National Vulvodynia Association

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Treatment of Vulvar Pain Syndrome

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Introduction

According to the most recent definition by the International Society for the Study of Vulvovaginal Disease (ISSVD), vulvar pain syndrome consists of "vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or specific, clinically identifiable, neurological disorder." A recent population-based study suggests that the lifetime cumulative incidence of vulvar pain syndrome is 16 percent, indicating that approximately 14 million women in the United States alone may experience idiopathic vulvar pain during their lifetime.

There is currently no widely accepted scheme that classifies vulvar pain syndrome and differentiates it from other types of pelvic or genital pain. Vulvar pain syndrome is not included in disease classification systems, such as the International Classification of Disease (ICD-10), or in pain classification systems, such as that of the International Association for the Study of Pain. In 2003, the ISSVD revised its classification of vulvar pain syndrome based on two broad types of symptom presentations, namely localized vulvar pain and generalized vulvar pain. Localized refers to the involvement of a portion of the vulva, such as the vulvar vestibule, and generalized indicates the involvement of the entire vulva, composed of the labia majora, labia minora, clitoris, and vestibule.

The most common subtype of localized vulvar pain syndrome is *provoked vestibulodynia* (PVD), also known as vulvar vestibulitis syndrome. It is characterized by pain in the vulvar vestibule that is triggered by contact, whether sexual or nonsexual, e.g., tampon insertion. Dyspareunia, or painful intercourse, is one of its defining symptoms and the main presenting complaint. PVD is considered the most frequent form of vulvar pain syndrome in premenopausal women, with prevalence estimates ranging from 12 percent in the general population to 15 percent in general gynecologic practice. Women suffering from PVD typically describe their pain as a burning and/or cutting sensation.

Generalized vulvar pain syndrome, formerly known as dysesthetic or essential vulvodynia, is best described as a constant burning of the vulva, often including but not limited to the vestibule. The most common subtype of generalized vulvodynia is unprovoked. Although less prevalent than PVD, it is thought to affect six to seven percent of women in the general population. *Unprovoked generalized vulvodynia* (UGVD) is often considered to be a more debilitating condition because of the chronic, unrelenting nature of the pain.

In addition to disrupting sexual functioning and interfering with the reproductive process, there is preliminary

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evidence to suggest that vulvar pain syndrome can adversely affect general psychological well-being and overall quality of life. Despite a high prevalence rate and the fact that this urogenital pain condition was first described over 100 years ago, there has been a paucity of sound research to elucidate its descriptive characteristics, etiology, or treatment. In the understandable urgency to treat women afflicted with vulvar pain syndrome, interventions have been advanced without the benefit of randomized controlled outcome studies. This has resulted in a variety of approaches which have no known efficacy.

TREATMENT

Due to the lack of knowledge concerning the etiology of vulvar pain syndrome, the treatment literature is characterized by a wide variety of medical, surgical, cognitive-behavioral and alternative approaches directed at different proposed mechanisms or symptoms, with most attempts being unidimensional. In other words, proposed interventions tend to focus solely on one aspect of vulvar pain syndrome to the exclusion of others, and biopsychosocial models are the exception. In our 1997 review of the literature on PVD, we concluded that there were no effective treatments to date because there were no existing randomized trials comparing treatment and control groups. Since then, only a handful of randomized controlled treatment studies have been published. This is surprising in light of the fact that interest in vulvar pain has increased significantly over the last five years.

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MEDICAL TREATMENTS

Topical Applications

Medical interventions typically begin with minimally invasive treatments such as the topical application of different types of antifungal, corticosteroid, estrogen or other creams. It has been our experience that some type of corticosteroid cream is the most commonly prescribed first-line treatment and that many women self-medicate with, or are prescribed, antifungal agents. There is no published evidence, however, that any of these creams are efficacious. Cromolyn cream has also been suggested as a first-line treatment since it blocks mast cell degranulation, but studies examining the presence of mast cells in women with vulvar pain syndrome have yielded contradictory evidence. Interestingly, results from a randomized double-blind placebo study revealed that participants in both the therapy and the placebo groups exhibited statistically significant improvements in their symptoms, with no significant differences between groups. These findings point toward a potentially large placebo effect in the treatment of vulvar pain syndrome, which has also been documented in other pain syndromes.

