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Overlap Between Orofacial Pain And Vulvar Vestibulitis Syndrome

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Abstract

Objectives—To explore the prevalence of Orofacial Pain (OFP) among patients with Vulvar Vestibulitis Syndrome (VVS) and to examine the relationship between signs and symptoms of OFP and clinical characteristics of women with VVS; we specifically sought to investigate differences in psychological characteristics and self-reported severity of painful intercourse.

Methods—In this cross-sectional exploratory study, 137 women with VVS completed questionnaires that assessed self-reported levels of pain, anxiety, somatization, and presence of signs and symptoms suggestive of clinical and sub-clinical OFP. Demographic data were gathered from medical records.

Results—Orofacial Pain was found to be a highly prevalent (78%) condition among women with VVS. Compared to women with no OFP symptoms (n=30), those with symptoms (n=64) had higher levels of anxiety (45.0 vs. 37.8, Bonferroni adjusted p=0.017), somatization (125.2 vs. 96.0, Bonferroni adjusted p<0.001), and psychological distress (62.8 vs. 56.0, Bonferroni adjusted p=0.002). While we observed a similar trend among women with sub-clinical OFP (n=43), this trend only reached statistical significance with respect to somatization. Differences were not detected for demographics, duration of pain, and severity of pain during intercourse across the three groups.

Discussion—Orofacial Pain is a common condition among women with VVS. Because severity and duration of painful intercourse did not differ by OFP classification but psychological characteristics did, we must begin to question a uni-dimensional focus on vestibular mucosa as a reason for pain and persistent distress.

Keywords

vulvodynia; orofacial pain; vulvar vestibulitis syndrome; somatization; pain report

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Introduction

Vulvar Vestibulitis Syndrome (VVS), the most common type of chronic vulvovaginal pain, impairs the psychological, physical, and reproductive health of nearly 1 in 10 women at some point in their lifetime.[1] VVS is also known as localized vulvodynia, vestibulodynia, and, in 2004, was renamed as "provoked localized vulvodynia" by the International Society for the Study of Vulvovaginal Disease (ISSVD).[2, 3] However, the clinical diagnosis of VVS has not changed since it was originally introduced by Friedrich,[4] and is based on self-report of severe pain upon vaginal entry and tenderness to pressure localized within the vulvar mucosa (vestibule).[5] To date, the etiology of VVS remains poorly understood, and the diagnosis is made after excluding other known gynecological disorders in the face of persistent pain with genital contact (e.g., tampon use or intercourse).[6]

Although the current definition of VVS is based on a local pain conceptualization of this condition, an emerging body of evidence supports the notion of VVS as a complex pain disorder, akin to idiopathic musculoskeletal pain conditions, such as fibromyalgia and temporomandibular disorder [6, 7] In addition to higher pain on mucosal (vestibular) contact, women with VVS show increased pain sensitivity in non-genital sites.[6] A higher prevalence of psychological traits, such as somatization and anxiety, are also well documented in this population.[6] Collectively these observations suggest that women with VVS may have an alteration in pain processing pathways. In addition, these women may have psychological characteristics that facilitate the development of pain.[6, 7]

Granot and colleagues were the first to investigate the relationship between alterations in pain processing pathways- as demonstrated by heightened non-genital pain sensitivity- and psychological traits (such as anxiety) with treatment outcomes. They made an important observation in that subgroups of women with VVS differed in self-reports of anxiety, somatization and non-genital pain sensitivity.[8-10] Additionally, in their study, women with higher non-genital pain sensitivity and anxiety tended to respond poorly to conventional treatments for VVS.[8] This work, as well as that of others,[11-14] has led to a gradual shift away from the traditional conceptualization of VVS as primarily a mucosal inflammatory process.

We hypothesize that VVS is a group of disorders characterized by dysfunctions in the vestibular mucosa (i.e., heightened inflammatory response) and central pain processing pathways. However, the extent to which these dysfunctions contribute to the overall clinical picture varies among individuals.

In this study, we aimed to explore the overlap between Orofacial Pain (OFP) and VVS. We embarked on this study after noticing that a high percentage of women with VVS seen in our clinics complained of a distinct pattern of pain in their orofacial regions which was suggestive of an idiopathic pain condition such as temporomandibular disorder. We also noted that compared to women with no orofacial pain, those women with orofacial pain were more likely to report pelvic muscle tenderness during gynecological examination with an inability to relax pelvic muscles.

