

Vulvodynia

Managing Vulvodynia with Central Sensitization: Challenges and Strategies

Cristina Rubal, Augusto Pereira, Laura Calles Sastre, Belén Almoquera Pérez-Cejuela, Sofía Herrero Gámiz, Pilar Chaves, Tirso Pérez Medina

J Clin Med. 2023 Jun 5;12(11):3851. doi: 10.3390/jcm12113851.

<https://pubmed.ncbi.nlm.nih.gov/37298046/>

Background: Vulvodynia is defined as a chronic idiopathic vulvar pain condition. This study aimed to investigate the effect of central sensitization on the prognosis of neuromodulator treatment for vulvodynia. **Method:** A total of 105 patients with vulvodynia who underwent pelvic mapping pain exploration were included and scored according to the Convergence PP Criteria for pelvic pain and central sensitization. The patients were treated according to chronic pelvic pain guidelines, and their response to treatment was evaluated. **Results:** A total of 35 out of 105 patients (33%) with vulvodynia had central sensitization, which was associated with comorbidities, dyspareunia, pain with micturition, and pain with defecation. Dyspareunia and pain with defecation were independent prognostic factors for central sensitization. Patients with central sensitization experienced more pain during intercourse, urination, or defecation, had more comorbidities, and responded worse to treatment. They required more treatment, with a longer response time (over 2 months). Patients with localized vulvodynia were treated with physiotherapy and lidocaine, while patients with generalized vulvodynia were treated with neuromodulators. Amitriptyline was effective in treating patients with generalized spontaneous vulvodynia and dyspareunia. **Conclusions:** Overall, this study highlights the importance of considering central sensitization in the diagnosis and treatment of vulvodynia and the need for individualized treatment based on the patient's symptoms and underlying mechanisms. Vulvodynia patients with central sensitization had more pain during intercourse, urination, or defecation, and responded worse to treatment, requiring more time and medication.

Effectiveness of Two Transcutaneous Electrical Nerve Stimulation (TENS) Protocols in Women with Provoked Vestibulodynia: A Randomized Controlled Trial

Filippo Murina, Dario Recalcati, Stefania Di Francesco, Irene Cetin

Med Sci (Basel). 2023 Aug 2;11(3):48. doi: 10.3390/medsci11030048.

<https://pubmed.ncbi.nlm.nih.gov/37606427/>

Background: Vestibulodynia (VBD) is the most common form of vulvodynia. Because VBD is a pain disorder, transcutaneous electrical nerve stimulation (TENS) can be used as treatment. This study aims to evaluate the effects of two-parameter combinations (frequency and pulse duration) of TENS in reducing pain intensity and dyspareunia in VBD. **Methods:** A randomized, double-blind, controlled trial was conducted to study the effect of two different electrical stimulation treatment regimens on women with VBD receiving domiciliary TENS. Outcomes were the mean change from baseline at 60 and 120 days of burning/pain and dyspareunia (VAS), Vulvar Pain Functional Questionnaire (V-Q), Female Sexual Functioning Index (FSFI) and vaginal electromyography measurements. **Results:** A total of 78 subjects, 39 in each group, completed the trial. Patients in Groups 1 and 2 received a mean of 46.9 and 48.4 TENS sessions. By day 120, there was a 38.2% reduction in the burning/pain and a 52.1% reduction in the dyspareunia VAS scores in Group 1, as compared to 21.3% ($p = 0.003$) and 23.1% in Group 2 ($p = 0.01$), respectively. FSFI, V-Q, and muscle-strength measures also improved but were not statistically significant. **Conclusions:** Our findings showed the potential of TENS in the treatment of VBD.

Does the addition of electrical stimulation or kinesiotherapy improve outcomes of amitriptyline treatment for women with vulvodynia? A randomized clinical trial

Marcela Grigol Bardin, Paulo César Giraldo, Juliana Lenzi, Steven S Witkin, Ticiana Aparecida Alves De Mira, Melanie Morin

Int Urogynecol J. 2023 Jun;34(6):1293-1304. doi: 10.1007/s00192-023-05454-z. Epub 2023 Mar 16.
<https://pubmed.ncbi.nlm.nih.gov/36929279/>

Introduction and hypothesis: Women diagnosed with provoked vulvodynia frequently report a great deal of frustration in achieving symptomatic relief. Physical therapy and drug treatment are among the interventions most indicated by guidelines; however, whether those modalities are effective when combined remains unclear. The objective was to evaluate the effectiveness of adding a physical therapy modality compared with amitriptyline alone for the treatment of vulvodynia. **Methods:** Eighty-six women with vulvodynia were randomized to (G1) 25 mg amitriptyline, once a day ($n=27$), (G2) amitriptyline + electrical stimulation therapy ($n=29$) or (G3) amitriptyline + kinesiotherapy ($n=30$). All treatment modalities were administered for 8 weeks. The primary endpoint was the reduction in vestibular pain. Secondary measurements focused on sexual pain, frequency of vaginal intercourse, Friedrich score, and overall sexual function. Data were analyzed using intention-to-treat. **Results:** All treatment modalities resulted in a significant decrease in vestibular pain ($p<0.001$), sexual pain ($p<0.05$), Friedrich score ($p<0.001$), and an increase in the frequency of sexual intercourse ($p<0.05$). G3 was more effective than G1 at reducing sexual pain (G1: 5.3 ± 3.3 vs G3: 3.2 ± 2.7 ; $p=0.01$) and at improving sexual function (G1: 18.8 ± 9.8 vs G3: 23.9 ± 7.8 ; $p=0.04$). **Conclusion:** Kinesiotherapy and electrotherapy additions to amitriptyline administration as well as amitriptyline alone, were effective at improving vestibular pain in women with vulvodynia. Women receiving physical therapy had the greatest improvement in sexual function and frequency of intercourse at post-treatment and follow-up.

Treatment of Vestibulodynia with Submucosal Injections of IncobotulinumtoxinA into Targeted Painful Points: An Open-Label Exploratory Study

Paula Villa-Muñoz, Monica Albaladejo-Belmonte, Francisco J Nohales-Alfonso, Jose Alberola-Rubio, Javier Garcia-Casado

Toxins (Basel). 2023 Jul 25;15(8):476. doi: 10.3390/toxins15080476.
<https://pubmed.ncbi.nlm.nih.gov/37624233/>

The studies carried out to date on vulvodynia treatment with botulinum neurotoxin type A (BoNT/A) have followed generic injection protocols and reported contradictory outcomes on its effects. The aim of the present study was thus to propose a protocol for injecting BoNT/A into targeted painful points, to comprehensively assess the clinical effect of BoNT/A treatment and identify the risk/protective factors for successful treatment. Thirty-five vestibulodynia patients were treated with submucosal injections of incobotulinumtoxinA and assessed 8, 12 and 24 weeks after their treatment. Their clinical and pelvic statuses were assessed from self-reported questionnaires (Visual Analogue Scale (VAS), Female Sexual Function Index (FSFI), Marinoff's Dyspareunia Scale (MDS), Hospital Anxiety and Depression Scale (HADS), Catastrophizing Scale (CS)), physical examinations and surface electromyography (sEMG). The patients reported a reduction in provoked vestibulodynia ($<VAS, p < 0.01$), improved sexual function ($>FSFI, p < 0.01$; $<MDS, p = 0.01$) and psychological status ($<HADS, p < 0.01$), and lower pelvic floor hyperactivity at rest ($<sEMG \text{ amplitude}, p = 0.01$). Factors such as smoking, painful comorbidities, vulvar pain sensitivity and sexual function were significantly associated with successful treatment. The results indicate the beneficial effects of BoNT/A in treating vestibulodynia and reinforce the importance of adapting the treatment according to its clinical presentation and the patient's medical background.

