

Research Update E- Newsletter

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Vulvodynia

Pilot study of testing a clinical tool for pelvic physical examination in patients with vulvodynia

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Objectives: Vulvodynia diagnosis is based on medical history and physical examination. The study is aimed to evaluate the clinical usefulness of a pelvic floor physical examination (VAMP protocol) for vulvodynia diagnosis, applied during gynecological examination, proposed as educational and diagnostic tool. **Material and methods:** Pelvic physical examinations were performed for 650 non-pregnant female patients. A study group of 449 cases met the vulvodynia diagnostic criteria (120 with provoked, 104 with spontaneous, and 121 with mixed subtype) and were compared with those of 201 healthy individuals. Four anatomical regions were examined: the vulva (V) and anus (A) with a cotton swab, the internal pelvic muscles (M) with a digital examination of the levator ani, and the paraurethral (P) area with digital pressure. Only the maximum pain score for a given area was recorded, using a Numerical Rating Scale.

The four anatomical regions were recorded under the VAMP acronym. **Results:** Differences in mean scores VAMP protocol were statistically between vulvodynia and comparison group for V = 6.48 vs 0.98; M = 6.29 vs 1.05; and P = 6.89 vs 1.33, with exception of A = 0.03 vs 0.08. Patient age, weight, way of delivery, other concomitant diseases (e.g., dysuria, anal and bowel symptoms), vulvodynia subtype, and pain duration did not influence VAMP scores in patients with vulvodynia and comparison group.

Conclusions: Pelvic examination according to VAMP protocol can be applied in vulvar pain patients for diagnostic purposes. Besides of vulvodynia symptoms any other analyzed variables did not influence on scores of VAMP protocols. We found that cut-off score ≥ 3 even in one of V, M or P component of VAMP protocol can be considered as diagnostic criterium for vulvodynia. Component A (anus area) was not useful for vulvodynia diagnosis.

Internet-based treatment for vulvodynia (EMBLA) - Study protocol for a randomised controlled study

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Background: Vulvodynia is defined as vulvar pain for at least 3 months without a clear cause. To the best of our knowledge, there are no trials investigating the effects of internet treatment using CBT (Cognitive behavioural therapy) treatment with Acceptance and Commitment Therapy (ACT) components for women with vulvodynia. The aim of this study is to examine the effects of such a guided internet-based intervention on provoked vulvar pain during the waiting period before clinical treatment. **Methods:** We will randomise 52 patients to either guided internet-based intervention with CBT with (ACT) components or no intervention during the waiting period for treatment as usual. Online assessments are conducted at baseline, posttreatment, and at follow-up after 9 months. The primary outcome measure is provoked vulvar pain. Secondary outcomes are depression, anxiety, sexual function, and quality of life. Linear-mixed effect models will be used to assess the effect of the internet-based intervention on vulvar pain, pain acceptance, depression, anxiety, sexual function, and quality of life over time, by applying the intention-to-treat approach. Continuous data will be analysed with general linear models using intention-to-treat and also per protocol approaches to assess the effects of the intervention at different time points. Ordinal and binary data will be analysed with Mann Whitney's test, Fischer's exact test and multivariate logistic regression, respectively. **Discussion:** As a randomised controlled trial with short- and long-term follow-up points, the EMBLA study intends to provide a novel and better understanding regarding the treatment of vulvodynia and the role of internet-based treatment as a complement to standard care for women suffering from vulvodynia. The effects of vulvodynia on pain, sexual function, quality of life, depression, and anxiety are investigated. The study's results are expected to be of value in the planning of clinical care in the medical area. High dropout rates and technical difficulties associated with using the platform are common in similar studies.

Provoked Vestibulodynia

Evaluation of Gut Microbiota in Patients With Vulvovestibular Syndrome

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Background: Vulvovestibular syndrome (VVS) or vulvodynia is a chronic, heterogeneous and multifactorial disease that dramatically affects women's health and quality of life. Despite important advancements in understanding VVS etiology have been achieved in the past decades, VVS still remains an elusive and complex condition without identifiable causes and effective treatments. In the present observational, retrospective, case-control study, we sought to investigate whether gut dysbiosis developed in patients with VVS. **Methods:** To this aim, we compared both bacterial and fungal composition in VVS patients ($n = 74$; 34.3 ± 10.9 years old) with those of women without gynecological symptoms ($n = 13$ healthy control; 38.3 ± 10.4 years old). Furthermore, to assess whether gut ecology may have an impact on gut function, the degree of intestinal inflammation (calprotectin levels) and gut permeability (zonulin levels) were also evaluated. **Results:** VVS patient developed gut dysbiosis, mainly characterized by a significant increase of *Escherichia coli* along with increased colonization of

mold/yeast compared to healthy controls. Furthermore, fecal levels of zonulin indicated that in VVS patients gut dysbiosis translated into increased gut permeability. **Conclusion:** Our preliminary study, by demonstrating that alterations in gut microbiota and intestinal permeability are present in patients with VVS, highlights the novel notion that gut dysbiosis may be considered an important associated factor for VVS. These findings, if confirmed, may be clinically relevant and may help in choosing further diagnostic methods and more effective therapies for these patients.