The use of topical anesthetics has long been recommended in the treatment of vulvar pain syndrome, but only recently has a prospective study examined its effectiveness in women with PVD. Findings show that nightly applications of 5 percent lidocaine ointment for seven weeks resulted in a significant decrease in pain and a significant increase in the ability to have

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intercourse from pre- to post-treatment. However, the lack of a placebo control group does not allow us to conclude that lidocaine is effective, although it appears to help some patients.

Steinberg and colleagues recently conducted a retrospective chart review to evaluate whether capsaicin in an acid mantle base might show promise in the treatment of PVD. Since the application of capsaicin typically causes a strong burning sensation, patients were instructed to apply a 2 percent lidocaine gel for 10 minutes prior to the 20-minute capsaicin application. This treatment regimen was followed for a 12-week period. The study found a significant decrease in pain and increase in the ability to engage in intercourse from pre- to post-treatment, although the measurement of pain was rudimentary. It is unclear whether the observed effect of capsaicin cream partly involved a placebo response due to the lack of a control group, and whether it yielded more improvement than less painful topical applications such as lidocaine.

Finally, Walsh used a 0.2 percent nitroglycerin cream for four to six weeks to treat a group of women with four different types of vulvar pain syndrome: cyclic vulvovaginitis, PVD, generalized vulvodynia and vulvar dermatosis. Although a significant pre- to post-treatment decrease in pain was noticed, 76 percent of patients reported headache with each use, leading 29 percent of participants to drop out of the study prematurely.

The studies reviewed indicate that there are no effective topical applications for vulvar pain syndrome to date. Among the ointments evaluated, lidocaine and Cromolyn cream appear to be associated with fewer negative side effects.

Oral Medications

Systemic treatments, including oral antifungals, have been suggested as the next treatment stage following the absence of improvement with the aforementioned methods. Only one randomized controlled study examined the use of an oral medication for PVD with and without recurrent candidiasis. In a group of women adhering to a low oxalate diet with calcium citrate supplementation, Bornstein randomized half to a weekly oral dose of the antifungal fluconazole (150 mg) over a six-month period. Results showed that the addition of the systemic antifungal did not improve the outcome in these patients; 15 percent of women in the antifungal group had a satisfactory response, compared to 30 percent in the diet-only group.

Tricyclic antidepressants have been thought to be helpful in the treatment of UGVD, but not PVD. Munday reported on the successful use of tricyclic antidepressants in a mixed group of women suffering from either condition. Women in this group also received supportive psychotherapy, however, which may have contributed to their improvement. Nonetheless, this combination of treatments requires further study.

The anticonvulsant gabapentin (Neurontin) is recommended for women with UGVD who are either unresponsive to, or cannot tolerate the side effects of, tricyclic antidepressants. In a prospective study, 10 of 21 patients with various refractory urogenital pain syndromes reported a subjective improvement in their pain following a six-month trial of gabapentin. Ben-David and Friedman conducted an uncontrolled retrospective follow-up of 17 women suffering from UGVD treated with gabapentin and concluded that 14 experienced either partial or complete relief of pain following treatment. However, all of the above studies lacked adequate pain measurement and their retrospective nature does not allow us to reach any firm conclusions as to the effectiveness of gabapentin for this condition.

Overall, the studies on oral medication use for the treatment of vulvar pain syndrome have numerous methodological flaws that make it impossible to ascertain whether these interventions offer significant pain relief to affected women. However, due to their widespread use in the treatment of other pain syndromes, further research is warranted.

Injections

In the 1990s, vestibular interferon injections were used for PVD patients with a concomitant human papillomavirus infection, with reported success rates in retrospective studies ranging from 38 to 88 percent—the majority being around the 50 percent mark. However, this treatment is less in vogue today, partly due to the

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fact that human papillomavirus infections are no longer thought to be a causal factor in PVD. Additionally, this treatment option is time-consuming and has adverse side effects, including a low-grade fever and flu-like symptoms. It is thus questionable whether the downside of interferon injections justifies its limited success.

More recently, other types of injections have been proposed, namely the submucous infiltration of methylprednisolone and lidocaine into the vulvar vestibule. Murina assessed women with PVD who received weekly injections of methylprednisolone and lidocaine for three weeks, at decreasing doses. The authors report that 68 percent of participants responded favorably to treatment, although outcome measures were not specified. In a case report, Segal reported complete pain relief in one patient with PVD who received submucous infiltrations of betamethasone and lidocaine once a week for six weeks. Prospective controlled studies are needed to gain a clear picture of the efficacy of combined steroid–local anesthetic injections. Finally, botulinum toxin injections have also been attempted in two published case reports, but further research is needed to determine their impact on vulvar pain syndrome and related sexual dysfunction.