Immune mechanisms in vulvodynia: key roles for mast cells and fibroblasts

Elena Tonc, Gloriah K Omwanda, Kevin Arnold Tovar, Xiu Mei Emma Golden, Devavani Chatterjea
Front Cell Infect Microbiol. 2023 Jun 8;13:1215380. doi: 10.3389/fcimb.2023.1215380. eCollection 2023.
<https://pubmed.ncbi.nlm.nih.gov/37360527/>

Vulvodynia is a debilitating condition characterized by painful sensitivity to touch and pressure in the vestibular tissue surrounding the vaginal opening. It is often a "diagnosis of exclusion" of idiopathic pain made in the absence of visible inflammation or injury. However, the association between increased vulvodynia risk and a history of yeast infections and skin allergies has led researchers to explore whether immune mechanisms of dysregulated inflammation might underlie the pathophysiology of this chronic pain condition. Here we synthesize epidemiological investigations, clinical biopsies and primary cell culture studies, and mechanistic insights from several pre-clinical models of vulvar pain. Taken together, these findings suggest that altered inflammatory responses of tissue fibroblasts, and other immune changes in the genital tissues, potentially driven by the accumulation of mast cells may be key to the development of chronic vulvar pain. The association of increased numbers and function of mast cells with a wide variety of chronic pain conditions lends credence to their involvement in vulvodynia pathology and underscores their potential as an immune biomarker for chronic pain. Alongside mast cells, neutrophils, macrophages, and numerous inflammatory cytokines and mediators are associated with chronic pain suggesting immune-targeted approaches including the therapeutic administration of endogenous anti-inflammatory compounds could provide much needed new ways to treat, manage, and control the growing global pandemic of chronic pain.

Effectiveness of topical gabapentin in the treatment of vulvodynia: a narrative synthesis

Mehmet Ergisi, Alexander Law, Nishant Chaudhari, Stefania Tsatsari, Kim Lawson, Christopher Jenner
Front Pain Res (Lausanne). 2023 Jul 3;4:1159268. doi: 10.3389/fpain.2023.1159268. eCollection 2023.
<https://pubmed.ncbi.nlm.nih.gov/37465763/>

Vulvodynia is a leading cause of dyspareunia in premenopausal women, causing considerable morbidity and sexual dysfunction. A multimodal approach is used to treat vulvodynia. Alongside psychosocial interventions and physiotherapy, pharmacological treatment such as oral gabapentin are used in the

treatment of vulvodynia. Topical formulations of gabapentin have shown promise in animal models and case reports investigating its use in other pain conditions. The topical route also avoids the systemic complications of gabapentin such as somnolence, dizziness, and peripheral edema. This study aimed to perform a narrative synthesis of studies investigating the use of topical gabapentin in the treatment of vulvodynia. The primary outcome was a change in pain score following treatment with topical gabapentin. A broad literature search was performed, which identified four studies for inclusion. The included studies reported improved pain measures following treatment; however, conclusions cannot be made due to methodological heterogeneity and inherent limitations. These include lack of control arms, small sample sizes, lack of patient randomization, and use of combination treatments. Due to the paucity of evidence, this review supports the future implementation of double-blind randomized controlled trials to further investigate the efficacy of topical gabapentin in the treatment of vulvodynia.

Neuroproliferative dyspareunia in endometriosis and vestibulodynia

Agnes N Mwaura, Nisha Marshall, Michael S Anglesio, Paul J Yong
Sex Med Rev. 2023 Aug 5; qead033. doi: 10.1093/sxmrev/qead033.

<https://pubmed.ncbi.nlm.nih.gov/37544766/>

Introduction: Endometriosis is a common cause of deep dyspareunia, while provoked vestibulodynia is a common cause of superficial dyspareunia. The etiology of dyspareunia in both conditions is multifactorial and may include the role of local nerve growth (neurogenesis or neuroproliferation) that sensitizes pelvic structures and leads to pain with contact. **Objectives:** To review the evidence for neuroproliferative dyspareunia in endometriosis and provoked vestibulodynia. **Methods:** Narrative review. **Results:** The pelvic peritoneum and vulvar vestibule receive somatic and autonomic innervation. Various markers have been utilized for nerve subtypes, including pan-neuronal markers and those specific for sensory and autonomic nerve fibers. The nerve growth factor family includes neurotrophic factors, such as nerve growth factor and brain-derived neurotrophic factor, and their receptors. Studies of endometriosis and provoked vestibulodynia have demonstrated the presence of nerve fibers around endometriosis epithelium/stroma in the pelvic peritoneum and within the vulvar vestibule. The number of nerve fibers is higher in these pain conditions as compared with control tissue. Nerve growth factor expression by endometriosis stroma and by immune cells in the vulvar vestibule may be involved in local neuroproliferation. Local inflammation is implicated in this neuroproliferation, with potential roles of interleukin 1 β and mast cells in both conditions. Several studies have shown a correlation between nerve fibers around endometriosis and dyspareunia severity, but studies are lacking in provoked vestibulodynia. There are several possible clinical ramifications of neuroproliferative dyspareunia in endometriosis and provoked vestibulodynia, in terms of history, examination, biopsy, and surgical and medical treatment. **Conclusions:** A neuroproliferative subtype of dyspareunia may be implicated in endometriosis and provoked vestibulodynia. Additional research is needed to validate this concept and to integrate it into clinical studies. Neuroproliferative pathways could serve as novel therapeutic targets for the treatment of dyspareunia in endometriosis and provoked vestibulodynia.

Women's experiences of physical therapy treatment for vulvodynia

Emelie Johansson, Louise Danielsson

Physiother Theory Pract. 2023 Jul 11;1-11. doi: 10.1080/09593985.2023.2233600.

<https://pubmed.ncbi.nlm.nih.gov/37431750/>

Introduction: Vulvodynia is a common and complex pain syndrome with a negative impact on quality of life and sexual health. Physical therapy is still an underexplored treatment for vulvodynia. Women's experiences of their physical therapy treatment might shed light on meaningful aspects and essential keys to facilitate change. **Purpose:** To explore and describe women's experiences of physical therapy treatment for vulvodynia. **Methods:** A qualitative interview study, using qualitative content analysis. Fourteen women with a median age of 28 years and a median pain duration of 6.5 years participated. Digital interviews were conducted using a semi-structured interview guide with open-ended questions. **Results:** One theme, four categories and thirteen sub-categories were developed in the analysis. The theme, "Trying to become friends with your vulva," illuminate how the women approached and reconnected to their bodies in physical therapy. The treatment increased their awareness and provided explanations for their symptoms. Four categories described aspects of the theme: 1) untapped resources in a complex healthcare; 2) a matter of trust; 3) a guide to understanding your body; and 4) a new way forward but not the whole solution. **Conclusion:** Women with vulvodynia perceive physical therapy as a promising and yet unknown approach. Physical therapy treatment gives the opportunity to reconnect with the body and vulva in a new way, and to manage pain and muscle tension as part of a multidisciplinary treatment.