Predictors of vaginal penetration in women with Provoked Vestibulodynia

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This study examined whether time, treatment type, baseline individual differences, and treatment satisfaction affected the vaginal intercourse trajectories of women with Provoked Vestibulodynia (PVD) before and after psychological treatment. Women ($N = 130$) who received CBT or MBCT completed questionnaires prior to and 2-4 weeks, 6-, and 12-months following treatment. The odds of women engaging in vaginal penetration increased by 31% at each assessment. Baseline individual differences and treatment satisfaction predicted maintenance of or re-engagement in vaginal penetration at post-treatment. Findings suggest that women who refrain from vaginal intercourse after treatment differ from women who continue or resume this activity.

Specialized pro-resolving mediators reduce pro-nociceptive inflammatory mediator production in models of localized provoked vulvodynia

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Localized provoked vulvodynia (LPV) is the most common cause of chronic dyspareunia in premenopausal women, characterized by pain with light touch to the vulvar vestibule surrounding the vaginal opening. The devastating impact of LPV includes sexual dysfunction, infertility, depression, and even suicide. Yet, its etiology is unclear. No effective medical therapy exists; surgical removal of the painful vestibule is the last resort. In LPV, the vestibule expresses a unique inflammatory profile with elevated levels of pro-nociceptive proinflammatory mediators prostaglandin E_2 (PGE_2) and interleukin-6 (IL-6), which are linked to lower mechanical sensitivity thresholds. Specialized pro-resolving mediators (SPMs), lipids produced endogenously within the body, hold promise as an LPV treatment by resolving inflammation without impairing host defense. Ten of 13 commercially available SPMs reduced IL-6 and PGE_2 production by vulvar fibroblasts, administered either before or after inflammatory stimulation. Using a murine vulvar pain model, coupling proinflammatory mediator quantification with mechanical sensitivity threshold determination, topical treatment with the SPM, maresin 1, decreased sensitivity and suppressed PGE_2 levels. Docosahexaenoic acid (DHA), a precursor of maresin 1, was also effective in reducing PGE_2 in vulvar fibroblasts and rapidly restored mouse sensitivity thresholds. Overall, SPMs and their precursors may be a safe and efficacious for LPV. PERSPECTIVE: Vulvodynia, like many pain conditions, is difficult to treat because disease origins are incompletely understood. Here, we applied our knowledge of more recently discovered vulvodynia disease mechanisms to screen novel

therapeutics. We identified several specialized pro-resolving mediators as likely potent and safe for treating LPV with potential for broader application.

The Tampon Test as a Primary Outcome Measure in Provoked Vestibulodynia: A Mixed Methods Study

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Background: Provoked vestibulodynia (PVD) is characterized by severe pain, often induced by penetrative sex. This may lead to women abstaining from sexual intercourse, hence the recording of pain intensity levels in PVD research is often challenging. The standardized tampon test was designed as an alternative outcome measure to sexual intercourse pain and has frequently been used in clinical studies. **Aim:** The aim of this mixed methods study is to evaluate the tampon test as a primary outcome measure for an upcoming randomized clinical trial for women with PVD. **Methods:** An explanatory sequential design was applied, integrating quantitative and qualitative methods. In phase one, pain intensity levels were evaluated with the tampon test amongst 10 women, aged 18-33, with PVD. The test was repeated on day 1, 7 and 14. Pain intensity was rated on the Numerical Rating Scale (NRS), (0-10), 10 being worst possible pain. In phase two, the participants' experiences with the test were explored with semi-structured interviews using a descriptive and inductive qualitative design. All participants were recruited from the Vulva Clinic, Oslo University Hospital, Norway. **Outcomes:** The tampon test data and interviews were brought together to see how the interviews could refine and help to explain the quantitative findings. **Results:** The tampon test data demonstrated large intra- and inter-individual variability. Median tampon pain intensity was 4.5 (min=1.7; max=10; Q1=2.5; Q3=6). Many experienced the test as an inadequate representation of pain during intercourse as it was less painful, different in nature and conducted in an entirely different context. Four participants had a mean score of four or lower on the NRS, whilst concurrently reporting high levels of pain during sexual intercourse. **Clinical implications:** The findings indicate that the tampon test may underestimate severity of pain among some women with PVD. Participants with low pain scores would be excluded from studies where the tampon test is part of the trial eligibility criteria, even though severe pain was experienced during sexual intercourse. Large intra-individual variability in pain scores also reduces the test's ability to register clinical meaningful changes and hence necessitates repeated measurements per assessment time point. **Conclusion:** Although the tampon test has many advantages, this study indicates several potential problems with the application of the test as a primary outcome measure in PVD. In our opinion the test is most useful as a secondary outcome, preferably undertaken repeatedly in order to increase precision of the pain estimation.