Surgery

Vestibulectomy is the most commonly reported treatment for PVD and is consistently reported as achieving the best therapeutic outcome. Although surgical technique may vary, vestibulectomy is basically a 30-minute outpatient surgical procedure performed under general anesthesia, involving the excision of the vestibular area to a depth of 2mm and a width of 1cm, all the way up to the urethra, with vaginal advancement when necessary. Two critical reviews of the PVD surgery literature by Bergeron and Bornstein revealed vestibulectomy success rates ranging from 43 to 100 percent, with average success rates typically surpassing 65 to 70 percent. Uncontrolled published reports continue to attest to the success of this minor excisional surgery. Other retrospective studies have reported similar success rates using modified vestibulectomy—a slightly less invasive procedure. Finally, one study has shown that women with UGVD respond less favorably to a surgical approach than women with PVD and concluded that surgery should be proscribed for these patients.

In the majority of studies pertaining to surgery for vulvar pain syndrome, success is reported in terms of complete cure or significant improvement and measured by a one time self-report rating of pain during intercourse. These studies suffer from many methodological problems including lack of control groups, poor or absent specification of outcome, variations in surgical protocol, non-blind evaluation of outcome, and/or short or no follow-up. However, the large number of uncontrolled studies from many different centers consistently reporting success is striking. Despite this reported success, surgical interventions for PVD have been the source of much controversy, particularly surrounding the basic mechanism by which surgery produces its effect.

Bergeron and colleagues conducted the first randomized controlled treatment study of PVD comparing vestibulectomy, group cognitive-behavioral therapy (CBT), and biofeedback. The major results of this study support the efficacy of vestibulectomy. There were no changes in pain during the six-week baseline period, but there was significant improvement post-treatment and at six-month follow-up for all treatments. However, vestibulectomy resulted in approximately twice the pain reduction (47 to 70 percent depending on pain measure) of the two other treatments (19 to 38 percent). There were no changes in sexual function during the baseline period, but all three groups reported significant improvements in overall sexual functioning and frequency of intercourse at the six-month follow-up.

Recently, the authors carried out a 2.5-year follow-up of these study participants. All treatments resulted in significant improvement in pain over time. Vestibulectomy remained superior to the other treatments in its impact on vestibular pain during the gynecological assessment, but was equal to group CBT in terms of self-reported pain during intercourse.

COGNITIVE-BEHAVIORAL TREATMENTS

Sex Therapy and Pain Management

Cognitive-behavioral interventions for vulvar pain syndromes have been less frequently reported and

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Oral Contraceptives and Vulvodynia Risk

By Corey Binns, MS

Ms. Binns is a science and health writer based in New York City. She earned her masters degree from New York University's Science, Health and Environmental Reporting Program and has contributed to the New York Times *and* Scientific American.

Introduction

For young women in Europe and North America, hormonal contraception is the most common method of preventing pregnancy. The Centers for Disease Control and Prevention has named this method of family planning one of the 10 most important public health developments of the 20th century. Despite the birth control pill's popularity among health care providers and patients, it has come under scrutiny as a possible risk factor for vulvodynia.

Since the early 1990s, clinicians and researchers have considered the possibility that the use of oral contraceptive (OC) pills may increase the risk of vulvodynia. Yet the issue remains unresolved and controversial due to inconclusive and conflicting research findings. "We have to be careful about indicting oral contraceptives as a risk factor for vulvodynia," warns Bernard Harlow, PhD, the Mayo Professor and Division Head of Epidemiology and Community Health at the University of Minnesota School of Public Health. Harlow's recently published results from his population-based study suggest that the association of OC use and adult-onset vulvodynia is not as strong as researchers have concluded from clinic-based studies.

Pros and Cons of Oral Contraceptives

The birth control pill has well-established benefits. The modern low-dose oral contraceptive (< 50 mcg of ethinyl estradiol) is 99 percent effective at preventing pregnancy. It reduces the risk of bacterial pelvic inflammatory disease, as well as endometrial and ovarian cancers. In addition, low-dose pills that contain a combination of estrogen and progestin have been successful in treating acne and hirsutism (excessive hair growth in women).