After consultation with colleagues in orofacial pain research, we used a validated questionnaire to investigate the prevalence of signs/symptoms suggestive of OFP in our cohort of women with VVS. In addition, we investigated the relationship between OFP and self-reported pain during intercourse, as well as its association with psychological characteristics such as anxiety, somatization, and distress.

Materials and Methods

This cross-sectional questionnaire study was conducted between February 1, 2003 and October 31, 2005, and was approved by the institutional review board at the University of North Carolina at Chapel Hill. Women diagnosed with VVS during or after January 2002 were eligible for participation. In our clinical practice, the diagnosis of VVS is made by a subjective report of pain during intercourse and tenderness to touch elicited during a cotton swab exam; this diagnosis is only rendered after excluding other identifiable gynecological disorders.[5] Among participants, the diagnosis of VVS was confirmed by the review of medical records by two independent reviewers. Both reviewers were blinded to the subjects' responses to the questionnaires. In addition to confirming the diagnosis of VVS, the reviewers assessed eligibility. Disagreements on eligibility (n=4) were adjudicated by a third reviewer. Women who had VVS with other urogenital pain disorders (e.g., vaginismus, generalized vulvodynia, interstitial cystitis), dermatologic conditions (e.g., lichen sclerosis), chronic pelvic pain defined as non-menstrual daily pain localized to the pelvic region, and neuropathies (e.g., pudendal neuralgia) were excluded. A total of 196 women were eligible for participation and received both the consent forms and questionnaires. Participants were instructed by a cover letter in the study package to return the completed questionnaires and consent documents in a pre-stamped envelope. Of the 196 eligible women, 137 (70%) completed the questionnaires and comprise our sample.

The battery of questionnaires included assessments for psychological characteristics and self-reported pain. Additionally, participants were asked to complete a 9-item, validated questionnaire in order to assess signs and symptoms suggestive of OFP (e.g., temporomandibular disorder). Characteristics of the questionnaire are reviewed below.

Pain Questionnaire

Self-reported pain with intercourse was assessed by administering the Gracely Pain Scale, which asks women to rate the lowest, average and maximal pain with intercourse on a scale of 0−100.[15] Participants are instructed to select verbal descriptors of their pain by circling a word that best describes their pain experience. These verbal descriptors capture two important pain domains: 1) sensory (severity of physical pain), and 2) affective (emotional response to a given level of physical pain). A predetermined numerical value for each verbal descriptor was averaged to obtain a summary score for statistical analysis. Modified versions of this questionnaire are commonly used in assessing pain among patients with idiopathic pain disorders (e.g., temporomandibular disorder and fibromyalgia).

Psychological Questionnaires

We administered questionnaires to assess anxiety (*Speilberger State-Trait Anxiety Inventory)*, somatization (*Pennebaker Inventory of Limbic Languidness)*, and global psychological distress (*Brief Symptom Inventory-Global Severity Index)*. The following is a brief description of these questionnaires.

The *State-Trait Anxiety Inventory (STAI)* consists of two 20-item questionnaires, which assess an individual's current anxiety level and general propensity towards anxiety. This instrument has good reliability (retest reliability: r=.73 to .86, Cronbach's α=0.83 to 0.92) and is widely utilized in clinical research;[16] the norm for a female population of comparable demographics is 36 on both scales. As a comparison, the average score of an inpatient neuropsychiatric population is 47.7 and 46.6, respectively for the state and trait anxiety scales.[16]

The *Pennebaker Inventory of Limbic Languidness (PILL)* assesses somatization by capturing the frequency of occurrence of 54 common physical symptoms and sensations. It has high

internal consistency (α=0.88) and adequate test-retest reliability (0.70 for a two-month period);[17] the norm for the female population is 98−104. A high baseline somatization score is an independent risk factor for the development of a chronic pain state[7] and is shown to correlate well with the number of tender muscle sites, pain sensitivity and progression to chronicity.[18]

The *Brief Symptom Inventory (BSI)* consists of 53 items rating psychological distress in nine areas: somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.[19] A global severity index (GSI) is obtained by combining the number and intensity of reported symptoms. Internal consistency using Cronbach's α ranges from a low of 0.75 (psychoticism) to a high of 0.85 (depression). Test-retest validity for the global severity index score is 0.90;[19] the norm for the female population is 50, with a clinical cut-off of 63.[20]

