



Treatment of Vulvodynia: Pharmacological and Non-Pharmacological Approaches

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Abstract

Vulvodynia is a common, recurrent, vulvar pain condition with debilitating consequences for affected women's health and quality of life. The heterogeneity of women suffering from vulvodynia as well as its uncertain and likely multifactorial etiology pose a significant challenge to identifying any kind of "gold standard" treatment. Thus, treatment providers must be well versed in the various options and the evidence for each. In this review, we begin with pharmacological treatments, followed by non-pharmacological treatments, surgery, and finally multimodal treatments. For each approach, we briefly discuss the method, mechanism of action, and empirical support for the treatment. In sum, pharmacological treatments that *may be beneficial* but require further research include antinociceptive agents (lidocaine, capsaicin), anti-inflammatory agents (corticosteroids, interferon), neuromodulating medications (anticonvulsants and antidepressants), hormonal agents, and muscle relaxants (e.g., botulinum toxin). There is strong evidence to support and *recommend* non-pharmacological interventions including psychological therapy, pelvic floor physical therapy, as well as surgery (i.e., vestibulectomy for provoked vestibulodynia) for the treatment of vulvodynia. We conclude this review with a discussion of issues that may have hindered progress of treatment efficacy and effectiveness, and recommendations for moving the field forward.

Key Points

Psychological interventions, pelvic floor physical therapy, and vestibulectomy (for provoked vestibulodynia) are *recommended* empirically supported treatments for vulvodynia.

Pharmacological treatments that *may be beneficial* include antinociceptive agents (lidocaine, capsaicin), anti-inflammatory agents (corticosteroids, interferon), neuromodulating medications (anticonvulsants and antidepressants), hormonal agents, and muscle relaxants (e.g., botulinum toxin). These treatments all require further placebo-controlled study.

More rigorous randomized-controlled studies focusing on a multimodal approach are needed given that this approach is able to target multiple etiologies simultaneously.

1 Introduction

Vulvodynia is a diagnosis pertaining to vulvar pain lasting at least three months and without a clear identifiable cause [1]. Population-based studies estimate its prevalence to be 8% [2, 3], and new onset of vulvodynia occurs in approximately 4.3 cases per 100 women per year [4]. Vulvodynia adversely affects women and their romantic partners' sexual function and satisfaction, as well as their psychological and relationship health and well-being [5, 6]. The debilitating consequences of vulvodynia paired with its high prevalence translate into countless women searching for an effective treatment. Yet only 50% of treatment-seekers ever receive an accurate diagnosis, and they see an average of five health care providers before receiving a diagnosis [7, 8].

The *2015 Consensus Terminology and Classification of Persistent Vulvar Pain and Vulvodynia* [1] included the

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following pain descriptors: localized (i.e., a portion of the vulva) or generalized (i.e., the entire vulva), provoked or spontaneous, primary or secondary onset, and temporal pattern (e.g., intermittent). It remains unclear whether these descriptors characterize distinct etiological pathways or predict women's pain trajectories. Women with vulvodynia may have comorbid pain syndromes (e.g., fibromyalgia, painful bladder syndrome). Associated factors include genetics, hormones (e.g., pharmacologically induced), inflammation, musculoskeletal (hypertonic pelvic floor muscles, myofascial, biomechanical), neurologic mechanisms (central and peripheral), psychosocial factors (e.g., mood, interpersonal, sexual function), and structural defects (perineal descent) [1]. Given that multiple factors are frequently associated with the development and maintenance of this condition, vulvodynia is widely considered the result of a multifactorial process [1]. Identification of the relevant associated factors in individual women has important treatment implications and underscores that there is no one-size-fits-all approach to treatment.