The general position of the American College of Obstetricians and Gynecologists is that the benefits of oral contraceptives outweigh their risks. Reported risks associated with taking OCs are primarily cardiovascular-related and are especially relevant in women over 35 years of age who are heavy smokers. Athough some researchers recommend that doctors consider terminating the use of OCs in vulvodynia patients, others say that the research findings are not convincing enough to outweigh the pill's many benefits.

Review of the Literature

A small case-control study conducted by gynecologist Celine Bouchard, MD, at Saint Sacrement Hospital in Quebec City first suggested that vulvar vestibulitis might be related to OC use. The researchers found the strongest link between OCs and vulvar vestibulitis in women who started using them before age 17. According to a 1997 study comparing vulvar vestibulitis patients to a pain-free control group, patients had used OCs for a significantly longer period of time, i.e., 3.1 years vs. 1.9 years. Bouchard pointed out that since OCs down-regulate estrogen receptors, by starting them early in life or using them for a long time, the decrease in estrogen might result in a thin and fragile vestibular epithelium.

Bouchard corroborated these results in a 2002 study in which she found that women who used OCs were almost seven times more likely to develop vulvar vestibulitis than women who did not take them. Furthermore, women who began OCs before age 16 faced a nine times greater risk, which also increased with duration of use. The relative risk was higher when the OC used contained high levels of progesterone and androgen, and low levels of estrogen. Similarly, a 2002 survey of young Swedish women, in which 34 percent of respondents reported vulvar pain with intercourse, found that more than two years of OC use, as well as having intercourse on a regular basis from a young age, correlated with vulvar pain.

In 2003, Nina Bohm-Starke, MD, PhD, a gynecologist at the Karolinska Institutet Daderyd Hospital in Stock-

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holm, Sweden, assessed vulvar pain levels in healthy women, only half of whom took OCs. She reported that healthy women who took OCs containing 30 to 40 milligrams of ethinyl estradiol plus progrestins showed decreased pain thresholds in the vestibular mucosa. She also noted that the posterior vestibule was the most sensitive area for women using OCs. "We think that OCs might be a contributing factor to developing vulvodynia for some women," says Bohm-Starke. "We also propose that OCs may induce a mucosal sensitivity, because some women complain of mucosal dryness when they use them. We have also shown that healthy women taking OCs have a decreased pain threshold in the mucosa compared to women not taking them."

Alexander Greenstein, MD, a gynecologist at the Tel Aviv Sourasky Medical Center in Israel, administered a survey on OC usage to vulvar vestibulitis patients at his clinic. According to the survey's results, nearly 80 percent of the clinic's vulvar vestibulitis patients used low-dose estrogen OCs, a significant difference from the general population of Israeli women, in which 51 percent used low-dose estrogen OCs. Greenstein's results add further support to the argument that a low estrogen OC might be a risk factor for developing vulvodynia.

It should be noted that these clinic-based studies found correlations between the use of OCs and increased risk of vulvodynia *in some women*. The increased degree of risk was dependent on factors such as age of first use, duration of use and OC dosage level. The findings of these studies are highly suggestive, but far from conclusive.

In contrast, Harlow's analysis of population-based cases and controls found that oral contraceptive use was associated with a *non-significant* increase in the risk of vulvodynia; the only significant association was in women who started OCs before age 18. "The association is substantially less than what people thought," Harlow says of his own findings. "There appears to be some increased risk of vulvodynia with earlier age at first use of oral contraceptives, but I don't think the association accounts for a large incidence of vulvodynia."

Clinical Implications

Given the small number of studies and inconclusive results on OC use and vulvodynia risk, most health care providers continue to prescribe OCs. "I would not recommend that a patient stop taking the pill unless I had convincing data, but at this point we don't," explains Andrew Kaunitz, M.D., a gynecologist at the University of Florida College of Medicine and lead author of the American College of Obstetricians and Gynecologists' Practice Bulletin on hormonal contraception for women with pre-existing medical conditions. "Unintended pregnancy is a major problem for women and our society. When women stop the pill, they often use a less effective form of birth control or none at all. That is not good for our patients. We need solid evidence before recommending to our patients that they stop taking the pill."

Notwithstanding Bohm-Starke's findings that OCs put some women at greater risk of vulvodynia, she agrees with Kaunitz. "In general, we do not advise young women to avoid OC use due to a risk of developing vulvodynia," says Bohm-Starke. "I don´t think we have enough scientific proof yet to give such advice. OCs are a very effective contraception method and, in most cases, safe. We have to remember that OC use doesn't lead to pain in most women. However, we advise health care providers prescribing the pill to ask patients about vulvar discomfort and dyspareunia, in addition to gathering other medical information."