Treatment of Localized Vulvar Pain with Neural Therapy: A Case Series and Literature Review

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Background: Localized vulvar pain (LVP) is a common condition among fertile women, with physical and psychosexual implications. Treatment is complex with limited benefits. Neural therapy is a regulatory therapy that uses injections of local anesthetics in low concentrations in specific points to treat different

conditions. **Case presentation:** We present the cases of 5 women, ages 33-44 years, with LVP treated with procaine 0.5% injections in painful points. Complete relief from pain occurred in 2 patients, and significant improvement in 3. Only 1 or 2 sessions were required. Initial VAS score was ≥ 70 and decreased to ≤ 30 after the intervention. The improvement was maintained over time, with a minimum follow-up period of 6 months. None of the patients were able to have sex or use tampons due to pain, but they were able to resume after the intervention. **Conclusions:** In this case series, local injections of procaine showed a favorable outcome. Future randomized clinical trials could help elucidate the role of this intervention in LVP.

Correction to: #ItsNotInYourHead: A Social Media Campaign to Disseminate Information on Provoked Vestibulodynia

Lori A Brotto, Melissa Nelson, Lana Barry, Ciana Maher
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Provoked Vestibulodynia (PVD) is a type of localized vulvodynia (or pain in the vulva). The estimated prevalence of this condition is about 12% of the general population and approximately 20% of women under the age of 19. Many women who live with PVD suffer in silence for years before receiving a diagnosis. Whereas cognitive behavioral therapy (CBT) was already known to be effective for managing symptoms of PVD, there has recently been a published head-to-head comparison of CBT versus mindfulness-based therapy for the primary outcome of pain intensity with penetration. The trial revealed that both treatments were effective and led to statistically and clinically meaningful improvements in sexual function, quality of life, and reduced genital pain, with improvements retained at both 6- and 12-month follow-ups. We then undertook an end-of-grant knowledge translation (KT) campaign focused on the use of social media to disseminate an infographic video depicting the findings. Social media was strategically chosen as the primary mode of dissemination for the video as it has broad reach of audience, the public can access information on social media for free, and it presented an opportunity to provide social support to the population of women with PVD who are characterized as suffering in silence by starting a sensitive and empowering dialogue on a public platform. In this paper, we summarize the social media reach of our campaign, describe how and why we partnered with social media influencers, and share lessons learned that might steer future KT efforts in this field.

Co-morbid Disorders

An update on the management of chronic pelvic pain in women

K Vincent, E Evans
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<https://pubmed.ncbi.nlm.nih.gov/33682093/>

Chronic pelvic pain represents a major public health problem for women and impacts significantly on their quality of life. Yet it is under-researched and a challenge to manage. Women who suffer from chronic pelvic pain frequently describe their healthcare journey as long, via a variety of specialists and frustrating, with their pain often dismissed. Aetiological factors and associations are best conceptualised using the 'three P's' model of predisposing, precipitating and perpetuating factors. This integrates the numerous biological, psychological and social contributors to the complex, multifactorial nature of

chronic pelvic pain. Overall management involves analgesia, hormonal therapies, physiotherapy, psychological approaches and lifestyle advice, which like other chronic pain conditions relies on a multidisciplinary team approach delivered by professionals experienced and trained in managing chronic pelvic pain.

Dyspareunia in Women

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Dyspareunia is recurrent or persistent pain with sexual intercourse that causes distress. It affects approximately 10% to 20% of U.S. women. Dyspareunia may be superficial, causing pain with attempted vaginal insertion, or deep. Women with sexual pain are at increased risk of sexual dysfunction, relationship distress, diminished quality of life, anxiety, and depression. Because discussing sexual issues may be uncomfortable, clinicians should create a safe and welcoming environment when taking a sexual history, where patients describe the characteristics of the pain (e.g., location, intensity, duration). Physical examination of the external genitalia includes visual inspection and sequential pressure with a cotton swab, assessing for focal erythema or pain. A single-digit vaginal examination may identify tender pelvic floor muscles, and a bimanual examination can assess for uterine retroversion and pelvic masses. Common diagnoses include vulvodynia, inadequate lubrication, vaginal atrophy, postpartum causes, pelvic floor dysfunction, endometriosis, and vaginismus. Treatment is focused on the cause and may include lubricants, pelvic floor physical therapy, topical analgesics, vaginal estrogen, cognitive behavior therapy, vaginal dilators, modified vestibulectomy, or onabotulinumtoxinA injections.