Inflammation, lipids, and pain in vulvar disease

Megan L Falsetta, Krishna Rao Maddipati, Kenneth V Honn

Pharmacol Ther. 2023 Jun 5;248:108467. doi: 10.1016/j.pharmthera.2023.108467.

<https://pubmed.ncbi.nlm.nih.gov/37285943/>

Localized provoked vulvodynia (LPV) affects ~14 million people in the US (9% of women), destroying lives and relationships. LPV is characterized by chronic pain (>3 months) upon touch to the vulvar vestibule, which surrounds the vaginal opening. Many patients go months or years without a diagnosis. Once diagnosed, the treatments available only manage the symptoms of disease and do not correct the underlying problem. We have focused on elucidating the underlying mechanisms of chronic vulvar pain to speed diagnosis and improve intervention and management. We determined the inflammatory response to microorganisms, even members of the resident microflora, sets off a chain of events that culminates in chronic pain. This agrees with findings from several other groups, which show inflammation is altered in the painful vestibule. The vestibule of patients is acutely sensitive to inflammatory stimuli to the point of being deleterious. Rather than protect against vaginal infection, it causes heightened inflammation that does not resolve, which coincides with alterations in lipid metabolism that favor production of proinflammatory lipids and not pro-resolving lipids. Lipid dysbiosis in turn triggers pain signaling through the transient receptor potential vanilloid subtype 4 receptor (TRPV4). Treatment with specialized pro-resolving mediators (SPMs) that foster resolution reduces inflammation in fibroblasts and mice and vulvar sensitivity in mice. SPMs, specifically maresin 1, act on more than one part of the vulvodynia mechanism by limiting inflammation and acutely inhibiting TRPV4 signaling. Therefore, SPMs or other agents that target inflammation and/or TRPV4 signaling could prove effective as new vulvodynia therapies.

The impact of rurality on vulvodynia diagnosis and management: Primary care provider and patient perspectives

Valerie Webbe, Krisztina Bajzak, Diana L Gustafson

Can J Rural Med. 2023 Jul-Sep;28(3):107-115. doi: 10.4103/cjrm.cjrm_49_22.

<https://pubmed.ncbi.nlm.nih.gov/37417041/>

Objective: The objective of this study was to better understand how rurality impacts the knowledge, diagnosis and management of vulvodynia by primary care providers (PCPs) practising in the geographically disparate province of Newfoundland and Labrador, Canada. **Design:** This was a qualitative case study using questionnaires and semi-structured interviews with PCPs, compared with semi-structured focus groups and interviews with vulvodynia patients conducted in a previous study phase. **Results:** Ten family physicians and 6 nurse practitioners participated. Over half had baseline knowledge that vulvodynia has a relatively high prevalence, but most underestimated the likelihood they would see a patient with vulvodynia in their practice. Three barriers to discussing and managing vulvodynia emerged: (1) discomfort initiating sexual/vulvar health conversations; (2) concerns about protecting patient privacy and confidentiality; and (3) time constraints and building therapeutic relationships. These issues were largely corroborated by previous findings with vulvodynia patients. Rural-informed solutions might include: (1) supporting increased education in vulvodynia and sexual health more broadly, including funding to attend continuing professional education and developing more clinical tools; (2) following practice guidelines regarding standardised initiation of sexual health conversations; (3) incentivising retention of rural providers and extending appointment times by reconsidering fee-for-service structures; and (4) researching a tailored vulvodynia toolkit and the potential advantage of mobile health units. **Conclusion:** Rurality exacerbates common concerns in the identification and management of vulvodynia. Acting on recommended solutions may address the impact of rurality on the provision of timely care for those experiencing vulvodynia and other sexual health concerns.

Botulinum Toxin Injections as a Treatment of Refractory Vulvodynia in Adolescents: A Case Series

Julia Bhuiyan, Kaiane A Habeshian, Adam C Booser, Veronica Gomez-Lobo, Tazim Dowlut-McElroy
J Pediatr Adolesc Gynecol. 2023 Jun 8;S1083-3188(23)00340-6. doi: 10.1016/j.jpag.2023.06.001.
<https://pubmed.ncbi.nlm.nih.gov/37301425/>

Background: Vulvodynia involves vulvar discomfort that occurs in the absence of an identifiable cause. Because vulvodynia is often accompanied by myofascial pain and pelvic floor tension, transvaginal botulinum toxin (BT) injection into the pelvic floor has been proposed as a possible treatment.

Methods: Retrospective case series. **Results:** Three adolescents with vulvodynia had suboptimal response to treatment with several interventions, including neuromodulators (oral and topical), tricyclic antidepressants (oral and topical), and pelvic floor physical therapy. Subsequently, these patients underwent BT injections to the pelvic floor as treatment with varying responses. **Conclusions:** In select adolescent patients with vulvodynia, transvaginal BT injection into the pelvic floor can be an effective treatment. Further studies are needed to assess the optimal dosing, frequency, and sites of BT injections in the treatment of vulvodynia in pediatric and adolescent patients.

Sexual communication patterns in couples with vulvodynia-a case-control behavioral observation study

Elin Ekholm, Hanna Blaker, Lovisa Gottlander, Xiang Zhao, Steven J Linton, Marieke Dewitte, Ida K Flink
J Sex Med. 2023 Jul 31;20(8):1103-1114. doi: 10.1093/jsxmed/qdad085.
<https://pubmed.ncbi.nlm.nih.gov/37350134/>

Background: Sexual communication is a common target in psychological treatments for vulvodynia, and associations with sexual function and distress, as well as pain intensity, have been demonstrated.

However, structured observations of the communication patterns of couples with vulvodynia are lacking, as these are needed to guide treatment efforts. **Aim:** To explore (1) the sexual communication patterns in couples with vulvodynia in terms of observed communication quality (operationalized as validating and invalidating responses), self-reported sexual assertiveness, and self-disclosure and (2) associations between sexual communication quality and pain intensity. **Methods:** In a case-control design with within- and between-group comparisons, 62 couples engaged in videotaped discussions about their sexual relationship. Trained coders assessed the discussions by rating sexual communication (validation and invalidation) according to a structured behavioral coding scheme. Group differences in sexual communication quality were examined with parametric and nonparametric tests. Dyadic associations among observed communication quality, self-rated sexual assertiveness, and self-disclosure were examined within the actor-partner interdependence model. Multiple regression was used to test the predictive value of partners' validation/invalidation on the pain intensity of the women with vulvodynia. **Outcomes:** Observed communication quality (ie, validation and invalidation), self-reported sexual assertiveness, self-disclosure, and pain intensity. **Results:** Partners of women with vulvodynia were more invalidating toward their partners than those of women without pain. There were no significant differences in validating/invalidating communication between women in the 2 groups or in validation between partners. Partners' validating communication were significantly associated with women's lower pain intensity. The sexual communication patterns differed between couples with and without vulvodynia, and the associations between validating/invalidating responses and sexual assertiveness were stronger in the vulvodynia group than in the group without pain. Results on validation/invalidation and self-disclosure were inconclusive. **Clinical implications:** The results indicate a need to direct treatment interventions toward couples' sexual communication quality (ie, levels of validation and invalidation). **Strengths and limitations:** Strengths include systematic behavioral coding and dyadic analyses. Limitations include the cross-sectional design and self-selection of participants. **Conclusion:** This study demonstrated sexual communication patterns specific to couples with vulvodynia, and we conclude that validation and invalidation are important components of the sexual communication of couples with vulvodynia as they relate to sexual assertiveness, women's self-disclosure, and pain intensity.

