AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE
Menopausal MEDICINE
VOLUME 18, NUMBER 2 — MAY 2010
FOR CLINICIANS WHO PROVIDE CARE FOR WOMEN

Vulvodynia: An often-overlooked cause of dyspareunia in the menopausal population

NANCY PHILLIPS, MD, AND GLORIA BACHMANN, MD

Vulvovaginal pain may stem from various causes, affect women of all ages, and may or may not be associated with sexual activity (**TABLE 1**). Vulvodynia is defined as "vulvar discomfort, most often described as burning pain, occurring in the absence of relevant findings or a specific clinically identifiable neurologic disorder."[1] It is most commonly diagnosed in young women and is seldom considered in the diagnostic workup of peri- and postmenopausal women. For that population, diagnosis often focuses on genital atrophy; scant attention is given to other etiologies. This review describes the importance of a complete workup for such women.

Nancy Phillips, MD
Clinical Associate Professor
Department of ObGyn and Reproductive Services
UMDNJ—Robert Wood Johnson Medical School
New Brunswick, New Jersey

Gloria Bachmann, MD
Interim Chair
Associate Dean for Women's Health
Master Educators' Guild
UMDNJ—Robert Wood Johnson Medical School
New Brunswick, New Jersey

Disclosures
Dr Phillips reports no relevant commercial or financial relationships.
Dr Bachmann reports that she receives grants/research support from, and is a consultant to, Astellas Pharma US, Inc, Wyeth, Bayer HealthCare, Duramed Pharmaceuticals, Inc., Pfizer Inc, Boehringer Ingelheim Pharmaceuticals, Inc, Roche, Merck & Co., Inc., QuatRX Pharmaceuticals, Bionovo, GlaxoSmithKline, Femme Pharma Inc, Hormos Medical, Covance Inc, Novartis, Johnson & Johnson, Boston Scientific Corporation, Novo Nordisk, Inc, Procter & Gamble, and Xanodyne Pharmaceuticals Inc.

IN THIS ISSUE

S2 From the editor
NANETTE F. SANTORO, MD
S6 Is physical activity beneficial for hot flushes?
BARBARA STERNFELD, PHD

Vulvodynia definition and etiology

Vulvodynia is classified as generalized or localized, and provoked or unprovoked (**TABLE 2**).

Its exact etiology remains unknown. It has not been consistently linked to candidiasis, human papillomavirus, high urinary oxalates, sexual abuse, or any specific infectious, hormonal, allergic, or inflammatory processes.[2] Recent theories include abnormalities of embryologic development and genetic or immune factors.[3,4] The pain ultimately results from a neuropathic process that may

TABLE 1 Causes of vulvovaginal pain

INFECTIOUS
- Vaginitis (yeast, bacterial vaginosis, Trichomonas)
- Herpes simplex
- Bartholinitis

NEOPLASTIC
- Vulvar intraepithelial neoplasia
- Paget's disease
- Vaginal/vulvar cancer

ALLERGIC
- Contact dermatitis

INFLAMMATORY
- Vulvar dystrophies
- Lichen planus
- Eczema

ANATOMIC
- Trauma
- Vaginismus

NEUROLOGIC
- Referred musculoskeletal pain (disc disease, hip, back)
- Multiple sclerosis
- Pudendal nerve entrapment or injury
- Postherpetic neuralgia

VULVODYNIA
- Unexplained

CONTINUED ON PAGE S3

CONTINUED FROM PAGE S1

be central, peripheral, or both.

Vulvodynia is a diagnosis of exclusion. Examination is essentially normal, although erythema may be present.

Patient evaluation

The medical history obtained from a menopausal patient with vulvovaginal pain should include targeted questions about the nature and timing of the pain. The presence of coexistent menopausal symptoms, vaginal discharge, vulvar lesions, and other sexual problems, as well as sexual contacts, should be determined. Systemic symptoms and current medical conditions and medications should be documented. In addition to complaining of dyspareunia with coital activity, women with vulvodynia often note constant or intermittent burning, itching, rawness or irritation, or pain with any touch. They may report a history of severe pain associated with gynecologic exams or with the use of vaginal preparations.