Historically, treatment recommendations have proceeded from non-pharmacological to pharmacological treatments, followed by surgical intervention in some cases. This approach has largely been based on clinical experience and the small number of randomized-controlled trials (RCTs) for individual treatments. The heterogeneity of women suffering from vulvodynia poses a significant challenge to identifying any kind of "gold standard" treatment. This review will begin with an overview of pharmacological treatments, followed by non-pharmacological treatments, surgery, and finally multimodal treatments. For each treatment, the method, mechanism of action, and empirical support will be discussed. *Recommended* treatments are those with favorable results following adequately powered RCTs, whereas *not recommended* treatments include those that demonstrated no benefit or did not outperform placebo conditions in adequately powered RCTs. Treatments deemed as *potentially beneficial* include those that have demonstrated mixed findings in a small number of studies or have shown promise in uncontrolled or underpowered RCTs, but that require additional study before recommendations regarding efficacy can be made. The review will conclude with a discussion of issues that may have impeded progress of treatment efficacy and effectiveness, and thoughts for future directions. It should be noted that much of the review will discuss research that focuses on a subtype of localized vulvodynia, provoked vestibulodynia (PVD; pain localized to the vulvar vestibule on contact) given that it is most common, especially among premenopausal women [8], and hence has received more research attention.

2 Pharmacological Options

Researchers have devoted a great deal of attention to pharmacological treatments of vulvodynia relative to non-pharmacological treatments. The use of various antinociceptive, anti-inflammatory, and neuromodulating agents comes from evidence that women with vulvodynia have increased innervation and/or sensitivity of nociceptors in the vulvar mucosa [9–11], as well as greater inflammation and increased nerve density in the vestibular tissue [12].

2.1 Antinociceptive Agents

Topical lidocaine was previously recommended as a first-line treatment for vulvodynia [13] based on promising results in uncontrolled trials [14, 15]. However, in the only double-blind placebo-controlled RCT ($N = 133$), Foster et al. [16] compared four treatment arms: desipramine with placebo cream, placebo tablets with topical lidocaine, combination desipramine and lidocaine, and placebo tablets and placebo cream. No group differences for pain reduction via the tampon test (i.e., pain experienced when inserting and removing a tampon) were observed. Although secondary outcomes (i.e., intercourse pain, vulvar algesiometry, and cotton swab test) demonstrated improvement post-treatment, there was no difference between the lidocaine and placebo groups. Based on this evidence, lidocaine is no longer recommended as a first-line treatment for vulvodynia [17]. However, given that this was only a single relatively small trial, further placebo-controlled studies should be conducted, with potential investigation into subgroup responders, before firmly recommending against lidocaine.

Two small uncontrolled pilot studies ($Ns = 26$ and 27) examined the use of multilevel nerve blockade (i.e., caudal epidural blockade, a transvaginal pudendal block, and local infiltration of the vestibule with bupivacaine) in women with generalized and provoked vulvodynia [18, 19]. The researchers observed improvements in pain ratings post-treatment [18, 19], but mixed findings for improvements in sexual functioning. RCTs are needed.

Capsaicin is a vanilloid receptor agonist that leads to desensitization of the receptors with systematic exposure [20]. Compared to controls, women with vulvodynia have increased density of vanilloid receptors in their vestibular tissue [21]. Uncontrolled studies using capsaicin reported improvements in pain and sexual frequency [22, 23]; however, these studies combined capsaicin with topical lidocaine to minimize the side effect of burning pain making it difficult to isolate the effects. A small RCT ($n = 23$; 9 treatment, 14 controls), published only in abstract form, demonstrated a 77% reduction in pain for those in the treatment group, compared to no change in pain for those in the control group

[24]. Larger placebo-controlled studies are needed to determine if capsaicin is effective and the appropriate dosing.

2.2 Anti-Inflammatory Agents

Case reports and case series have found symptomatic improvement following treatment with interferon when women with vulvodynia also show signs of human papillomavirus (HPV) infection [25–30]. Interferon decreases production of inflammatory cytokines, which are higher in the hymenal tissue of women with vulvodynia [17]. In the only placebo-controlled cross-over trial, women with vulvodynia and koilocytosis on biopsy ($N=17$) were treated with a serial intradermal vulvar injection of interferon alpha 2-b or serial injection of saline [31]. No improvement in vulvodynia symptoms were observed with the saline treatment. Following interferon treatment, 15 of 17 women reported complete resolution of their pain. Within this study, a second control group without HPV showed no improvements with interferon treatment. Interferon treatment may be considered for women with vulvodynia and histologic findings suggestive of HPV infection, if other treatments have failed.