A feasibility trial of online Acceptance and Commitment Therapy for women with provoked vestibulodynia

Pernilla Maathz, Lance M McCracken, Viktor Eriksson, Fredrika Säde, Gunilla Aneblom, Åsa Rikner, Alkistis Skalkidou, Monica Buhrman

Scand J Pain. 2023 Jul 3;23(3):476-482. doi: 10.1515/sjpain-2022-0146. Print 2023 Jul 26.

<https://pubmed.ncbi.nlm.nih.gov/37401654/>

Objectives: Acceptance and Commitment Therapy (ACT) is an established treatment for chronic pain. However, it is a form of treatment that have not yet been applied much in the treatment of persistent vulvar pain disorders. This study examines the feasibility and preliminary effects of online ACT for patients with provoked vestibulodynia. **Methods:** Women diagnosed with provoked vestibulodynia were assigned randomly either to online ACT or to a waitlist control group. Feasibility was assessed in terms of recruitment potential, treatment credibility, completions rates, retention in trial, and data quality. Participants completed measures of pain with sexual activity, sexual functioning, emotional and relational adjustment, and potential treatment processes before and after treatment. **Results:** Of the 111 women who were invited to participate in the study, 44 were included (39.6 % recruitment rate). Thirty seven participants (84.1 %) completed the pre-treatment assessment. Participants who received online ACT rated treatment credibility positively, and completed on average 4.31 (SD=1.60) of the six

treatment modules. Of participants, 34 provided post treatment data, giving a trial retention rate of 77 %. Effects of online ACT, as compared to waitlist, were large for pain acceptance and quality of life, medium for anxiety and pain catastrophizing, and small for sexual satisfaction, pain with sexual activity, and relationship adjustment. **Conclusions:** With some adjustments to recruitment procedures, a full scale randomized controlled trial of online ACT for provoked vestibulodynia appears feasible.

Chronic Pelvic Pain

Pelvic pain in women after childbirth and physiotherapy

Michaela Hroncová

Ceska Gynekol. 2023;88(3):214-220. doi: 10.48095/cccg2023214.

<https://pubmed.ncbi.nlm.nih.gov/37344188/>

Objective: There are many types of pelvic pain. Pelvic plexus pain, coccyx pain, pain from episiotomy scars, and vulvodynia are frequently seen in postpartum women. The aim of this study was to conduct a systematic review of studies on pelvic pain in postpartum women to assess the effect of physiotherapy interventions on each type of pain. **Methods:** A comprehensive literature review was conducted by searching on PubMed, Ovid Embase and Scopus Web of Science using the key words - pelvic pain, women after childbirth, pelvic girdle pain, coccygodynia, episiotomy, vulvodynia, and physiotherapy. The author reviewed all the identified articles and selected articles for inclusion according to relevance to the topic. **Conclusion:** Based on the analysis of the above studies, it can be concluded that a comprehensive physiotherapy designed for postpartum women that includes manual techniques, behavioral techniques, relaxation of hypo-tonic and shortened muscles and strengthening of hypotonic muscles can positively affect a wide range of pain and associated dysfunctions of the pelvic floor and trunk muscles.

The impact of combined contraceptive vaginal ring on vaginal environment: an observational, longitudinal study

Filippo Murina, Alessandra Graziottin, Stefania Di Francesco, Dario Recalcati

Eur J Contracept Reprod Health Care. 2023 Aug;28(4):234-237.

doi: 10.1080/13625187.2023.2228440. Epub 2023 Jul 7.

<https://pubmed.ncbi.nlm.nih.gov/37417287/>

Purpose: To assess the relationship between combined contraceptive vaginal ring (CVR) and vaginal microbiome using 16S rRNA gene sequencing. **Materials and methods:** We enrolled 20 women for 8 weeks in an open-label study using CVR (NuvaRing®) that delivered 15 mcg ethinylestradiol and 120 mcg etonogestrel daily. The vaginal microbiome was assessed at baseline and after 2 months by sequencing the 16S rRNA genes amplified from the total genomic DNA isolated from the sample. **Results:** Bacterial distribution richness and equity did not significantly change after 2 months, and the dominant bacterial strain was *Lactobacillus crispatus*. Only one woman with a history of vestibulodynia and recurrent vulvovaginitis showed an increase in bacterial biodiversity, with a switch to the relative abundance of anaerobic bacteria. **Conclusions:** Our results suggest that CVR does not adversely affect the composition and structure of the vaginal microbiome. However, special care should be taken in patients with a history of vestibulodynia and/or recurrent vulvovaginal infections.

A scoping review: sexual activity and functioning before and after surgery for femoroacetabular impingement (FAI), labral tears, and hip dysplasia

Jenny Niedenfuehr, David M Stevens

Sex Med Rev. 2023 Aug 18;qead036. doi: 10.1093/sxmrev/qead036.

<https://pubmed.ncbi.nlm.nih.gov/37596240/>

Introduction: There is limited information on sexual activity and functioning for patients with hip abnormalities, specifically femoroacetabular impingement (FAI), labral tears, and hip dysplasia, before and after surgical interventions. **Objectives:** The aim of this review was to synthesize the existing literature on sexual activity and functioning for patients with FAI, labral tears, and/or hip dysplasia before and after their respective surgeries. **Methods:** We performed a rigorous, comprehensive search on multiple databases including PubMed, EMBASE, CINAHL, and Web of Science. Subject headings and a search string of key terms including Medical Subject Headings were used systematically to search these databases. The reference list was reviewed with an additional reviewer to reduce bias. **Results:** A total of 726 articles were found during the search, which were narrowed down to 22 articles that included at least 1 hip abnormality in relation to sexual functioning, sexual pain, or sexual activity. FAI, labral tears, and hip dysplasia can affect sexual activity, functioning, and positioning, and corrective surgery generally improves these metrics. Surgery improved vulvodynia, clitorodynia, and scrotal pain symptoms for some patients, though arthroscopy resulted in some instances of temporary pudendal nerve dysfunction. **Conclusion:** This review may serve as an important resource for surgeons, healthcare providers, researchers, physical therapists, and patients to understand the relationship between the hips and sexual functioning, and to bridge the gaps among the disciplines of orthopedics, pelvic floor physiology, and sexual health. Hip anatomy impacts sexual activity, functioning, and positioning as well as vulvodynia and scrotal pain symptoms for some patients, and a comprehensive hip evaluation by a qualified hip specialist should be considered for patients with such complaints.