Persistent Genital Arousal Disorder

Prevalence of Persistent Genital Arousal Disorder in 2 North American Samples

Robyn A Jackowich, Caroline F Pukall

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Background: Persistent genital arousal disorder (PGAD) is a highly distressing, understudied condition characterized by persistent genital arousal (eg, genital sensations, sensitivity) in the absence of sexual desire. Currently, there is limited information about the prevalence of PGAD based on its proposed diagnostic criteria ("PGAD criteria"). **Aim:** This study sought to assess the prevalence of PGAD criteria in 2 North American samples: a large, non-clinical sample of Canadian undergraduate students (Study 1), and a nationally representative sample from the U.S. (Study 2). **Methods:** The incoming class of undergraduate students (N = 1,634) enrolled in the Introduction to Psychology course at a Canadian university and a nationally representative sample of U.S. participants (N = 1,026) responded to questions about each PGAD criterion, and distress associated with these experiences. **Outcomes:** 5 self-report questions were developed based on each of the Leiblum and Nathan 2001 PGAD criteria, and a measure of associated distress was included. The U.S. sample (Study 2) also responded to questions about medical comorbidities and their knowledge of the term "PGAD." **Results:** 1.1% (n = 4; Study 1) to 4.3% (n = 22; Study 2) of men and 0.6% (n = 7; Study 1) to 2.7% (n = 14; Study 2) of women reported experiencing all 5 PGAD criteria at a moderate to high frequency. Even greater proportions of

participants reported experiencing all 5 criteria at any frequency (6.8-18.8%). Although ratings of associated distress varied, participants who were distressed by these symptoms most frequently endorsed the first PGAD criterion: physiological genital arousal in the absence of sexual excitement or desire. These results are similar to previously reported rates of PGAD. **Clinical implications:** A non-trivial number of individuals may experience PGAD, and it should be screened for by healthcare practitioners. **Strengths & limitations:** This study is the first to use 2 large, non-clinical samples to assess the prevalence of PGAD symptoms. However, barriers to reporting symptoms, such as shame or embarrassment, may have resulted in underestimates of prevalence in the present sample. **Conclusion:** The prevalence of the 5 PGAD criteria in 2 large non-clinical samples ranged from similar to higher than rates reported in previous research. However, distress ratings associated with each of the 5 criteria varied, with most respondents describing them primarily as neutral or non-distressing. Jackowich RA, Pukall CF. Prevalence of Persistent Genital Arousal Disorder in 2 North American Samples. *J Sex Med* 2020;17:2408-2416.

Healthcare Experiences of Individuals With Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia

Robyn A Jackowich, Stéphanie C Boyer, Samantha Bienias, Susan Chamberlain, Caroline F Pukall
Sex Med. 2021 Apr 17;9(3):100335. doi: 10.1016/j.esxm.2021.100335.
<https://pubmed.ncbi.nlm.nih.gov/33878624/>

Introduction: Persistent genital arousal disorder/genito-pelvic dysesthesia (PGAD/GPD) is a distressing condition characterized by persistent, unwanted sensations of genital arousal (eg, feelings of being on the verge of orgasm, and of lubrication, swelling, tingling, throbbing) that occur in the absence of sexual desire. Although PGAD/GPD is associated with significant impairments in psychosocial functioning, the healthcare (HC) experiences of affected individuals are not well understood. **Aim:** The aims of this study were to examine the barriers to HC, the costs of HC, and the associations among HC experiences, symptoms, and psychosocial outcomes in those with PGAD/GPD symptoms. **Methods:** One hundred and thirteen individuals with PGAD/GPD symptoms completed an online, cross-sectional self-report questionnaire about their HC history and experiences. **Main outcome measures:** Self-reported HC barriers, and financial costs associated with PGAD/GPD HC. Validated measures of HC experiences (eg, comfort communicating with HC practitioners [HCPs]), and psychosocial (eg, depression, anxiety) and PGAD/GPD symptom outcomes. **Results:** The majority of participants (56.6%) reported waiting at least 6 months to seek HC for PGAD/GPD symptoms. Those who sought HC approached many HCPs (46.0% approached 6+ HCPs). Several barriers to HC were identified (eg, lack of HCP knowledge of PGAD/GPD), and high costs were reported. A series of multiple linear regression analyses found an association between HC experiences, psychosocial, and symptom outcomes. Specifically, decreased comfort communicating with one's HCP was associated with greater depressive and anxiety symptoms. **Conclusion:** High costs and numerous barriers to seeking HC for PGAD/GPD symptoms were identified, and discomfort communicating with an HCP about PGAD/GPD was associated with increased symptoms of depression and anxiety. These results highlight the need for more awareness of this condition in order to improve care for this population.

International Society for the Study of Women's Sexual Health (ISSWSH) Review of Epidemiology and Pathophysiology, and a Consensus Nomenclature and Process of Care for the Management of Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia (PGAD/GPD)

Irwin Goldstein, Barry R Komisaruk, Caroline F Pukall, Noel N Kim, Andrew T Goldstein, Sue W Goldstein, Rose Hartzell-Cushmanick, Susan Kellogg-Spadt, Choll W Kim, Robyn A Jackowich, Sharon J Parish, April Patterson, Kenneth M Peters, James G Pfaus