To rule out other causes of pain, a comprehensive physical and pelvic exam should include examination of the vulva and vagina, wet prep and cultures (as indicated), palpation to assess levator spasm and bladder or urethral tenderness, and bimanual exam to rule out pelvic pathology. Neurologic examination should be performed as indicated. Areas where pain is most intense should be mapped by exerting gentle pressure over the vulva, clitoris, and vestibule with a moist cotton swab. Posttreatment pain mapping will help ascertain whether management is successful, as evidenced by improved patient tolerance to areas that had been tender.

In the absence of visible genital pathology, and if not contraindicated, a trial of topical estrogen may be helpful if the patient reports dryness and has diminished lubrication. If symptoms resolve, estrogen should be titrated to the minimal dose that provides desired results.

If no or inadequate response to treatment is observed, a diagnosis of vulvodynia is confirmed, regardless of patient age.

Women with vulvodynia often note constant or intermittent burning, itching, rawness or irritation, or pain with any touch.

Vulvodynia management: Therapeutic options

The best treatment for vulvodynia is as elusive as its etiology. Simple measures may help: wearing absorbent underwear, as well as loose clothing in the perineal area, and using mild, unscented soaps and detergents. Vulvar irritants (TABLE 3) should be avoided. Patient diaries may help uncover potential offensive triggers. Cold packs applied to the vulvar area may provide temporary relief.

The application of topical lidocaine (2% or 5% cream or ointment) may be used for symptomatic and therapeutic treatment. Application may initially result in an escalation of burning symptoms, which usually resolve when the anesthetic takes effect. Ointments are generally less irritative than creams. Diluting the lidocaine by mixing it with a tolerated substance, such as mineral oil or estrogen cream, may be helpful, especially at initiation of treatment. For localized vulvodynia, applying lidocaine to a cotton ball and placing it over the affected area overnight will assure a constant therapy and aid sleep.[5]

In small trials, physical therapy and biofeedback for pelvic floor retraining has been shown to provide vulvovaginal pain relief and facilitate intercourse. Some experts feel that these modalities will only benefit patients with levator spasm on exam or evidence of vaginismus[6]; others maintain that all vulvodynia patients have a degree of pelvic muscle hypertonus, and these options should always be considered.[7] Internal and external soft tissue mobilization, trigger point pressure, and exercises for posture, back, and pelvic floor are some examples of these interventions.

Pharmacologic agents

Oral tricyclics have been used for many years, although not all data confirm their superiority over other options.[8] Therapy begins at 10 mg of nortriptyline or amitriptyline at bedtime, and increases in 10 mg increments to a maximum daily dose of 75 mg. Anticholinergic and cardiac side effects may occur even at low doses; the clinician should titrate upward over several weeks.

Gabapentin has shown promising results. This agent produces fewer anticholinergic side effects than the

TABLE 2 Classification of vulvodynia

GENERALIZED

- Involvement of the entire vulva

LOCALIZED

- Involvement of a portion of the vulva, such as the vestibule

SUBDIVIDED
(generalized or localized PLUS)

- Provoked (present only with contact, sexual or nonsexual)
- Unprovoked (present without contact)
- Mixed (provoked and unprovoked)

Adapted from: Moyal-Barracco M, Lynch PJ. 2003 ISSVD terminology and classification of vulvodynia: a historical perspective. J Reprod Med. 2004;49:772-777.

tricyclics but may be sedating or cause ataxia. Various dosing regimens have been evaluated, but a small initial dose of 100 mg at bedtime, increasing by 100 mg every 2 to 7 days to a maximum of 3600 mg/d in divided doses, is a reasonable approach in an older population.

Scant data suggest that pregabalin 250 mg to 450 mg may be beneficial. Pregabalin-induced remission in a 62-year-old woman with a 20-year history of vulvodynia has been reported.[9] A clinical trial is being conducted at The Cleveland Clinic.