Applications of botulinum toxin to the female pelvic floor: Botulinum toxin for genito-pelvic pain penetration disorder and chronic pelvic pain in women

Barbara I Karp, Pamela Stratton

Toxicon. 2023 Jul;230:107162. doi: 10.1016/j.toxicon.2023.107162. Epub 2023 May 16.

<https://pubmed.ncbi.nlm.nih.gov/37201800/>

Chronic pain conditions like genito-pelvic pain penetration disorder and chronic pelvic pain cause significant morbidity in women worldwide and yet are underdiagnosed and undertreated. While the use of botulinum toxin for pain conditions has expanded, there are few randomized controlled studies of botulinum toxin for pelvic pain conditions in women. This paper provides an update on the current status and context for considering botulinum toxin treatment for these conditions to complement and expand currently available approaches. High quality clinical trials to evaluate safety and efficacy and to determine optimal doses and approaches to injection are urgently needed.

Are pelvic pain and increased pelvic floor muscle tone associated in women with persistent noncancer pelvic pain? A systematic review and meta-analysis

Shaza Kadah, Sze-Ee Soh, Melanie Morin, Michal Schneider, W Catarina Ang, Lucy McPhate, Helena Frawley

J Sex Med. 2023 Jul 28;qdad089. doi: 10.1093/jsxmed/qdad089.

<https://pubmed.ncbi.nlm.nih.gov/37507352/>

Background: The association between pelvic pain and pelvic floor muscle (PFM) tone in women with persistent noncancer pelvic pain (PNCPP) is unclear. **Aim:** To synthesize the evidence of the association between pelvic pain and PFM tone in women with PNCPP. **Methods:** A systematic review was conducted via MEDLINE, Emtree, Embase, CINAHL, PsycINFO, and Scopus to identify relevant studies. Studies were eligible if pelvic pain and PFM tone outcome measures were reported among women aged >18 years. The National Heart, Lung, and Blood Institute's Quality Assessment Tool for Observational Cohort and Cross-sectional Studies was used to assess study quality. Studies were pooled by assessment of PFM tone via a random effects model. Associations between the presence of pelvic pain and PFM tone were assessed with odds ratio (OR), while linear associations were assessed with Pearson or Spearman correlation. **Outcomes:** Pelvic pain measures (intensity, threshold, and frequency) and resting PFM tone in women with PNCPP, as evaluated by any clinical assessment method or tool. **Results:** Twenty-four studies were included in this review. The presence of pelvic pain was significantly associated with increased PFM tone as assessed by digital palpation (OR, 2.85; 95% CI, 1.66-4.89). Pelvic pain intensity was inversely but weakly associated with PFM flexibility when evaluated through dynamometry ($r = -0.29$; 95% CI, -0.42 to -0.17). However, no significant associations were found between pelvic pain and PFM tone when measured with other objective assessment methods. **Clinical implications:** Pelvic pain and increased PFM tone may not be directly associated; alternatively, a nonlinear association may exist. A range of biopsychosocial factors may mediate or moderate the association, and clinicians may need to consider these factors when assessing women with PNCPP. **Strengths and limitations:** This review was reported according to the PRISMA guidelines. All possible findings from relevant theses and conference abstracts were considered in our search. However, nonlinear associations between pelvic pain and increased PFM tone were not assessed as part of this review. **Conclusion:** Pelvic pain may be linearly associated with increased PFM tone and decreased PFM flexibility when measured with digital palpation or dynamometry; however, this association was not observed when other aspects of PFM tone were assessed through objective methods. Future studies are required using robust assessment methods to measure PFM tone and analyses that account for other biopsychosocial factors that may influence the association.

Laser Treatment for Patients With Vulvodynia and Interstitial Cystitis/Bladder Pain Syndrome: A Case Series (The UNICORN-3 Study)

Nobuo Okui, Machiko Aurora Okui, Yuko Kouno, Kaori Nakano

Cureus. 2023 Jul 12;15(7):e41786. doi: 10.7759/cureus.41786. eCollection 2023 Jul.

<https://pubmed.ncbi.nlm.nih.gov/37449291/>

Introduction Interstitial cystitis/bladder pain syndrome (IC/BPS) is a chronic pain disorder characterized by urgency, frequency of urination, and pelvic pain. Women with IC/BPS often experience sexual dysfunction, vulvodynia, and vaginal health issues. Combined erbium and neodymium yttrium aluminum garnet (YAG) laser treatments targeting the vagina and vulva have shown promise in improving symptoms. Our study aims to investigate the effectiveness of these combined laser treatments in women with IC/BPS and vulvodynia. **Methods** Women diagnosed with vulvodynia and IC/BPS underwent combined laser treatment using vaginal erbium:YAG laser (VEL) and neodymium:YAG laser (Nd:YAG). Various parameters were evaluated, including the vulvodynia test, numeric rating scale (NRS-11) for pain, interstitial cystitis symptom index and problem index (ICSI and ICPI), pelvic pain and urgency/frequency symptom score (PUF), and mean urination volume/daily urination frequency in a three-day urination diary. Treatment was administered three times, with intervals of one month between each session, and follow-up evaluations were conducted at six and 12 months. All statistical analyses were designed and programmed by the AI chatbot GPT-4 (chatGPT-4). **Results** Fifteen female

patients diagnosed with vulvodynia and IC/BPS were treated with three sessions of VEL + Nd:YAG. Significant improvements were observed in the vulvodynia test, NRS-11 scores, PUF, ICSI scores, ICPI scores, mean urination volume, and daily urination frequency at six and 12 months ($p < 0.01$). Short-term improvements in IC/BPS pain scores correlated with improvements in the vulvodynia test ($p = 0.007$), suggesting a synergistic effect. However, no significant correlations were found at 12 months. Conclusion Combined laser treatments targeting the vagina and vulva showed significant therapeutic effects in women with IC/BPS and vulvodynia. The addition of Nd:YAG to the VEL treatment enhanced outcomes. Short-term improvements in IC/BPS pain scores correlated with improvements in the vulvodynia test, indicating a synergistic effect. Long-term improvements in both vulvodynia and IC/BPS symptoms may occur independently. These findings highlight the importance of comprehensive approaches for treating coexisting vulvodynia and IC/BPS.

Persistent Genital Arousal Disorder

Selective Serotonin Reuptake Inhibitors, Post-Treatment Sexual Dysfunction and Persistent Genital Arousal Disorder: a systematic review

Livio Tarchi, Giuseppe Pierpaolo Merola, Ottone Baccaredda-Boy, Francesca Arganini, Emanuele Cassioli, Eleonora Rossi, Mario Maggi, David S Baldwin, Valdo Ricca, Giovanni Castellini
Pharmacoepidemiol Drug Saf. 2023 Jun 9. doi: 10.1002/pds.5653.