Lastly, to examine the prevalence of signs and symptoms suggestive of idiopathic pain disorders in the orofacial region, we administered a 9-item, validated screening survey. This survey is commonly used to identify incident cases of temporomandibular disorder, and is validated against the 'gold standard' physical exam; the sensitivity (100%) and specificity (81%) of this screening survey is high (G. D. Slade, PhD, unpublished data, November, 2005). Participants are queried on the frequency and duration of symptoms such as headache, facial and jaw pain, grinding, and clenching. Two independent reviewers (DZ and WM) masked to the subjects' identification and responses to psychometric questionnaires classified women into the following three categories: OFP, sub-clinical OFP, or no OFP. We classified women as having OFP if they had been previously been diagnosed with temporomandibular disorder or endorsed greater than three episodes of headache or 'sinus pain' per week, and experienced both provoked and spontaneous orofacial pain. We classified women as having sub-clinical OFP if they denied spontaneous orofacial pain but endorsed provoked orofacial pain, and reported greater than three episodes of headache or 'sinus pain' per week. In addition, in order to be classified in the sub-clinical OFP category, subjects had to report use of night guard, grinding or clenching. The agreement between the two reviewers was high (Weighted Kappa (κ) = 0.81, 95% CI (0.71, 0.90)). OFP was defined using three categories instead of two (OFP versus not) due to our *a priori* hypothesis that a large proportion of patients would not fit into either dichotomous category. This hypothesis was based on our previous clinical experience and a common belief among most pain experts that patients with these conditions represent a spectrum of disease rather than a dichotomy.

Data Analysis

Statistical analysis was performed using SAS software (version 9.1; SAS Institute Inc., Cary, NC). We performed bivariate analyses using one way analysis of variance (ANOVA) or Fisher's Exact tests to determine if there were differences in patient characteristics amongst the groups classified by OFP (OFP, sub-clinical OFP, no OFP). These characteristics include age, race, education, parity, marital status, duration of pain, and number of prior physicians seen for similar symptoms. Differences in mean intercourse related pain (Gracely Pain Severity Scale) and psychometric assessments were compared for all groups using the ANOVA test. All tests comparing the three groups were conducted at α=0.05. If overall differences were detected ($p<0.05$), Bonferroni procedures were used to adjust the p-values resulting from multiple pairwise comparisons tests ($p\text{-value}_{Bon,adj}$)

Results

Seventy-eight percent (n=107) of the participants had signs and symptoms suggestive of idiopathic pain conditions in the orofacial region (e.g., temporomandibular disorder). Of those, thirty-one percent (n=43) were classified as having sub-clinical OFP and forty-seven percent (n=64) were classified as having OFP. Demographic characteristics among these subgroups

did not differ (Table 1). In general, participants were highly educated, young, Caucasian women with an average duration of 5 years of painful intercourse. We did not observe any differences with respect to the duration and severity of self-reported pain during intercourse among the subgroups of women with VVS. Similarly, verbal descriptors indicating sensory and affective domains of pain during intercourse did not differ among the subgroups (Table 1).

However, we observed significant and robust differences in the psychological characteristics among the three subgroups (Table 2). Among our cohort of women with VVS, those with OFP had significantly higher levels of anxiety (Speilberger State-Trait Anxiety Inventory), somatization (Pennebaker Inventory of Limbic Languidness) and global psychological distress (Brief Symptom Inventory-Global Severity Index) as compared to those without OFP (Table 2).

Women with OFP had the highest scores on all measured psychometric indices, while those without OFP had the lowest. Women with sub-clinical OFP, however, consistently fell within these two limits. For example, while women with sub-clinical OFP were similar to those without OFP with respect to psychological distress (BSI-Global Severity Index), they differed significantly on somatization (PILL, Table 2). The highest mean score on somatization was seen among women with OFP (125.2, 2 SD above norm), followed by women with sub-clinical OFP (111, 1 SD above norm). Women without OFP had mean score lower than average for the general population (103.3) (Table 2).