Deborah Coady, MD, a New York City gynecologist in private practice, says she hesitates before starting some of her patients on the pill. "In my regular gynecology practice, I have begun to think twice about prescribing the pill to young women who might have conditions such as hyper-tense pelvic floor muscles, low back or pelvic injury, severe allergies, eczema, recurrent urinary tract infections, vaginitis and/or irritable bowel syndrome. By not prescribing it, however, many women miss out on its benefits."

Bohm-Starke encourages her patients who have vulvar pain and take an OC to try stopping it. "If a young woman

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starts to feel pain, we advise her to take a break from the pill to see if she improves," says Bohm-Starke. "Women with vulvar vestibulitis syndrome (VVS) who have been successfully treated and are able to resume intercourse can try an OC. If they start to feel dry, sensitive, or the pain returns, a different contraception method would be more appropriate." Similarly, Drs. Alexander Greenstein, and Liora Abramov, of the Sex Therapy Clinic of Lis Maternity Hospital in Tel Aviv, report, "During physical examinations of young women with VVS, we were surprised to find atrophic vulvar tissue similar to what we see in menopausal women. In this group of patients, cessation of the pill usually resulted in significant improvement."

According to Andrew Goldstein, MD, director of the Center for Vulvovaginal Disorders in Washington, DC, discontinuing the pill does not necessarily correct the problem. "In my clinical practice I see patients with severe vestibulodynia (vulvar vestibulitis) who take oral contraceptives that have lowered their free testosterone to the point that the hormone is undetectable. Since this contributes to the thinning and dryness of the vestibular mucosa, I prescribe topical estradiol and testosterone cream to be applied to the vestibule," he says. Goldstein estimates that over 60 percent of these patients experience complete resolution of their symptoms within six to eight months.

Future Studies

One thing that is certain is that more studies are needed before any conclusions can be drawn about whether OC use is a risk factor for vulvodynia. Large populations must be studied and data must include both the age of first OC use and age of onset of vulvodynia symptoms. "None of the studies that I have read are performed in a prospective way which can answer the question of whether OC use is one of the causes of vulvodynia," says Bohm-Starke. "In other words, you need a population of young women to start using OCs, who are then followed to see how many develop vulvodynia. You could also compare different types of OCs to see if the risk varies. To my knowledge this study has not been performed."

Harlow concurs that the design of previous studies has been less than ideal, because most research has focused on relatively small groups of women who visit the gynecologist on a regular basis. "I'm concerned about the results of previous studies based on clinical subjects and controls," says Harlow. "We know that probably less than 50 percent of women with vulvodynia seek care. By only studying clinical patients, they are looking at an unrepresentative sample of women."

Since most research thus far has focused on women who are already under the care of vulvodynia specialists, and many of these women didn't seek help for several years after their symptoms started, little is known about risk factors for vulvodynia in the general population. This summer, NIH grant recipients at the University of Michigan, Barbara Reed, MD, and Hope Haefner, MD, will begin a longitudinal population-based study of 2,500 women to investigate genetic susceptibility and the role of hormonal factors in the onset of vulvodynia. "In my own research, we have not seen any convincing evidence of an association between OC use and the presence of vulvodynia," Reed notes. "However, there are a number of studies that suggest there might be a relationship between their use and vulvodynia. Unfortunately, the studies were inconsistent in their findings, and none were prospective; hence, they could not determine whether OC use predated the onset of vulvodynia and was associated with new onset of disease."

Reed suggests that the use or non-use of OCs might have been associated with other factors that varied between those with vulvodynia and those without, such as the presence of genital symptoms; the presence or history of Candida vulvovaginitis; varied menstrual symptoms; or the desire and financial ability to buy the most effective form of contraceptive rather than risking pregnancy at a young age. "This possibility of confounding factors, or of factors that modify the effect of another factor on the presence of vulvodynia, often limit the interpretation of risks suggested in cross-sectional studies," she explains.

Reed and Haefner's study will identify women with and without symptoms of vulvodynia, who will then be followed for three years. A number of factors that may be associated with vulvodynia onset and remission will

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Recent NIH and NVA Vulvodynia Grants

In May 2008, the National Institute of Child Health and Human Development awarded a third research grant to University of Michigan co-investigators Barbara Reed, MD, professor of family medicine, and Hope Haefner, MD, professor of obstetrics and gynecology and co-director of the Center for Vulvar Diseases. This grant will fund a five-year project investigating the role of genetic factors and hormone use in the development of vulvodynia.