<https://pubmed.ncbi.nlm.nih.gov/37294623/>

Adverse effects of selective serotonin reuptake inhibitors (SSRIs) on sexual function have been an important area of research for many years. However, the duration of SSRI-associated sexual adverse effects, and their possible persistence after treatment discontinuation, is still uncertain. The aims of the current systematic review were firstly to identify existing evidence of sexual dysfunction following SSRI discontinuation, and to provide an account of reported symptoms and proposed treatment options; and secondly, to establish whether current literature allows accurate estimates of the prevalence of such sexual dysfunction. Therefore, a systematic review was conducted on PubMed, Embase and Google Scholar; papers with clinical data regarding patients with persistent sexual dysfunction after SSRI treatment suspension were included. Overall, two retrospective interventional studies, six observational studies and 11 case reports were judged eligible for inclusion. It was not possible to determine reliable estimates of prevalence. Similarly, a cause-effect relationship between SSRI exposure and persistent sexual impairment could not be ascertained. Nonetheless, the potential for continued sexual disturbances despite discontinuation could not be entirely ruled out. There is a need to investigate a possible dose-response relationship between SSRI exposure and persistent sexual adverse effects. Treatment options for persistent dysfunctions remain limited, but novel therapeutic approaches may be required in order to address an otherwise neglected need for sexual well-being.

Predictors of Psychosocial and Functional Outcomes in Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia: Application of the Fear Avoidance Model

Robyn A Jackowich, Éveline Poirier, Caroline F Pukall
J Pain. 2023 Aug 18;S1526-5900(23)00509-6. doi: 10.1016/j.jpain.2023.08.008.

<https://pubmed.ncbi.nlm.nih.gov/37598985/>

Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia (PGAD/GPD), which affects up to 4.3% of individuals, is a distressing and poorly understood condition characterized by persistent, unwanted, and often painful sensations of genito-pelvic arousal (e.g., throbbing) in the absence of sexual desire. PGAD/GPD is associated with significant negative impacts on psychosocial wellbeing and daily functioning. Recent research has indicated that PGAD/GPD shares many similarities with other forms of chronic genito-pelvic pain. This study applied the Fear Avoidance (FA) Model of chronic pain to PGAD/GPD to identify cognitive and behavioral factors associated with psychosocial and functional outcomes. A total of 263 individuals with PGAD/GPD symptoms completed a cross-sectional online survey of symptom intensity, cognitive and behavioral predictors (symptom catastrophizing, hypervigilance to symptoms, symptom fear and avoidance, self-efficacy), depression symptoms, and role functioning. Symptom catastrophizing, fear of symptoms, avoidance of symptoms, and hypervigilance to PGAD/GPD symptoms were significantly correlated with poorer psychosocial and functional outcomes, whereas higher self-efficacy was significantly associated with lower depression and better role functioning. Two serial parallel mediation models examined the fear avoidance pathway from PGAD/GPD symptom intensity to depression symptoms and role functioning. In both models, the pathway through symptom catastrophizing, fear of symptoms, and symptom avoidance was significant, but the pathway through symptom catastrophizing, fear of symptoms, and symptom hypervigilance was not. The results of this study provide support for the applicability of the FA Model to PGAD/GPD. Interventions targeting fear avoidance factors may help to reduce PGAD/GPD symptom intensity, distress, and increase psychological wellbeing and daily functioning. PERSPECTIVE: This article provides support for the applicability of the Fear Avoidance Model of chronic pain to Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia (PGAD/GPD). These results suggest that interventions targeting fear-avoidance cognitions and behaviors (catastrophizing, fear, avoidance, hypervigilance) may help to reduce PGAD/GPD symptom intensity and improve psychological wellbeing and daily functioning.

Pudendal Neuralgia

Novel implantation technique for pudendal nerve peripheral nerve stimulation for treatment of chronic pelvic pain

Christopher M Lam, Sarah A Keim, Usman Latif

Reg Anesth Pain Med. 2023 Jul 6;rapm-2023-104551. doi: 10.1136/rapm-2023-104551.

<https://pubmed.ncbi.nlm.nih.gov/37419506/>

Background: Chronic pelvic pain (CPP) is a pervasive, difficult to treat condition affecting up to 26% of the global female and 8.2% of the global male population. Considered a form of chronic regional pain syndrome (CRPS), it is medically complex and often refractory to multimodal management. Neuromodulation has become increasingly popular in treatment of chronic neuropathic pain conditions, including CPP and CRPS. Dorsal column spinal cord stimulation and dorsal root ganglion stimulation have had some success for managing CPP meanwhile peripheral nerve stimulators (PNS) have been suggested as another viable option. However, few studies in the literature have reported successful use of PNS in treatment of CPP. Here, we detail a possible technique for pudendal PNS lead placement for management of CPP. **Method:** This article describes a novel cephalad to caudad fluoroscopic guided technique for pudendal nerve PNS lead placement and implantation. **Results:** A cephalad to caudal-medial fluoroscopic guided approach as described within to successfully implant a percutaneous pudendal nerve PNS for management of CPP. **Conclusions:** The pudendal nerve PNS lead placement technique noted within can be used to avoid many of the important neurovascular structures near the

pelvic outlet. Further studies are needed to validate the safety and efficacy of this therapy modality but it may be a viable management option for patients with medically refractory CPP.

Pudendal Neuralgia: Two case reports with laparoscopic nerve decompression

N Habib, G Centini, J S Klebanoff, R Fernandes, M Giorgi, G N Moawad, J Bakar
Facts Views Vis Obgyn. 2023 Jun;15(2):181-187. doi: 10.52054/FVVO.15.2.073.
<https://pubmed.ncbi.nlm.nih.gov/37436058/>

Pudendal neuralgia (PN) is a rare and underestimated condition. The reported incidence by the International Pudendal Neuropathy Association is 1/100000. However, the actual rate may be significantly higher, with a propensity for women. It is most frequently caused by an entrapment of the nerve at the level of the sacrospinous and sacrotuberous ligament, also known as pudendal nerve entrapment syndrome. Due to the late diagnosis and inadequate management, pudendal nerve entrapment syndrome often leads to considerable reduction in the quality of life and high health care costs. The diagnosis is made using Nantes Criteria, in conjunction with the patient's clinical history and physical findings. Clinical examination with an accurate assessment of the territory of the neuropathic pain is mandatory to set the therapeutic strategy. The aim of the treatment is to control the symptoms and it usually starts with conservative approaches which include analgesics, anticonvulsants, and muscle relaxants. Surgical nerve decompression can be proposed after failure of conservative management. The laparoscopic approach is a feasible and appropriate technique to explore and decompress the pudendal nerve, and to rule out other pelvic conditions that can cause similar symptomatology. In this paper, the clinical history of two patients affected by compressive PN is reported. Both patients underwent laparoscopic pudendal neurolysis suggesting that the treatment for PN should be individualised and carried out by a multidisciplinary team. When conservative treatment fails, laparoscopic nerve exploration and decompression is an adequate option to propose and should be performed by a trained surgeon.

Dermatological Conditions

LASER treatment in gynaecology -A randomized controlled trial in women with symptomatic lichen sclerosus

Elke Krause, Stephanie Neumann, Marina Maier, Sara Imboden, Laura Knabben, Michael D Mueller, Annette Kuhn

Eur J Obstet Gynecol Reprod Biol. 2023 Aug;287:171-175. doi: 10.1016/j.ejogrb.2023.06.003. Epub 2023 Jun 8.