Discussion

In our cohort, approximately 8 out of 10 women with VVS had chronic orofacial pain. The most common and widely studied form of chronic orofacial pain -temporomandibular disorder- affects 7−15% of the adult population; 80% of the treated cases are women in their early to mid-adulthood.[21] At the present, we can not irrefutably make a statement about the prevalence of a specific category of OFP. However, on formal evaluation by an orofacial pain specialist (as part of an ongoing follow up study) the majority of our participants have signs and symptoms of temporomandibular disorder.

It is intuitively perplexing as to why an idiopathic orofacial pain disorder (affecting 10% of the general population)[22] is highly prevalent among women with idiopathic genital pain. Another related question that comes to mind is the mechanism by which the distribution of signs and symptoms of OFP mirror the spectrum of psychological characteristics among women with VVS. Women with VVS and symptoms of OFP had higher levels of anxiety, somatization, and psychological distress; duration and severity of self-reported pain with intercourse did not differ among categories of OFP.

The association between psychological traits and OFP among women with VVS may, in part, be explained by specific genetic variants which mediate the activities of central pain regulatory pathways. For example, polymorphism of the gene encoding catechol-o-methyltransferase (COMT) is a potent and independent risk factor for the development of chronic pain conditions, such as temporomandibular disorder.[23] Furthermore, the associations between the haplotype variations for the β2 adrenergic receptor and psychological traits, such as anxiety and somatization, have been identified.[24]

We hypothesize that subgroups of women with VVS may share the same genetic vulnerability as women with temporomandibular disorder.[7] Thus, the associations between certain psychological traits and signs/symptoms of OFP among women with VVS suggest that an inherent susceptibility may permit or even precede the development of VVS in certain women. We therefore speculate that women with VVS are a heterogeneous population and that the

observed clinical phenotype is composed of several interactive biological and psychological factors.

Based on our findings and an emerging body of evidence, we hypothesize that the experience of pain with attempted intercourse may be governed by two interdependent processes: 1) a biologic impairment in pain regulatory mechanisms (similar to what is seen among women with temporomandibular disorder and other idiopathic pain conditions), and 2) a genetic predisposition to a heightened inflammatory response in vulvar mucosa. Mucosal sensitivity, though a necessary component of the clinical manifestation of VVS, may not be sufficient for the development of this disorder in all women. Experience of pain, though clinically similar, could in fact be primarily driven by different pathophysiologic processes, some that are centrally mediated (i.e., biochemical abnormality in pain processing) and some that are peripherally mediated (i.e., biochemical abnormality in the inflammatory cascade in the mucosa).

While these results are intriguing, it is important to note that our population reflects the severe end of the spectrum of patients with VVS seen in a referral-based university clinic. The findings from our patient population may not be generalizable to VVS patients seen in primary care. Furthermore, the 137 women who completed the questionnaires that allowed classification of OFP status may differ in important ways from those not reached or not willing to participate in research. It is difficult to hypothesize the direction of bias due to non-response. However, it is unlikely that women who opted against participation or could not be contacted would change our findings because the classification of these women would likely fall equally among the three subgroups. Lastly, we did not use the 'gold standard'[22] clinical exam for diagnosis of OFP but instead used a validated questionnaire used to identify temporomandibular disorder, the most common form of OFP. This may have resulted in a higher prevalence of OFP. However, the differences across groups with respect to psychosocial variables are in agreement with previous research in temporomandibular disorder [25]and support the likelihood that our categories based on questionnaire responses adequately classified OFP groups.

This study is cross-sectional and therefore temporal sequence cannot be established. Specific psychological traits may precede or be modified by chronic pain disorders.[6] Psychological traits may be consequences of living with chronic pain; more importantly, however, such traits may precede the development of chronic pain and be amplified with disease progression.

Research in chronic pain disciplines (e.g., orofacial pain, fibromyalgia) requires conceptual models that examine the interplay between psychological and biological factors and their ultimate effect on pain pathophysiology. This model is lacking in VVS. Our findings provide additional evidence in support of VVS being an idiopathic pain disorder akin to fibromyalgia and TMD. To that end, we must: 1) objectively measure the clinical presentation of VVS as it relates to the vulvar mucosa, pelvic floor muscles, psychological traits, and central pain processing mechanisms; 2) investigate the potential for distinctive subtypes of VVS; and 3) develop a conceptual framework, incorporating these measures, in order to guide research in the pathophysiology and treatment of VVS.

