and relationship components [1]. Patients with localized and generalized vulvar pain need varying degrees of sexual counseling and emotional support.

Sex therapy, couples counseling, psychotherapy, or a combination of these can be very helpful. Patients need assurance that referral for any type of emotional therapy does not mean that the clinician has concluded that the pain is not real. Sharing a model that integrates mind and body can help allay fears that the patient already may have about their pain being psychological. When managing patients with vulvodynia, psychosexual and psychological issues must be considered in addition to the patients' other needs [1].

Cognitive behavior therapy (CBT) has been used in women with vulvodynia with encouraging results and has shown to be more effective than other forms of therapy [42]. CBT was noted to be comparable with surgery in a prospective, randomized study [43] and comparable with surgery after 2 years in terms of self-reported pain during coitus among 28 women assigned for CBT, electromyographic biofeedback, or vestibulectomy in a small randomized, controlled study [44].

CONCLUSIONS

Vulvodynia is a complex disorder that is frequently frustrating to both clinician and patient. It is important to recognize that rapid resolution of symptomatic vulvar pain is unusual even with appropriate therapy and that no single treatment is successful in all women. Pain mitigation may take weeks to months and may not be complete. Expectations for improvement need to be realistically addressed with the patient. Emotional and psychological support is important for many patients, and sex therapy and counseling may be beneficial.

Despite many published studies on treatment of vulvar pain, management needs to be individualized to each individual patient. Future research should aim at evaluating a multimodal approach along with more research on the etiology.

Resources

Current information on vulvar pain is available at the National Vulvodynia Association (www.nva.org) and the Vulvar Pain Foundation (www.vulvarpainfoundation.org). Books on general sexuality and other self-help books more specifically addressing sexual pain are available.

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