<https://pubmed.ncbi.nlm.nih.gov/37352640/>

Objective: Aim of our study was to evaluate the therapeutic effect of laser treatment in vulvar lichen sclerosus, mainly the reduction of existing symptoms as itching, burning and pain. We asked about the different outcome by using different application doses. **Study design:** We conducted a prospective randomized double-blind dose-controlled trial in our dysplasia unit specializing vulvar disorders. 67 patients with active LS were included. LS was confirmed by biopsy or by the validated CSS (clinical scoring system of vulvar LS). Computer generated randomization resulted in two groups, each group received a different application dose. (LDG- low dose group, NDG- normal dose group) During the study period of 18 weeks all participants received three laser applications in three subsequent sessions of

three weeks. Two follow-ups six and twelve weeks after the first application was performed. At every visit, the participants filled in the VAS (visual analogue scale) for recording the actual vulvar symptoms as itching burning or pain on a range from 0 to 10. **Results:** Before treatment the mean VAS-Score was 4.3 (STD \pm 2.4) in the NDG and 5.1(\pm 2.6) in the LDG. After 18 weeks, the mean reduction was -2.4 (\pm 2.3) for NDG and -2.7 (\pm 2.8) for LDG. Four patients (two of each group) reported more pain after than before treatment. Both groups show significant lower VAS-Scores 18 weeks after the treatment than before therapy ($p < 0.0001$). The reduction of symptoms after 18 weeks between NDG and LDG was not significant ($p = 0.6244$). **Conclusion:** Laser treatment with the microablative CO2 laser leads to a significant improvement for symptoms of LS. A higher dosage of laser radiation shows no benefit concerning the symptoms. We have not observed any serious adverse events during this study.

The urinary, vaginal and gut microbiota in women with genital lichen sclerosus - A case-control study

Sofie Nygaard, Katrine Gerlif, Caspar Bundgaard-Nielsen, Jean Saleh Media, Peter Leutscher, Suzette Sørensen, Annemarie Brusén Villadsen, Louise Thomsen Schmidt Arenholt

Eur J Obstet Gynecol Reprod Biol. 2023 Aug 8;289:1-8. doi: 10.1016/j.ejogrb.2023.08.004.

<https://pubmed.ncbi.nlm.nih.gov/37591024/>

Background: Lichen sclerosus (LS) is a chronic, autoimmune skin disease predominantly located in the anogenital region in women. In recent years, the role of the human microbiota in the pathogenesis of autoimmune diseases, including LS, has received interest. **Objectives:** The study aimed to evaluate and compare the composition of the urinary, vaginal and gut microbiota in women with LS versus non-affected controls. **Study design:** Women diagnosed with LS ($n = 16$) and matched controls ($n = 14$) were enrolled in the study. From each participant, midstream urine, upper and lower vaginal swabs, as well as faecal samples, were collected. The microbiota composition was assessed using 16S ribosomal RNA (rRNA) gene sequencing of the V4 hypervariable region. **Results:** We observed no LS-specific clustering in either of the four anatomic niches, using either hierarchical cluster analysis or weighted beta diversity metrics. However, for unweighted UniFrac, significant differences in the urinary and lower vaginal microbiota were observed when comparing women with LS to controls. These findings indicate that while the two groups have microbiota dominated by the same bacteria, variations do occur amongst less abundant bacteria. The LEfSe analysis revealed a higher relative abundance of the genus *Streptococcus* in the urinary and lower vaginal microbiota in women with LS compared to controls. Additionally, a higher relative abundance of phylum Euryarchaeota was observed in the gut microbiota in women with LS compared to controls. **Conclusion:** In this study, we demonstrated several differences amongst less abundant bacteria in the urinary, lower vaginal and faecal microbiota when comparing women with LS to controls. However, further research is required to assess whether these microbiota differences are causative or merely a result of the underlying LS disease.

Cross-Polarization Optical Coherence Tomography for Clinical Evaluation of Dermal Lesion Degrees in Vulvar Lichen Sclerosus

A L Potapov, M M Loginova, A A Moiseev, S G Radenska-Lopovok, S S Kuznetsov, I A Kuznetsova, N N Mustafina, I K Safonov, N D Gladkova, M A Sirotkina

Sovrem Tekhnologii Med. 2023;15(1):53-60. doi: 10.17691/stm2023.15.1.06. Epub 2023 Jan 28.

<https://pubmed.ncbi.nlm.nih.gov/37388751/>

The aim of the study was to identify different degrees of dermal lesions in vulvar lichen sclerosus (VLS) using cross-polarization optical coherence tomography (CP OCT) based on attenuation coefficient to

detect disease early manifestations and to monitor the effectiveness of treatment. **Materials and methods:** The study included 10 patients without pathology and 39 patients with VLS diagnosed histologically. CP OCT was performed *in vivo* on the inner surface of the labia minora, in the main lesion area. From each scanning point, a 3.4×3.4×1.25-mm³ 3D data array was obtained in 26 s. CP OCT examination results were compared with histological examination of specimens stained with Van Gieson's picrofuchsin. Quantitative analysis of OCT images was performed by measuring the attenuation coefficient in co-polarization and cross-polarization. For visual analysis, color-coded charts were developed based on OCT attenuation coefficients. **Results:** According to histological examination, all patients with VLS were divided into 4 groups as per dermal lesion degree: initial (8 patients); mild (7 patients); moderate (9 patients); severe (15 patients). Typical features of different degrees were interfibrillary edema up to 250 μm deep for initial degree, thickened collagen bundles without edema up to 350 μm deep for mild degree, dermis homogenization up to 700 μm deep for moderate degree, dermis homogenization and total edema up to 1200 μm deep for severe degree. Pathological processes in dermis during VLS like interfibrillary edema and collagen bundles homogenization were visualized using CP OCT method based on values of attenuation coefficient in co- and cross-polarization channels. However, CP OCT method appeared to be less sensitive to changes of collagen bundles thickness not allowing to distinguish thickened collagen bundles from normal ones with enough statistical significance. The CP OCT method was able to differentiate all degrees of dermal lesions among themselves. OCT attenuation coefficients differed from normal condition with statistical significance for all degrees of lesions, except for mild. **Conclusion:** For the first time, quantitative parameters for each degrees of dermis lesion in VLS, including initial degree, were determined by CP OCT method allowing to detect the disease at an early stage and to monitor the applied clinical treatment effectiveness.

Differential proteomic expression profiles in vulvar lichen planus as compared to normal vulvar tissue, vulvar lichen sclerosus, or oral lichen planus: An exploratory study

Fangyi Xie, Surendra Dasari, Maria Deschaine, Casey A Gleue, Julio C Sartori-Valinotti, Rochelle R Torgerson, Mark D P Davis, M Cristine Charlesworth, Alexander Meves, Julia S Lehman
Exp Dermatol. 2023 Jun 15. doi: 10.1111/exd.14854.

<https://pubmed.ncbi.nlm.nih.gov/37317627/>

Vulvar lichen planus (VLP) is a chronic inflammatory disease which adversely affects patients' quality of life. The pathogenesis of VLP is unknown although Th1 immune response has been implicated. We aimed to discover specific tissue-based protein biomarkers in VLP compared to normal vulvar tissue (NVT), vulvar lichen sclerosus (VLS) and oral lichen planus (OLP). We used laser capture microdissection-liquid chromatography-tandem mass spectrometry to assess protein expression in fixed lesional mucosal specimens from patients with VLP (n = 5). We then compared proteomic profiles against those of NVT (n = 4), VLS (n = 5), OLP (n = 6) and normal oral mucosa (n = 5), previously published by our group. IL16, PTPRC, PTPRCAP, TAP1 and ITGB2 and were significantly overexpressed in VLP compared to NVT. Ingenuity pathway analysis identified antigen presentation and integrin signalling pathways. Proteins overexpressed in both VLP versus NVT and OLP versus NOM included IL16, PTPRC, PTPRCAP, TAP1, HLA-DPB1, HLA-B and HLA-DRA. This proteomic analysis revealed several overexpressed proteins in VLP that relate to Th1 autoimmunity, including IL16. Overlapping pathways, including those involving IFN γ and Th1 signalling, were observed between VLP, VLS, and OLP.