Over the past decade, research on a number of chronic pain syndromes has found that subtle variations in certain genes can make an individual highly sensitive to pain and more susceptible to developing a chronic pain disorder. For example, by analyzing slight differences in the gene that produces a certain enzyme (COMT), researchers can predict the risk of developing temporomandibular joint disorder. In recent years, studies on vulvodynia have also identified a number of genetic variations that lead to immunological changes in some women with Vulvar Vestibulitis Syndrome.

Reed and Haefner expect to find an increased prevalence in one or more pain-associated genetic variations in women with vulvodynia. They will also study the influence of previous and current exogenous hormone use on the risk of vulvodynia onset and persistence. Prior studies have found an association between vulvodynia and/or vulvar sensitivity and hormonal exposure, such as oral contraceptive use or hormone therapy, but findings in this area have been inconsistent.

To date, most vulvodynia research has used a cross-sectional design, in which data is collected at a single point in time, and study participants have typically been women referred to vulvodynia specialty clinics. Consequently, little is known about the natural history of vulvodynia and risk factors associated with its occurrence, persistence and resolution in the general population of women. In contrast, Reed and Haefner's new study will use a longitudinal design and a geographically-defined population-based group of 2,500 women.

The specific aims of this study are to: (i) assess the prevalence, incidence, persistence and remission rates of vulvodynia, with clinical confirmation and DNA analysis, and (ii) determine the association between pain-related genetic variations and hormonal influences, singly and in combination, and the incidence, persistence and remission of vulvodynia. This comprehensive study should substantially contribute to our understanding of the combined role of genetic factors and hormone exposure in the onset, maintenance and remission of vulvodynia, facilitating future studies on pathophysiology, treatment and prevention.

NVA Awards Two Research Grants

In December 2007, NVA awarded a research grant for the study of pelvic floor muscle function in women with Vulvar Vestibulitis Syndrome (VVS). The recipients of this award were Dr. Linda McLean, associate professor in the school of rehabilitation therapy, and Dr. Caroline Pukall, assistant professor of psychology, both of Queen's University in Ontario, Canada. Their study objectives are to determine whether, when compared to a control group, women with VVS demonstrate: (i) heightened activity of the superficial pelvic floor muscles in response to vestibular pressure and/or stretching of the introitus, or vaginal opening; (ii) heightened activity of the deep pelvic floor muscles in response to introital pressure; (iii) anticipatory reactions of the superficial and/or deep pelvic floor muscles in response to introital pressure or stretching; and (iv) heightened activity of remote muscles (biceps and trapezius muscles) in anticipation of, or in response to, introital pressure or stretching. This study is the first to investigate possible differences in the tonic and reactive contractility of pelvic floor muscles in women with VVS and to differentiate superficial and deep pelvic floor muscle response in this group of women. The results are expected to shed light on the etiology and/or maintenance of the disorder and contribute to future clinical assessment and management of women with VVS. If the data reveal significant differences between superficial and deep pelvic floor muscle response in VVS patients, the investigators plan to seek funding to do the same study with women who have generalized vulvodynia.

NVA also awarded a grant to vulvodynia pioneer William Ledger, MD, chairman emeritus of the department of obstetrics and gynecology at New York Presbyterian Hospital, and Steven Witkin, PhD, director of the division of immunology and infectious diseases in the department of obstetrics and gynecology at Weill Medical College of Cornell University. Ledger and

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NVA Announces Career Award Recipient

In 2006, the NVA established the Dr. Stanley C. Marinoff Vulvodynia Career Development Award in recognition of Dr. Marinoff's invaluable contributions to the field of vulvodynia. The award is given annually to a junior faculty member who demonstrates a serious clinical or research interest in vulvodynia. The NVA is pleased to announce that the 2008 recipient of the award is Beri Ridgeway, MD, who is currently completing a fellowship in female pelvic medicine and reconstructive surgery at The Cleveland Clinic in Ohio.