Corticosteroids have strong anti-inflammatory effects by reducing the production of interleukin- β , which researchers have found to be elevated in the hymenal tissue of women with vulvodynia [32]. Smaller and likely underpowered RCTs using high potency topical steroids have shown negligible effects [33, 34]. Case reports and series using combined local subcutaneous infiltration of lidocaine and a steroid (methylprednisolone or betamethasone) to the vestibule have shown some success [35–37]. In the largest RCT ($N=97$) Bergeron et al. [38] randomly assigned women to topical hydrocortisone 1% (twice daily) or group CBT (12 sessions). Both groups showed a significant improvement in pain and sexual functioning post-treatment, but effects were larger among those in the CBT group. At this time, more controlled studies are needed before corticosteroids (either topical or injections) are recommended for treatment of vulvodynia [17].

Recent studies have provided more evidence for the role of inflammation in the pathophysiology of vulvodynia, supporting further investigation into anti-inflammatory treatments. Other potential anti-inflammatory agents include cromolyn (a mast cell stabilizer), enoxaparin (a low molecular weight heparin with anti-heparinase activity), cutaneous fibroblast lysate (containing anti-inflammatory cytokines), and meloxicam (Cox-2 inhibitor) [39–42]. Evidence from small RCTs, suggest no benefit to cromolyn relative to placebo [39], and modest improvements in vulvar pain following enoxaparin, fibroblast derived lysate [40, 41], and topical meloxicam with lidocaine [42]. Although potentially beneficial, further research including larger samples is needed before these treatments can be recommended.

2.3 Neuromodulating Agents

There is a long history of the use of anticonvulsants and antidepressants as treatment for vulvodynia. Gabapentin is thought to attenuate depolarization of nociceptors resulting in decreased pain [43]. In their critical review, Spoelstra et al. [44] concluded that while results seem promising for both oral and topical gabapentin [45–52], RCTs are needed. A recent placebo-controlled crossover RCT ($N=89$) found no difference between women treated with long acting oral gabapentin as a solitary treatment versus placebo for pain outcomes [53], but did observe improvements in sexual function in the gabapentin group among those with pelvic floor muscle pain [53]. Uncontrolled studies have also shown the potential benefits of topical gabapentin [47, 50], but placebo-controlled studies are needed before it can be recommended. Other studies have examined the use of pregabalin [51, 54], lamotrigine [55], and carbamazepine [56], but more rigorous RCTs are needed before any treatment recommendations can be made.

Antidepressant medications are thought to exert their pain mediating effects by increasing the release of inhibitory neurotransmitters (noradrenalin and serotonin), which play a role in modulating signalling from peripheral nociceptors [43]. Large retrospective and prospective uncontrolled studies have shown favourable results for amitriptyline [51, 52, 57–62]; however, two small controlled trials did not show any benefit [33, 63]. In the RCT described earlier, Foster et al. [16] did not observe any benefit of desipramine over placebo for pain during the tampon test. Smaller uncontrolled studies and case reports of other antidepressants (e.g., escitalpram, nortriptyline, venlafaxine, milnacipran) alone or in combination with other medications [45, 53, 61, 64], as well as the use of topical amitriptyline alone or with baclofen [57, 65] have observed favourable effects. The mixed findings suggest that more and larger RCTs are necessary before recommending the use of antidepressant medications for vulvodynia.

2.4 Muscle Relaxants

Botulinum toxins (BoNT) are a group of neurotoxins produced by Clostridium bacteria, with most research focused on the BoNT type A (BoNT-A). BoNT blocks the release of acetylcholine as well as other neurotransmitters and neuropeptides at the neural synapse, which causes a localized and temporary muscular paralysis and analgesic effects [66, 67]. Case reports and small, prospective, uncontrolled studies have shown that women with vulvodynia report significant improvement in pain and sexual functioning with the injection of 10–100 units of BoNT-A [68–73], with effects maintained two years post-treatment [69]. In an RCT ($N=64$) women with vulvodynia were

randomized to receive 20 units of BoNT-A or saline in the bulbospongiosus muscles [74]. Both groups reported a significant reduction in pain and improved sexual functioning post-treatment; however, there was no difference between BoNT-A and saline treatment. Of note, the BoNT-A dose was lower than in previous uncontrolled studies, which may account for the lack of differences observed in this small RCT. Additional placebo-controlled trials are warranted given the promising findings from early prospective studies.