[Possibilities of multiphoton microscopy for the diagnosis of the vulvar lichen sclerosis]

[Article in Russian]

S G Radenska-Lopovok, A L Potapov, M M Loginova, V V Elagin, A E Bychkova, M M Karabut, S S Kuznetsov, A V Asaturova, I A Kuznetsova, I A Apolikhina, N D Gladkova, M A Sirotkina
Arkh Patol. 2023;85(3):29-39. doi: 10.17116/patol20238503129.

<https://pubmed.ncbi.nlm.nih.gov/37272438/>

Background: Vulvar lichen sclerosis (VLS) is a chronic and recurrent dermatosis of an inflammatory nature with severe focal atrophy of the skin. Connective tissue changes are polymorphic and are still not taken into account in histological diagnostics due to the difficulty of interpreting routine histological methods. In this work, we use multiphoton microscopy (MPM) as a new imaging technique that provides detailed information about the organization of collagen fibers in the dermis based on a non-linear second harmonic generation (SHG) process. **Objective:** To determine the degree of connective tissue damage in lichen sclerosis using standard histological techniques and to reveal the diagnostic capabilities of multiphoton microscopy. **Material and methods:** We studied 42 biopsies with a histopathological diagnosis of VLS and 10 biopsies of normal vulvar skin. Histological, histochemical and immunohistochemical evaluation was used in comparison with MPM data. Quantitative analysis included the determination of the thickness, length of collagen fibers and the average intensity of the SHG signal. **Results:** A comprehensive study of the skin showed 4 groups of changes that can be regarded as the degree of the dermis damage: initial, mild, moderate, severe. The affected area at the initial and mild degree has subtle changes, however, it is reliably identified by quantitative analysis of the SHG signal. So, the initial degree is characterized by thin (1.3-1.8 μm) long (56-69 μm) collagen fibers, with a moderate degree, the fibers are thickened (3.4-4.3 μm) and fragmented (22-37 μm). The affected area in moderate and severe cases undergoes homogenization, which is associated with the deposition of extremely thin (0.6-0.9 μm) short (16-28 μm) collagen fibers and the expression of type V collagen. **Conclusion:** Multiphoton microscopy in the second harmonic generation mode is a reliable method for identifying collagen fibers in tissues. The study made it possible to identify 4 degrees of the dermis damage in vulvar lichen sclerosis.

Fat Grafting in Vulvar Lichen Sclerosis: Long Term Follow-Up

Veronica Boero, Massimiliano Brambilla, Eugenia Di Loreto, Giulia Emily Cetera, Sonia Cipriani, Francesca Boggio, Ermelinda Monti, Giada Libutti, Carlotta Caia, Fabio Parazzini

J Low Genit Tract Dis. 2023 Aug 8. doi: 10.1097/LGT.0000000000000766.

<https://pubmed.ncbi.nlm.nih.gov/37551790/>

Objective: The rationale for the use of autologous fat grafting in the treatment of vulvar lichen sclerosis (VLS) consists in reduction of inflammation, regeneration of tissues, volume increase, and pain fiber control. The main outcome of our study was the evaluation of patients' satisfaction after treatment. Secondary outcomes included modifications in symptoms, psychosexual wellbeing, vulvar hydration, and histology after surgery. **Methods:** Eligible for this study were women aged 18-85 years with a histological diagnosis of VLS who underwent at least one autologous vulvar fat grafting at our center, between 2010 and 2019. In 2021, all women underwent a clinical reevaluation, comprehensive of vulvoscopy, vulvar biopsy, and handing out of validated questionnaires. **Results:** Overall, 88.7% of patients declared themselves very satisfied/satisfied with the procedure. All symptoms were improved postsurgery; in particular, the difference was statistically significant for pruritus, burning, and dyspareunia ($p < .05$). Sexual function was also improved at time of reevaluation, as were depressive and anxiety symptoms ($p < .05$). No cases of vulvar intraepithelial neoplasia or cancer occurred during

follow-up and vulvar architecture remained stable, although patients reported a significantly reduced need for topical steroids ($p < .0001$). Lastly, in postoperative biopsies, inflammatory infiltrate was stable or reduced, and the distribution of elastic fibers was comparable or restored in most patients.

Conclusions: Patient satisfaction with fat grafting is detectable up to 11 years after surgery, and as such, it may represent a valid therapeutic option in selected cases of VLS

Pregnancy, parturition and postpartum considerations among patients with vulvar lichen sclerosis: A retrospective cross-sectional online survey

Alyssa B Shaffer, Sarah T Cigna, Rachel Pope, Jill M Krapf

BJOG. 2023 Jul 9. doi: 10.1111/1471-0528.17601.

<https://pubmed.ncbi.nlm.nih.gov/37424180/>

Objective: Characterise VLS and obstetric considerations among women during pregnancy, parturition and postpartum. **Design:** Retrospective cross-sectional online survey, 2022. **Setting:** International, English-speakers. **Population:** Self-identified individuals aged 18-50 diagnosed with VLS with symptom onset prior to pregnancy. **Methods:** Participants recruited from social media support groups and accounts, completed a 47-question survey including yes/no, multiple answer, and free-text responses. Data were analysed with frequency, means and the Chi-square test. **Main outcome measures:** VLS symptom severity, mode of delivery, perineal laceration, source and sufficiency of information provided about VLS and obstetrics, anxiety about delivery, and postpartum depression. **Results:** Of 204 responses, 134 met inclusion criteria, encompassing 206 pregnancies. Mean respondent age was 35 years (SD 6) and mean age of VLS symptom onset, diagnosis and birth, was 22 (SD 8), 29 (SD 7) and 31 (SD 4) years, respectively. Symptoms decreased in 44% ($n = 91$) of pregnancies and increased during the postpartum period in 60% ($n = 123$). In all, 67% ($n = 137$) of pregnancies resulted in vaginal birth and 33% ($n = 69$) in caesarean birth. Anxiety for delivery due to VLS symptoms was reported by 50% ($n = 103$); 31% ($n = 63$) experienced postpartum depression. Of respondents previously diagnosed with VLS, 60% ($n = 69$) used topical steroids prior to pregnancy, 40% ($n = 45$) were treated during pregnancy and 65% ($n = 75$) postpartum. In all, 94% ($n = 116$) reported receiving an insufficient amount of information on the topic. **Conclusion:** In this online survey, we found reported symptom severity remained unchanged or decreased during pregnancy, but increased postpartum. Use of topical corticosteroids decreased during pregnancy compared with before and after pregnancy. Half of the respondents reported anxiety regarding VLS and delivery.