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Table 1

Characteristics of the Study Participants

Patient Characteristics	n	No OFP Mean ± SD or Freq (%)	n	Sub-clinical OFP Mean ± SD or Freq (%)	n	Clinical OFP Mean ± SD or Freq (%)	*P* *
Age	30	31.1 ± 8.3	43	31.6 ± 8.8	64	31.7 ± 6.9	.947
VVS classification	30		43		63		.139
Primary		5 (17%)		16 (37%)		19 (30%)	
Secondary		22 (73%)		26 (60%)		36 (57%)	
Uncertain		3 (10%)		1 (2%)		8 (13%)	
White	30	26 (87%)	43	41 (95%)	64	59 (92%)	.388
College education or beyond	24	22 (92%)	33	27 (82%)	61	57 (93%)	.255
Nulliparous	30	23 (77%)	43	33 (77%)	64	48 (75%)	1.000
Married	30	21 (70%)	43	36 (84%)	64	50 (79%)	.385
Duration of painful intercourse (months)	30	55.9 ± 45.7	42	71.4 ± 44.0	64	64.3 ± 57.5	.449
Number of prior physicians seen	22	2.6 ± 1.6	34	2.9 ± 2.0	49	3.1 ± 2.7	.648
Intercourse related pain (GPS)							
Low	30	32.6 ± 30.2	39	38.1± 32.3	61	38.6 ± 27.7	.642
Average	30	52.8 ± 28.4	39	54.8 ± 31.4	61	61.9 ± 27.1	.278
High	30	70.9 ± 30.1	39	72.4 ± 27.9	61	81.2 ± 19.6	.097
Affective Word	30	12.7[§] ± 8.4	39	13.5[§] ± 7.6	60	15.2[//] ± 8.9	.359
Sensory Word	30	33.4[¶] ± 18.5	38	35.2[#] ± 17.4	59	34.8[#] ± 18.6	.913

OFP, orofacial pain syndrome. GPS, Gracely Pain Scale.

[*] Significance testing based upon ANOVA test for continuous variables and Fisher's Exact Tests for categorical.

[§] Slightly intolerable.

[//] Slightly intolerable to very distressing.

[¶] Intense.

[#] Intense to very intense.

Table 2

Psychological Characteristics of Subgroups of Women with Vestibulitis

Psychological scores	No OFP n=30 Mean (SD)	Sub-clinical OFP n= 43 Mean (SD)	Clinical OFP n=64 Mean (SD)	P*	Multiple Comparisons Bonferroni Adjusted Results	Population n	Norm* (no OFP) Mean (SD)
STAI- state†	35.9 (10.9)	38.6 (12.6)	41.8 (11.8)	.075	----	246	31.8 (9.3)
STAI- trait‡	37.8 (11.0)	39.6 (10.7)	45.0 (12.1)	.008	Clinical > No OFP	243	36.6 (8.9)
PILL-somatization§	96.0 (17)	111.0 (23.7)	125.2 (25.8)	<.001	All significant	240	103.3 (20.6)
BSI-GSI//	56.0 (9.2)	57.5 (9.9)	62.8 (9.4)	.002	Clinical >Sub-clinical and No OFP	231	53.5 (10.0)
Anxiety	53.3 (11.9)	55.2 (10.2)	60.6 (8.7)	.001	Clinical >Sub-clinical and No OFP	243	48.8 (11.7)
Somatization	49.1 (13.5)	54.3 (13.3)	59.5 (11.5)	.001	Clinical > No OFP	243	46.1 (12.2)
Depression	50.5 (13.6)	52.7 (12.5)	59.3 (11.7)	.002	Clinical >Sub-clinical and No OFP	243	51.1 (11.7)

*Population norm derived from the participations of a 3 year prospective study on incidence of temporomandibular disorder, the most common form of OFP; the scores are based on participants who did not develop OFP over the study period. [18] Significance testing based upon ANOVA test.

†STAI-S, Spielberger State Anxiety Inventory describing situational or state related anxiety

‡STAI-T, Spielberger Trait Anxiety Inventory describing general propensity (trait) toward anxiety

§PILL, Pennebaker Inventory of Limbic Languidness

//BSI-GSI, Brief Symptom Inventory -Global Severity Index, composite score for psychological distress with individual subscale scores