Uncontrolled studies have shown potential improvement in vulvodynia patients with the use of vaginal diazepam—a benzodiazepine with muscle relaxing properties [75]. Murina et al. [76] conducted an RCT ($N = 42$) randomizing patients with vulvodynia and moderate to severe pelvic floor hypertonic dysfunction to transcutaneous electrical nerve stimulation (TENS) alone or TENS with vaginal diazepam. Greater improvement in pain and pelvic floor function was observed in the TENS plus vaginal diazepam group than the TENS alone group.

2.5 Hormonal Agents

There is some evidence suggesting increased incidence of vulvodynia among women using combined hormonal contraception (CHC), leading to speculation that relative estrogen or testosterone deficiency may contribute to the development of vulvar pain [77]. Two RCTs sampling women with secondary vulvodynia that developed while using CHC have tested the effect of local estrogen replacement with conjugated equine estrogen (CEE) [78, 79]. Langlais et al. [79] ($N = 20$) reported significant improvements in superficial dyspareunia relative to placebo using topical CEE, whereas Bazin et al. [78, 79] ($N = 61$) did not observe any improvement in dyspareunia relative to placebo using intravaginal application of CEE. A case series study ($N = 50$) reported that topical estradiol and testosterone compound cream applied to the vestibule twice daily for an average of 20 weeks was associated with reduced pain during the cotton swab test [38, 80]. The cessation of CHC and addition of topical estrogen alone or in combination with testosterone may be a reasonable first-line treatment in women who develop vulvodynia while on CHCs, especially if the patient history and physical exam reveal evidence of vulvar dryness and atrophy. However, prospective RCTs are still needed.

3 Non-Pharmacological Options

Current evidence and international consensus guidelines support non-pharmacological treatments including psychological interventions and pelvic floor physical therapy as first-line interventions for the management of vulvodynia [17]. Alternative approaches including acupuncture, hypnosis, and laser therapy will also be discussed.

3.1 Psychological Interventions

Psychological interventions for vulvodynia have primarily been cognitive-behavioral therapy (CBT) and delivered in individual, group, and couple formats. The treatment aims to reduce pain and its associated distress, improve sexual function and satisfaction for both partners, and strengthen the couple relationship. These aims are achieved through psychoeducation and by introducing strategies that (1) target the maladaptive thoughts, emotions, behaviors and couple interactions that are associated with vulvodynia (e.g., avoidance, catastrophizing, excessive anxiety), and (2) increase adaptive coping (e.g., communication skills, expanding the sexual repertoire away from painful intercourse) [81].

In one of the first RCTs, women with PVD ($N = 78$) were randomized to surgical vestibulectomy, biofeedback, or group CBT. At 6-month post intervention follow-up, those who received CBT reported significant improvements in their pain during intercourse, but those who underwent vestibulectomy reported the greatest pain reduction [82]. At 2.5-years follow-up, there were no longer any differences in pain during intercourse between women in the vestibulectomy and CBT groups, and improvements in pain, sexual function, and psychological adjustment were maintained for all treatment groups. Importantly, women who received CBT had a lower attrition rate than those who underwent vestibulectomy, and were more satisfied with their treatment than women who received biofeedback [82].

Another RCT ($N = 97$) randomized women with PVD to a 13-week treatment of corticosteroid cream or group CBT [38]. Women in both groups reported significant improvements in pain and sexual function from baseline to post-treatment and 6-months later, although the CBT group reported significantly greater improvements at the 6-months. Again, the women in the CBT group reported higher treatment satisfaction than those in the corticosteroid group. A final RCT ($N = 50$) examined the efficacy of individual CBT in comparison to supportive psychotherapy. Those randomized to the CBT group reported greater improvements in pain and sexual function from

pre- to post-treatment compared to the supportive therapy, with gains maintained one year later [83]. These results suggest that CBT entails targeted components, beyond the supportive elements of therapy.

Given the large body of evidence indicating that romantic partners both impact and are impacted by vulvodynia, Bergeron and colleagues developed a 12-session couple-format treatment for PVD, based on acceptance-based CBT approaches [84, 85]. A prospective pilot study found that women reported significant pre- to post-treatment improvements in pain during intercourse and sexual functioning, and both partners' reported improvements in sexual satisfaction and other psychological and relational outcomes [85]. While limited by a small sample size ($N = 8$ couples), a couples-based approach may be beneficial and its efficacy is currently being evaluated in a large-scale RCT [84].