Any oral regimen that produces desired efficacy should be titrated to the lowest dose that results in acceptable symptomatic relief.

Topical formulations of both gabapentin (2%-6%, formulated by a compounding pharmacy) and amitriptyline 2%/baclofen 2% have shown moderate success in small numbers of patients.[10,11] These are appealing as a potential means of decreasing systemic drug levels and subsequently decreasing unwanted side effects. More clinical experience and controlled trials are needed to establish efficacy.

TABLE 3 Common vulvar irritants

- Bubble baths
- Condoms
- Douches and vaginal sprays
- Excessive or chronic vaginal discharge
- Laundry detergents
- Lubricants
- OTC ointments, lotions, yeast treatments
- Sanitary pads or panty liners
- Soaps (scented, colored, antibacterial)
- Spermicides
- Thong or noncotton underwear

TABLE 4 Treatment options for vulvodynia

Treatment	Regimen
Gabapentin[a]	Initial dose: 100 mg at bedtime Increase by 100 mg every 2-7 days Maximum dose: 3600 mg/d in divided doses
Oral tricyclics[a] (amitriptyline, nortriptyline)	Initial dose: 10 mg at bedtime Increase by 10 mg every 1-4 weeks Maximum dose: 75 mg at bedtime
Physical therapy	Perineal massage, biofeedback with progressive muscle relaxation
Pregabalin[a]	Initial dose: 250 mg orally Maximum dose: 450 mg orally
Topical baclofen 2%/amitriptyline 2%[a]	Apply twice daily
Topical gabapentin (2%-6%)[a]	Apply sparingly twice daily
Topical lidocaine (2%-5%)[a]	Apply as needed as with intercourse, or Apply soaked cotton ball to affected area overnight
Nerve blocks (intralesional, pudendal, caudal-epidural)	Steroids (triamcinolone acetonide, methylprednisolone) Anesthetics (lidocaine, bupivacaine)
Surgery	For localized vestibulodynia

[a]Off-label use; dosages represent commonly prescribed regimens.

Any oral regimen that produces desired efficacy should be titrated to the lowest dose that results in acceptable symptomatic relief.

Additional treatment options

Additional treatment options include nerve blocks, which may be intralesional, pudendal, or even caudal-epidural, using a combination of steroids (triamcinolone acetonide, methylprednisolone) and anesthetics (bupivacaine, lidocaine). Although intra-lesional injections are often done in a primary care setting, blocks that are more regional are usually referred to an anesthesiologist or pain center.

Surgical options, such as vestibulectomy, are reserved for localized disease, especially vestibulodynia, and should be considered for the most resistant cases and after other options have failed. The woman must be fully informed about surgical risks and benefits. Limited data in postmenopausal patients are available. Presurgical topical estrogen therapy will help postoperative healing of vaginal tissue. After surgery, a period of pelvic rest will be required to ensure incision healing, followed by use of a vaginal dilator prior to attempted intercourse. Success rates as high as 80% have been reported postsurgically,[7] but few data apply to the peri- and postmenopausal population.

Psychosocial factors

Psychosocial evaluation and therapy may be useful in therapeutic success. Women with vulvodynia, as with any chronic pain condition, are often depressed or anxious. Secondary sexual dysfunctions may develop, and intimate relationships become

TABLE 5 Treatment guidelines

- All medications should be started at the lowest dose and titrated upward at a slow rate, over at least 2-4 weeks per advancement in dose.
- Only one treatment should be introduced at a time.
- Pain and symptom diaries should be kept to help guide and monitor treatment.
- In the absence of direct adverse interactions, multiple therapies may be used simultaneously, although little to no data are available to support this strategy.
- Physical therapy is a helpful adjunct to medical treatment.
- Counseling should be offered as appropriate (longstanding disease, history of abuse, coexisting sexual dysfunctions, or relationship difficulties).
- Surgery should be reserved for localized vestibulodynia only after failure of medical therapy.

stressed. A multidisciplinary approach overseen by the gynecologist can be beneficial.