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Background: Persistent genital arousal disorder (PGAD), a condition of unwanted, unremitting sensations of genital arousal, is associated with a significant, negative psychosocial impact that may include emotional lability, catastrophization, and suicidal ideation. Despite being first reported in 2001, PGAD remains poorly understood. **Aim:** To characterize this complex condition more accurately, review the epidemiology and pathophysiology, and provide new nomenclature and guidance for evidence-based management. **Methods:** A panel of experts reviewed pertinent literature, discussed research and clinical experience, and used a modified Delphi method to reach consensus concerning nomenclature, etiology, and associated factors. Levels of evidence and grades of recommendation were assigned for diagnosis and treatment. **Outcomes:** The nomenclature of PGAD was broadened to include genito-pelvic dysesthesia (GPD), and a new biopsychosocial diagnostic and treatment algorithm for PGAD/GPD was developed. **Results:** The panel recognized that the term PGAD does not fully characterize the constellation of GPD symptoms experienced by patients. Therefore, the more inclusive term PGAD/GPD was adopted, which maintains the primacy of the distressing arousal symptoms and acknowledges associated bothersome GPD. While there are diverse biopsychosocial contributors, there is a common underlying neurologic basis attributable to spontaneous intense activity of the genito-pelvic region represented in the somatosensory cortex and its projections. A process of care diagnostic and treatment strategy was developed to guide the clinician, whenever possible, by localizing the symptoms as originating in any of five regions: (i) end organ, (ii) pelvis/perineum, (iii) cauda equina, (iv) spinal cord, and (v) brain. Psychological treatment strategies were considered critical and should be performed in conjunction with medical strategies. Pharmaceutical interventions may be used based on their site and mechanism of action to reduce patients' symptoms and the associated bother and distress. **Clinical implications:** The process of care for PGAD/GPD uses a personalized, biopsychosocial approach for diagnosis and treatment. **Strengths and limitations:** Strengths and Limitations: Strengths include characterization of the condition by consensus, analysis, and recommendation of a new nomenclature and a rational basis for diagnosis and treatment. Future investigations into etiology and treatment outcomes are recommended. The main limitations are the dearth of knowledge concerning this condition and that the current literature consists primarily of case reports and expert opinion. **Conclusion:** We provide, for the first time, an expert consensus review of the epidemiology and pathophysiology and the development of a new nomenclature and rational algorithm for management of this extremely distressing sexual health condition that may be more prevalent than previously recognized. Goldstein I, Komisaruk BR, Pukall CF, et al. International Society for the Study of Women's Sexual Health (ISSWSH) Review of Epidemiology and Pathophysiology, and a Consensus Nomenclature and Process of Care for the Management of Persistent Genital Arousal Disorder/Genito-Pelvic Dysesthesia (PGAD/GPD).

Making a Difference: Persistent Genital Arousal Disorder

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[https://www.smr.jsexmed.org/article/S2050-0521\(21\)00013-5/fulltext](https://www.smr.jsexmed.org/article/S2050-0521(21)00013-5/fulltext)

As sexual medicine providers, researchers and educators, we are very familiar with how aging can affect sexual function—erectile dysfunction and genitourinary syndrome of menopause are obvious examples—and we know how to treat these. We also see adults with lifelong congenital problems such as chordee or neuroproliferative vestibulodynia. Finally, there are sexual health issues that may have resulted from an accident such as Peyronie's disease. But what about a child with a lifelong sexual health issue that few recognize, let alone provide appropriate diagnosis or treatment? During COVID-19 many children and young adults are having social development issues due to their inability to have what we knew as a normal life—they can no longer sit in a classroom all day, smiling at friends, eating lunch together at the cafeteria and making social plans for the weekend. We can all empathize. Now imagine a child not old enough to be sexual who cannot sit still in the classroom because she constantly feels her genitals engorged and cannot concentrate on her teacher, or he needs to masturbate in order to relieve himself and pay attention to the lesson. Think about the teenager whose friends hang out in the mall or at each other's houses on the weekend....where does that leave the young adult who has unwanted spontaneous orgasms and would be embarrassed to spend any length of time with friends? What must go on in the minds of young adults with lifelong persistent genital arousal disorder? How do these young women and men traverse the fragmented socialization that is their world, learning to date, trying to separate from their parents, preparing for college, when COVID-19 is the least of what is not normal in a world in which they suffer from persistent genital arousal disorder/genito-pelvic dysesthesia (PGAD/GPD)?

Pudendal Neuralgia

Clinical efficacy evaluation and prevention of adverse reactions in a randomized trial of a combination of three drugs in the treatment of cancerous pudendal neuralgia