Antidepressants and anticonvulsants are often the first-line medicines used to treat vulvodynia, but randomized placebo-controlled trials to determine the efficacy of these medications are scarce. With her NVA award and matching funds from The Cleveland Clinic, Dr. Ridgeway will investigate the efficacy of the anticonvulsant pregabalin (Lyrica) in the treatment of vulvodynia. Pregabalin has been shown to be effective in the treatment of other chronic pain disorders such as post-herpetic neuralgia, diabetic neuropathy and fibromyalgia. Dr. Ridgeway's primary objective is to determine whether, and to what extent, pregabalin relieves pain in women suffering from either generalized vulvodynia or vulvar vestibulitis syndrome. In addition, she will assess the medication's tolerability and its effect on quality of life. Dr. Ridgeway's aim is to add to the growing body of evidence-based literature on treatment efficacy, so women and their health care providers can make more informed treatment decisions.

For additional information on the Career Development Award and/or to read summaries of previous recipients' projects, please visit http://www.nva.org/for_medical_professionals/career_development_award.html. ■

Grants

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Witkin's long-term research collaboration and numerous publications have shown that women with VVS can be differentiated into subgroups based on: (i) the presence or absence of variations in specific genes involved in the immune response, (ii) the relative production of pro- and anti-inflammatory cytokines, (iii) an allergic response to seminal fluid, and (iv) whether or not symptoms began with the first attempt at sexual intercourse.

One of Ledger and Witkin's major research findings is that some women with VVS exhibit genetic variations that increase their capacity to initiate inflammation and reduce their ability to terminate inflammation. Specifically, they show a deficiency in Interleukin-1 receptor antagonist production, which increases susceptibility to inflammation, coupled with an increase in Interleukin-1-Beta production, which reduces the ability to terminate inflammation. With their NVA grant, Ledger and Witkin will apply this novel research finding to the treatment of women with VVS. They will (i) investigate whether women with VVS benefit from treatment with Anakinra, an Interleukin-1 receptor antagonist that is already being used to treat rheumatoid arthritis, an inflammatory condition, and (ii) try to predict which patients, based on their genetic makeup, would benefit from this treatment.

Make a Research Donation

The NVA recently issued its annual request for research proposals from the medical community. We are committed to funding studies that will increase our knowledge base and lead to the development of effective vulvodynia treatments. Please make a tax-deductible contribution to the NVA Medical Research Fund by visiting our home page at www.nva.org (click on 'donate or renew' in the left column) or contact Gigi Brecheen at gigi@nva.org or 301-949-5114. ■

E-Mail Updates

To keep informed on the latest vulvodynia news, sign up for our bimonthly electronic newsletter, *NVA Update*. Simply send an email to gigi@nva.org with the words 'E-mail address' in the subject line or sign up on our web site: www.nva.org (click on 'e-news' box in right-hand corner). We treat all contact information, including e-mail addresses, as confidential.

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include sex therapy, pelvic floor physical therapy, biofeedback and cognitive-behavioral pain management. Sex therapy has been conducted based on the assumption that an increase in desire and arousal, as well as a decrease in pelvic floor muscle contraction, might impact some of the mechanisms that mediate idiopathic vulvar pain. Indeed, women with PVD have consistently shown dramatic impairment in sexual desire, arousal, and orgasm in comparison to women without vulvar pain. Two different studies report success rates ranging from 43 to 68 percent with a combination of sex therapy and behavioral pain management, although treatment protocols were either unstandardized or multidisciplinary.

My colleagues and I investigated the efficacy of group cognitive-behavioral sex therapy combined with pain management in two different randomized studies of women with PVD. In the first study, described above (*See* Surgery section), participants in the cognitive-behavioral therapy (CBT) group reported significant improvement in pain during intercourse at a 2.5-year follow-up. In this regard, there was no difference between the CBT and vestibulectomy groups. On other pain measures, however, women in the vestibulectomy group reported more improvement than those in the CBT group. In another ongoing study, we randomly assigned women with PVD to either apply a corticosteroid cream or receive CBT for a 13-week treatment period. At post-treatment, women in both groups reported significant reduction in pain and improvement in sexual outcome standardized measures, but women in the CBT group were significantly more satisfied with their treatment, catastrophized less about pain and reported more global improvement in sexual functioning. Although these results are preliminary, they suggest that CBT may yield, overall, better results than a corticosteroid cream. As a whole, studies focusing on CBT indicate that it is a promising, noninvasive treatment which may be underutilized.