A summary of treatment options is shown in **TABLE 4**, and general guidelines for treatment are reviewed in **TABLE 5**.

Vulvodynia management: Special considerations

All treatment options discussed here are off-label for premenopausal patients. In aging women, additional factors must be considered.

Few randomized, controlled trials assess vulvodynia treatments; because the incidence of vulvodynia in the menopausal population is low, even less data are available.

Older patients are more likely to have chronic medical conditions, increasing the potential for drug interactions and the impact of side effects, such as sedation or constipation. Medical clearance or specialist consultation may be warranted.

Older patients are more likely to have chronic medical conditions, increasing the potential for drug interactions and the impact of side effects.

The coexistence of vulvodynia and atrophy may demand the use of estrogen or other nonhormonal therapies for vulvovaginal atrophy, in addition to those aimed at treating vulvodynia. Use of topical estrogen may be alternated with other topical agents, whereas oral estrogen or vaginal inserts or rings may be used concomitantly.

Vulvodynia symptoms resolve slowly with any therapeutic option. Several weeks are often needed for appreciable relief. In an older population, therapies—especially systemic medications—may be increased slowly over time frames that are longer than usual, and expected intervals for symptom improvement should be adjusted.

Conclusion

This condition can occur in women across the life cycle.[12,13] The diagnosis of vulvodynia should be considered the etiology for women who report vulvar burning and tenderness, especially when noted with sexual contact or any type of vulvar pressure. Although estrogen therapy may be used as a first-line therapy in older women, vulvodynia management strategies should be considered in women with no obvious pathology and an inadequate response to estrogen intervention. ■

References

1. Moyal-Barracco M, Lynch PJ. 2003 ISSVD terminology and classification of vulvodynia: a historical perspective. J Reprod Med. 2004;49:772-777.
2. American College Obstetricians and Gynecologists. ACOG Committee Opinion No. 345: Vulvodynia. Obstet Gynecol. 2006;108:1049-1052.
3. Witkin SS, Gerber S, Ledger WJ. Differential characteristics of women with vulvar vestibulitis syndrome. Am J Obstet Gynecol. 2002;187:589-594.
4. Witkin SS, Gerber S, Ledger WJ. Influence of interleukin-1 receptor antagonist gene polymorphisms on disease. Clin Infec Dis. 2002;32:204-209.
5. Zolnoun DA, Hartmann KE, Steege JF. Overnight 5% lidocaine ointment for the treatment of vulvar vestibulitis. Obstet Gynecol. 2003;102:84-87.
6. Stewart EG, Barbieri RL. Clinical manifestations and diagnosis of generalized vulvodynia. http://www.uptodate.com/patients/content/topicdo?topicKey=~iuZuSngHDPOHgPu.
7. Goldstein AT, Burrows L. Vulvodynia. J Sex Med. 2008;5:5-14; quiz 15.
8. Brown C, Wan J, Bachmann G, et al. Self-management, amitriptyline and amitriptyline plus triamcinolone in the management of vulvodynia. J Womens Health (Larchmt). 2009;18:163-169.
9. Jerome L. Pregabalin-induced remission in a 62-year-old woman with a 20-year history of vulvodynia. Pain Res Manag. 2007;12:212-214.
10. Boardman LA, Cooper AS, Blais LR, et al. Topical gabapentin in the treatment of localized and generalized vulvodynia. Obstet Gynecol. 2008;112:579-585.
11. Nyirjesy P, Lev-Sagie A, Mathew L, et al. Topical amitriptyline-baclofen cream for the treatment of provoked vulvodynia. J Lower Gen Tract Dis. 2009;13:230-236.
12. Sutton JT, Bachmann GA, Arnold LD, et al. Assessment of vulvodynia symptoms in a sample of U.S. women: a follow-up national incidence survey. J Womens Health (Larchmt). 2008;17:1285-1292.
13. Bachmann GA, Rosen R, Pin VW, et al. Vulvodynia: a state-of-the-art consensus on definitions, diagnosis and management. J Reprod Med. 2006;51:447-456.