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Background: To explore the clinical efficacy, safety, and prevention of major adverse reactions of the nonsteroidal anti-inflammatory drug celecoxib combined with OxyContin and Pregabalin in the treatment of cancerous pudendal neuralgia. **Methods:** A total of 51 patients presenting with pelvic malignancies with cancerous pudendal neuralgia were selected, and random number table method was used to allocate them to either the experimental group (n=27) or control group (n=24). The control group was treated with OxyContin combined with Pregabalin, and the experimental group was treated with Celecoxib on the basis of the control group. **Results:** At 24 hours after treatment, the clinical effective rate of the experimental group was 92.6%, which was significantly higher than the 66.7% of the control group (P<0.05). The numerical rating scale (NRS) scores of the 2 groups of participants on the 7th and 14th days after treatment were lower than before treatment (P<0.05), and the NRS scores of the participants in the experimental group had decreased more significantly. At the same time, the average

daily consumption of OxyContin on the 7th and 14th day of the experimental group was lower than that of the control group ($P < 0.05$). Compared with the control group, the incidence of constipation and dysuria in the experimental group was significantly reduced ($P < 0.05$). Co-occurring in both groups during treatment, 10 participants with urinary dysfunction were treated with tamsulosin hydrochloride sustained-release capsules, no urinary retention occurred, catheterization was avoided, tamsulosin hydrochloride sustained-release capsules could be stopped after 1 week, and urination was smooth ($P < 0.05$). After treatment, the quality of life of the 2 groups of participants had improved compared to before treatment, and the improvement was more significant in the experimental group.

Conclusions: When treating patients with cancerous pudendal neuralgia with OxyContin and Pregabalin, the addition of celecoxib has a significant effect, which can effectively improve the patient's pain, improve their quality of life to a certain extent, and reduce the consumption of OxyContin. Lowering the dose of OxyContin reduces the occurrence of adverse reactions related to the drug, especially the incidence of constipation and urinary retention. Tamsulosin hydrochloride sustained-release capsules can effectively relieve urinary disorders caused by OxyContin.

The Clinical Efficacy of High-Voltage Long-Duration Pulsed Radiofrequency Treatment in Pudendal Neuralgia: A Retrospective Study

Cheng-Long Wang, Tao Song

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Background: Patients with pudendal neuralgia (PN) experience long-lasting chronic pain, hyperalgesia, and comorbid emotional disorders, such as depression and anxiety. Treatment via conventional pulsed radiofrequency (PRF) current carries a significantly high rate of failure. **Objective:** To determine the safety and clinical efficacy of high-voltage, long-duration PRF application to the pudendal nerve in patients with PN. **Study design:** Observational retrospective design, self before-after controlled clinical trial. **Materials and methods:** We analyzed the records of 70 patients of our hospital with diagnosed PN. Treatment consisted of PRF application to the pudendal nerve, using computed tomography guidance to target the pudendal nerve at the level of the ischial spine or ischial tuberosity of the affected side. PRF was applied with the following parameters: temperature 42°C, frequency 2 Hz, pulse width 20 ms, field intensity ramped gradually from 40 to 90 V, duration 900 sec. The therapeutic effect was evaluated by collecting patient scores for the visual analog scale (VAS), SF-36 health survey questionnaire (SF-36), and patient health questionnaire (PHQ-9) before treatment and at 1-, 4-, and 12-week follow-ups after PRF treatment. Data were analyzed by paired t-test with $p < 0.05$ considered to be statistically significant.

Results: VAS, SF-36, and PHQ-9 scores at 1, 4, and 12 weeks after high-voltage long-duration PRF treatment were significantly improved relative to their respective pretreatment baseline scores ($p < 0.05$ for all). The effective rate at 12 weeks after high-voltage long-duration PRF was up to 88.6%.

Limitations: A small sample size and lack of a control group. **Conclusions:** High-voltage long-duration PRF provided significant short-term (at least 12 weeks) pain relief to most patients with PN; it also improved subjective measures of depression and quality of life over the same duration of time.

Diagnostic and therapeutic algorithm for pudendal nerve entrapment syndrome

María José Luesma, Inés Galé, José Fernando

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Pudendal nerve entrapment syndrome is widely unknown and often misdiagnosed or confused with other pelvic floor diseases. The aim is to develop a diagnostic and therapeutic algorithm based on a review of the existing literature. For its diagnosis, an anamnesis will be carried out in search of possible aetiologies, surgical history, and history of pain, assessing location and irradiation, intensity on the visual analogue scale, timing, triggering factors and rule out alarm signs. A physical examination will be performed, looking for trigger points or areas of fibrosis with transvaginal / transrectal palpation of the terminal branches of the nerve. With a doubtful diagnosis, an anaesthetic block of the pudendal nerve can be performed. Once the diagnosis is confirmed, the treatment will begin staggered with lifestyle changes, drug therapy and physiotherapy. In view of the failure of these measures, invasive therapies such as botulinum toxin injection, pulsed radiofrequency and decompression surgery or spinal cord stimulation will be used.

Dermatological Conditions

Clobetasol Compared With Fractionated Carbon Dioxide Laser for Lichen Sclerosus: A Randomized Controlled Trial

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Objective: To compare 6-month safety and efficacy outcomes of fractionated CO₂ laser (laser) with topical clobetasol propionate (steroid) for treatment of symptomatic vulvar lichen sclerosus.