Pelvic Floor Physical Therapy and Biofeedback

Therapeutic effectiveness of biofeedback was initially reported in Glazer's retrospective study involving a group of women with mixed types of vulvar pain. Out of 33 participants, 17 reported pain-free intercourse after treatment. Another retrospective follow-up of 43 women with unprovoked generalized vulvodynia confirmed long-term gains resulting from biofeedback treatment. In a subsequent prospective study, 15 of 29 women with PVD reported experiencing negligible pain with intercourse following four to six months of daily biofeedback exercises. Although lacking control groups, these studies suggested that hypertonic pubococcygeal muscles, which surround the vagina and anus and form part of the pelvic floor, may play a role in the etiology or maintenance of vulvar pain syndrome. Since then, one controlled study has demonstrated that women with PVD have significantly more hypertonic pelvic floor muscles than normal-matched controls, confirming Glazer's initial hypothesis and further supporting the use of pelvic floor physical therapy and/or biofeedback in the treatment of vulvar pain syndrome.

Bergeron and colleagues carried out a retrospective telephone interview study of 35 PVD patients who had received physical therapy, including biofeedback. Physical therapy was successful for 51 percent and unsuccessful for the rest. Overall, self-reported pain during intercourse and gynecologic examinations was significantly reduced pre- to post-treatment, as was self-reported pain frequency, pain interference with intercourse and fear of pain. Sexual functioning also improved pre- to post-treatment with a significant increase in frequency of intercourse, sexual desire and arousal.

Recently, another physical therapy modality—pelvic floor electrical stimulation – was assessed prospectively in a group of 29 women with vestibular pain resulting in dyspareunia and, for nine participants, vaginismus. Results showed that after 10 weeks of weekly electrical stimulation, participants reported significantly improved pain levels and sexual function as per standardized measures.

Overall, the results of these reviewed studies suggest that physical therapy can be a noninvasive, low-risk treatment option for PVD, although randomized controlled trials are necessary to confirm the efficacy of this intervention. Finally, there is an emerging trend toward combining cognitive-behavioral sex therapy and pain management with pelvic floor physical therapy, in an effort to offer women with vulvar pain syndrome an approach that deals with multiple aspects of their disorder.

See TREATMENT, page 11

Treatment

(from page 10)

ALTERNATIVE TREATMENTS

One prospective pilot study suggested that acupuncture, which has been shown to be an effective treatment for some types of chronic pain, may prove beneficial for women with PVD. Another case study reported that hypnotherapy completely relieved pain in a woman with PVD and that gains were maintained at a one-year follow-up. Considering the low adverse effects of these two alternative interventions, and their use in the treatment of other pain conditions, more rigorous studies are warranted to evaluate their efficacy.

CONCLUSION

Treatment interventions for vulvar pain syndrome have largely been devised on a trial and error basis. Medical treatments are the most common, but have limited empirical support. Surgery outcome reports are numerous and claim moderately high success, but these studies are not well-controlled, apart from one randomized treatment study which confirmed the efficacy of vestibulectomy in the treatment of PVD. Cognitive-behavioral studies are few in number, but may be a promising, noninvasive adjunct approach. Alternative treatments need to be further studied to assess their potential usefulness in the treatment of vulvar pain syndrome. In particular, research on the treatment of vulvar pain syndrome has suffered from its lack of alignment with current conceptualizations of chronic and recurrent pain, which emphasize their multidimensional nature and incorporate the interdependent roles of biological, cognitive, emotional, behavioral and interpersonal factors that contribute to their development and maintenance. This has been reflected in the types of treatments that are studied—the vast majority being biomedical—and in the narrow range of measures used to document treatment-associated changes. It is likely that significant improvement in all aspects of vulvar pain syndrome will require the adoption of multimodal, multidisciplinary approaches. These approaches must be studied in order to document empirically their hypothesized advantages over unimodal treatment models.

(*Editor's note: A footnoted version of this article is available upon request by contacting Chris Veasley at* chris@nva.org or 401-398-0830.) ■

Oral Contraceptives

(from page 7)

be analyzed. They propose that this population-based study will accurately determine the relationship between vulvodynia and hormonal status, including the use of oral contraceptives and hormone therapy.

"Our knowledge about the impact that OC use and/or hormone therapy might have on the onset of symptoms of vulvodynia is incomplete, with current data being limited by inconsistent findings between studies, the cross-sectional nature of the studies, and the possible bias inherent in population selection," states Reed. "Prospective, population-based studies are expected to more clearly define the possible relationship between hormonal factors (natural or medicinal) and vulvodynia, and are expected to provide information that will result in evidence-based recommendations for women with, or at risk for, vulvodynia."

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