Brotto et al., have incorporated mindfulness into a 4-session group CBT program [86–88], which is consistent with evidence of the effectiveness of mindfulness in the treatment of other chronic pain conditions [89]. In a quasi-experimental design using a wait-list control comparison group ($N = 85$), women in the mindfulness group reported significant improvements from pre- to post-treatment, and from post-treatment to 6-month follow-up in pain catastrophizing and hypervigilance, cotton-swab provoked allodynia, and sexual distress, but not in pain during intercourse [86]. Taken together, there is strong evidence supporting the efficacy of psychological treatments for vulvodynia; it is therefore a recommended first-line treatment.

3.2 Pelvic Floor Physical Therapy

There is considerable evidence linking vulvodynia to pelvic floor muscle (PFM) dysfunction (e.g., [17, 90, 91]). Women with vulvodynia display hypertonicity in the PFM and poorer PFM strength and control [17]. The goal of pelvic floor physical therapy (PFPT) is to restore proper function to the PFM and tissues, decrease neural tension and vulvovaginal pain and in some cases, improve sexual function [92].

Manual PFPT includes a variety of techniques (e.g., stretching, massage, and myofascial trigger points) to facilitate muscle relaxation, improve circulation, and increase mobility. Although limited by small samples, three prospective studies show promising results for decreasing self-reported pain during intercourse following use of vaginal dilators alone [93–95]. To date, no RCTs have examined the effect of other forms of manual therapy alone in vulvodynia; however, a randomized feasibility study provided preliminary support for the use of myofascial trigger point release for pelvic pain disorders [96].

Retrospective and prospective studies examining the effectiveness of assisted therapies have observed significant improvements in self-reported pain, dyspareunia, and sexual

functioning following peripheral neuromodulation with TENS, with some evidence that these effects are maintained over time [97–99]. Two RCTs, one involving TENS and the other including TENS with vaginal diazepam showed modest improvements in pain and pelvic floor instability compared to placebo-controlled conditions [76, 94] whereas the addition of palmitoethanolamide and transpodydin was not supported [100]. Morin et al. [101] conducted a triple-blind, parallel-group, RCT to examine the efficacy of central neuromodulation (transcranial direct-current stimulation; TDCS) for PVD. There was no evidence to support the use of TDCS for pain reduction or improved sexual function.

Initial uncontrolled, non-randomized studies using biofeedback via electromyographic (EMG) observed moderate reductions in reported vestibular pain [102, 103]. In their prospective randomized study Danielsson et al. [15] compared 4-months of EMG biofeedback to topical lidocaine. No group differences were observed; however, positive outcomes (e.g., reported vestibular pain, sexual function, and quality of life) were maintained 12 months later for both groups. In the RCT [82] comparing CBT, EMG biofeedback, and vestibulectomy described earlier, women receiving EMG biofeedback reported on average a 35% reduction in pain and this was maintained at the 2.5 year follow-up; however, both the CBT and vestibulectomy conditions produced greater improvements in reported pain.

Most of the existing research has examined a comprehensive multimodal approach to PFPT, which includes the manual and assisted therapies described above with other approaches including education and at home exercises. Retrospective and prospective studies show that the majority of women (71–76%) report significant improvements in their intercourse pain, pain during gynecological examinations, and sexual functioning following 6 to 10 sessions of multimodal PFPT [97, 104–110]. A pilot RCT ($N = 20$) comparing CBT and multimodal PFPT showed that both interventions produced significant decreases in self-reported pain [111]. In sum, a systematic review ($K = 43$ studies) found that PFPT is effective for decreasing pain during intercourse and improving sexual function [92]. It is therefore currently recommended as a first-line treatment for vulvodynia [112].

3.3 Alternative Approaches

Acupuncture, hypnosis, and laser therapy are alternative approaches with few adverse effects; however, these approaches require more thorough investigation regarding their efficacy. The western view of acupuncture is that the placement of needles at specific pain points releases endorphins and opioids, the body's natural analgesics, resulting in pain reduction [113]. To date, three small uncontrolled and non-randomized studies have demonstrated mixed support for the treatment of vulvodynia with acupuncture [114–116].