Methods: We conducted a single-center randomized controlled trial that compared fractionated CO₂ laser with steroid treatment for patients with biopsy-proven lichen sclerosus. Randomization was stratified by prior clobetasol propionate use. The primary outcome was mean change in Skindex-29 score at 6 months. A total sample size of 52 participants were recruited to detect a mean difference of 16 points on the Skindex-29 (SD±22) with 80% power, based on a one-sided two-sample t test with $\alpha=0.05$, accounting for 10% attrition. Secondary outcomes included validated subjective and objective measures. Intention-to-treat, per protocol, and regression analysis based on prior steroid exposure were performed. **Results:** From October 2015 to July 2018, 202 women were screened, 52 were randomized, and 51 completed a 6-month follow-up. No significant difference was found in baseline demographics, symptoms, and physician assessment scores. There was greater improvement in the Skindex-29 score in the laser arm at 6-months (10.9 point effect size, 95% CI 3.42-18.41; P=.007). Overall, 89% (23/27) of patients in the laser group rated symptoms as being "better or much better" compared with 62% (13/24) of patients in the steroid group, P=.07. More patients (81%, 21/27) were "satisfied or very satisfied" with laser treatment compared with steroid treatment (41%, 9/24); P=.01. After stratification for previous steroid use, the significant change of Skindex-29 score was only seen in the previously exposed group. There was one adverse event in each group: minor burning and blistering at the laser site and reactivation of genital herpes 1 week after starting steroid. **Conclusion:** Fractionated CO₂ laser treatment showed significant improvement in subjective symptoms and objective measures compared with clobetasol propionate, without serious safety or adverse events at 6 months.

Fractionated Carbon Dioxide Laser for the Treatment of Vulvar Lichen Sclerosus: A Randomized Controlled Trial

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Objective: To estimate the efficacy of fractionated carbon dioxide (CO₂) laser therapy for vulvar lichen sclerosis. **Methods:** We conducted a prospective, double-blind, randomized, sham-controlled, trial conducted in a clinic specializing in vulvar disorders. The study participants were 40 women with active vulvar lichen sclerosis confirmed with biopsy who were abstaining from topical and systemic treatments for at least 4 weeks before enrollment. Women were randomized in a 1:1 ratio to receive either five sham laser treatments or five fractionated CO₂ treatments in a 24-week period. Study participants, treating clinicians, and the evaluating pathologist were blinded. The primary endpoint was the change in the histopathology scale score between pretreatment and posttreatment biopsies. We estimated 20 per group for 80% power to detect a 40% reduction in the histopathology scale score with up to 10% attrition. A secondary endpoint was the change in the validated CSS (Clinical Scoring System for Vulvar Lichen Sclerosus). **Results:** From November 2018 to June 2020, 40 women were randomized to participate in the trial, and 37 women (19 fractionated CO₂, 18 sham) were included in an intention-to-treat (ITT) analysis. Three women were excluded from the ITT analysis because they did not have posttreatment biopsies and, therefore, a posttreatment histopathology scale score could not be obtained. There was a 0.20 reduction (improvement) in histopathology scale score from baseline in the active treatment group (95% CI -1.1, 0.80, P=.74) and a 0.1 increase from baseline in the sham treatment group (95% CI -0.90, 1.0, P=.91). The change in histopathology scale score between the active and sham arm was not statistically significant (95% CI -1.14, 1.06, P=.76). **Conclusion:** Fractionated CO₂ is not an effective monotherapy treatment for vulvar lichen sclerosis.

Microablative fractional radiofrequency as a therapeutic option for vulvar lichen sclerosis: a pilot study

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Objectives: To assess the clinical response to and the histomorphometric effects of microablative fractional radiofrequency (MFR) in women with symptomatic vulvar lichen sclerosis (VLS).

Methods: This was a pilot study on the use of MFR for the treatment of VLS. Upon recruitment and at each treatment session, all participants were examined and each of their symptoms were rated on a visual analog scale. After the procedure, the participants completed a satisfaction questionnaire. We compared the morphometric findings of vulvar biopsies performed at enrollment and after the last treatment session. The participants were divided into three groups according to previous treatment with corticosteroids: G1, no previous treatment; G2, treated for up to 5 years; and G3, treated for >5 years. **Results:** This study included 26 women. After two to three sessions, most participants in all groups became either "asymptomatic" or "much better" than before treatment and were "very satisfied" or "satisfied" with the intervention. Pruritus and burning sensation were the most frequently reported symptoms. Nearly 40% of the participants in all groups reported complete remission of symptoms. The improvement was rated as moderate or higher by 80%, 76%, and 66% of the women in

groups 1, 2, and 3, respectively. The improvement of symptoms persisted for 11 months (range, 7-16 months), on average, after the treatment. Type III collagen concentration significantly increased and was associated with important symptom improvement. Tissue trophism and vascularization also increased but did not reach statistical significance, probably because of the small number of cases.