In a wait-list controlled RCT ($N = 36$), Schlaeger et al. [117] found that vulvar pain and intercourse pain were significantly reduced, and overall sexual functioning significantly improved, following acupuncture. Hypnotherapy has been shown to alleviate the subjective experience of pain in other populations [118]. Evidence from a case study [119] and an uncontrolled, non-randomized pilot study ($N = 8$) [118], observed that hypnotherapy (6 to 12 sessions) was associated with reported improvements in pain (e.g., gynecologic examination, intercourse, and non-coital), and psychosexual functioning (e.g., sexual satisfaction) from pre- to post-intervention.

Evidence for treatment with energy devices such as fractional CO₂ laser therapy and low-level laser therapy (LLLT) is mixed, and currently there is an FDA warning against the use of energy devices to perform “vaginal rejuvenation,” and for procedures to treat symptoms related to sexual function, because of concerns regarding adverse events [120, 121]. In a case series, women with either vestibulodynia ($N = 37$) or genitourinary syndrome of menopause ($N = 33$) underwent three sessions of fractional ablative CO₂ laser treatment. No group differences were observed; however, 67.4% of women reported significant improvements in pain during intercourse, and improvements were maintained at four-month follow-up [120]. In a small ($N = 34$) double-blind, placebo-controlled RCT [121], 12 sessions of LLLT resulted in a greater proportion of women (i.e., 78%) reporting some improvement (using a 100-point pain scale) in their intercourse pain following treatment relative to their intercourse pain at the time of recruitment compared to those (i.e., 44%) in the placebo sham LLLT condition. No group differences were observed for any other outcomes (e.g., pain during Q-tip examination, daily and intercourse pain using the visual analog scale, tampon test). Although sham controlled multicenter trials are underway, there is currently insufficient evidence for fractional CO₂ laser or LLLT as a treatment for vulvodynia.

4 Surgery

In comparison to other treatment approaches, vulvar vestibulectomy surgery has been studied extensively [122]. Vestibulectomy can include partial or complete excision of the vestibular mucosa with, or without, a vaginal advancement flap [123]. In general, the literature is difficult to compare because of variability in surgical procedures, lack of control conditions, poorly defined outcomes and definitions of “success”, and lack of follow-up [17]. Of note, the evidence only supports vestibulectomy as an effective treatment for localized PVD. It is contraindicated for generalized vulvar pain disorders and non-provoked vestibulodynia [123].

In a systematic review ($K = 33$ studies), Tommola et al. [123] found that vestibulectomy resulted in significant self-reported relief of dyspareunia in 79% of patients, some relief in 89% of patients, and no relief in 12% of patients. In studies ($K = 6$) that examined pain and tenderness of the vestibular mucosa following surgery via the cotton-swab test, lack of tenderness was reported for 70% to 85% of women following surgery [82, 124]. In addition, Tommola et al. [123] observed significant improvements in sexual functioning following vestibulectomy and that these effects were maintained 12 to 30 months following surgery [82, 125–128]. Moreover, women are generally highly satisfied with the procedure [129, 130]. Complications are infrequent and can include bleeding, infection, increased pain, scar tissue, wounds, and cyst formation [5, 17].

Some experts have questioned why vulvar vestibulectomy is typically recommended only after less invasive interventions are unsuccessful [17, 110]. In their observational case-controlled study, Tommola et al. [110] observed similar long term outcomes for pain and sexual function when comparing women with severe PVD who were treated with conservative interventions and those who received vestibulectomy surgery. Such findings highlight that conservative treatment might be preferable as a first-line intervention.

5 Multimodal Approaches

Consistent with recommendations of the *Fourth International Consultation on Sexual Medicine for women’s sexual pain disorders* [17], and the evidence for multiple etiological pathways in vulvodynia, a multidisciplinary model of care that can targets pain pathways simultaneously is considered optimal. Multimodal treatment that combines interventions (e.g., PFPT, CBT, oral gabapentin) rather than preceding sequentially may support a more expedient treatment process and promote greater engagement from both patients and clinicians, possibly leading to less resistance to any single modality [131]. There are a small number of published uncontrolled quantitative [44, 132–134] and qualitative studies [88, 135–137] evaluating a multimodal treatment, typically combining psychotherapy, physical therapy, and prescriptive therapy. Results indicate that women experienced improvements in their pain as well as their ability to manage the pain, and psychological and sexual well-being, and that the benefits may also extend to partners of the women. The lack of RCTs makes it unclear whether a multimodal approach is superior to any single modality, but findings are promising.

6 Conclusions

Our updated review of the literature supports the conclusions from the *Fourth International Consultation on Sexual Medicine* [17] that, currently, the best treatment options for vulvodynia are psychological interventions, pelvic floor physical therapy, and vestibulectomy (for provoked vestibulodynia). More rigorous studies are needed focusing on a multimodal approach given its ability to target multiple etiologies simultaneously. Pharmacological treatments that *may be beneficial* and considered as second-line avenues include antinociceptive agents (lidocaine, capsaicin), anti-inflammatory agents (corticosteroids, interferon), neuromodulating medications (anti-convulsants and antidepressants), hormonal agents, and muscle relaxants. These treatments all require further placebo-controlled study. An important consideration is that the definition of “successful” treatment varies considerably across health care providers and affected women and couples. Symptoms may be reduced following treatment but still persist to some degree, or symptoms may reoccur even following more invasive treatment such as surgery [82, 138]. Thus complete resolution of pain is often an unrealistic goal. For some, pain reduction or enhanced pain management skills may be sufficient for increasing women’s quality of life, and can be an important end-point of treatment in and of itself.

There are some methodological, theoretical, and clinical issues that may have hindered advances in the treatment of vulvodynia. First, a major limitation is the lack of placebo-controls, with the few placebo-controlled trials clearly demonstrating strong placebo effects [139]. Some treatments (e.g., vestibulectomy, physical therapies) have not been subjected to a placebo-controlled trial, likely due to the logistics of performing a sham version of these treatments. Although these treatments have demonstrated strong efficacy in other study designs—including in RCTs, which compared against other supported treatments—whether they lead to improvements beyond placebo cannot be fully determined. A second challenge has been the neglect of the romantic partner in treatment, despite painful intercourse being an inherently interpersonal problem [6]. Partners can be included in any treatment by inviting them to participate in appointments and providing them with education and/or involving them in the treatment itself. Partner support or resistance to treatment can play a major role in compliance with a treatment protocol and subsequent outcomes [140].

Third, the heterogeneity of women suffering from vulvodynia poses significant challenges for treatment trials. There is evidence that they differ in several characteristics including age of onset, location and quality of the

pain, and presence of comorbidities [4, 141, 142] but see also [143]. Such differences may imply various underlying pathophysiology, experienced consequences (i.e., sexual, psychological), and treatment responsiveness, although evidence of empirically-derived subgroups is sparse. Unfortunately, although there are a limited number of well-designed RCTs studies of vulvodynia, very few differentiated among potential subtypes. When women with different characteristics or etiologies are examined together as a single group, it is possible that treatment efficacy for a subgroup of women will be masked by those for whom the treatment is ineffective, rendering the overall findings non-significant [144]. As researchers uncover the underlying mechanisms and etiology of different forms of vulvodynia, they can develop corresponding treatment algorithms to guide decision-making in a more evidence-based manner. King, Rubin, and Goldstein [145] published such an algorithm to differentiate between vulvar pain subtypes based on the associated factors outlined earlier. Some experts have suggested that classifying vulvodynia subtypes based on pain descriptors—including potential combinations of these characteristics—may be more useful than subgroups based on hypothesized etiology [1, 131].

Corsini-Munt et al. [146] outline a number of additional barriers and gaps in treatment knowledge and research of vulvodynia, as well as possible solutions to mitigate their effects. These include: (1) assessment of multiple domains of impairment beyond pain; (2) examining treatment predictors and moderators including the presence of co-morbid conditions; (3) inclusion of more diverse and representative samples; (4) explicitly testing the purported mechanisms of action; and (5) more effective and wider dissemination of empirically-supported treatment protocols. Collaboration across research teams and health disciplines may be the key to improving the size and representativeness of research participants, and enhancing efficacy by ensuring that treatments reflect the biopsychosocial complexity of vulvodynia.

Compliance with Ethical Standards

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