Does longer duration of corticosteroid treatment improve clearance in vulvar lichen sclerosis? Results from a single centre, comparative, open label study

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A complete clearance of vulvar lichen sclerosis (VLS) is achieved in a minority of patients treated with a standard 12-week duration corticosteroid treatment. The aim of this pragmatic, retrospective, open label, comparative trial was to assess the effectiveness, in terms of complete clearance, of a 24-week treatment with mometasone furoate 0.1% ointment (MMF) and to compare it with a 12-week therapy. We included VLS patients treated with MMF administered for five consecutive days/week for 24 weeks (group A). The following were assessed: (a) clearance in Global Subjective Score (GSS), Global Objective Score (GOS) or both, (b) changes of these parameters and dyspareunia at treatment completion compared to baseline, (c) safety profile. All these assessments were compared with the same outcomes recorded among VLS patients who had previously undergone a 12-week MMF treatment (group B). Twenty-nine patients were included in group A and 32 in group B. The rates of patients who achieved the clearance of GSS, GOS or both parameters did not significantly differ between groups A and B. The groups did not differ in any of the effectiveness outcomes assessed. A 24-week duration corticosteroid treatment does not seem to provide significant therapeutic benefits in comparison with standard 12-week courses, especially considering the occurrence of complete clearance.

Quality of Life in Vulvar Lichen Sclerosis Patients Treated With Long-Term Topical Corticosteroids

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Objective: The aim of the study was to investigate the quality of life in vulvar lichen sclerosis (VLS) patients treated with long-term, individualized topical corticosteroids. **Methods:** A prospective cross-sectional study comparing new pretreatment and long-term treated VLS patients attending a dermatogynecology practice in Sydney, Australia. Participants were invited to complete the Vulvar Quality of Life Index (VQLI). The VQLI scores were compared between the 2 groups.

Results: A total of 204 biopsy-proven VLS patients-68 new pretreatment and 136 treated patients on topical corticosteroids for 2 years or longer. Treated participants scored lower in all VQLI components, including total score (median = 2.0 [interquartile range {IQR} = 0.0-6.0] vs 13.5 [IQR = 7.5-22.0]; $p < .001$), symptoms (median = 0.5 [IQR = 0.0-0.5] vs 1.3 [IQR = 0.8-2.0]; $p < .001$), anxiety (median = 0.0 [IQR = 0.0-0.3] vs 0.8 [IQR = 1.1-2.0]; $p < .001$), activities of daily living (median = 0.2 [IQR = 0.0-0.3] vs 0.5 [IQR = 0.2-1.1]; $p < .001$), and sexuality (median = 0.0 [IQR = 0.0-0.7] vs 1.0 [IQR = 0.0-2.0]; $p < .001$). A higher proportion of treated patients achieved total scores of 0-5, representing nil to minimal impact of VLS on quality of life (98 [72.1%] vs 8 [11.8%]; $p < .001$). Mild and reversible adverse effects were developed in 11 patients (8.1%). Partially compliant patients were 12 times as likely to develop scarring progression than fully compliant patients (7 [22.6%] vs 2 [1.9%]; $p < .001$).

Conclusions: Long-term, individualized topical corticosteroid treatment is safe and effective in maintaining disease remission and improves the quality of life of VLS patients. Fully compliant patients demonstrate better treatment outcomes than partially compliant patients.

Clinic and demographic characteristics of pediatric patients with Lichen sclerosis

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Background: Lichen sclerosis (LS) is a chronic disease of the skin, for which the pathogenesis is not known. It can lead to various changes of the skin and the genital area, potentially leading to both functional as well as cosmetic problems for the patient, thus disrupting the quality of life. In this study; the purpose was to review the clinical characteristics and the treatments of the 15 pediatric patients under the age of 18 followed up in our out-patient clinic with a diagnosis of LS and to compare the findings with literature data. **Methods:** Between 2011 and 2017, the files of 15 patients diagnosed clinically and/or histologically with LS in our clinic were retrospectively examined. The demographic characteristics, clinic and laboratory findings, treatment options of the patients are reported. **Results:** Of the patients included in the study 14 were girls and one was a boy. The average age was 11.6 years (5-17 years), the average age for the initial disease was 7.8 years (2-13 years). The average duration of the disease at the diagnosis was 3.9 years. The most common form was genital vulvar type (8/14 girls) without anal and cutaneous involvement, and each of them suffered from itching. One of the cases had genital LS as well as extragenital morphea lesions. Two of the 15 patients were ANA positive. The other antibodies were negative. In two cases with extragenital involvement, lesions were widespread and they were in blachkoid form. **Conclusion:** LS is a chronic disease that progresses with recurrences and regressions. In our study, the most common LS type was genital type (60%). There was extragenital involvement in 6 patients (40%). Extragenital involvement was the most common on the trunk. Diagnosis, treatment and follow-up during childhood is highly important to prevent any possible future anatomical or psychological damage and genital malignancies.

Study of melanocyte density and epidermal thickness in vulvar lichen sclerosis lesions

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Objective: This study aimed to analyze changes in melanocyte density and epidermal thickness in vulvar lichen sclerosis (VLS). **Methods:** Vulvar skin tissues were collected from 15 VLS female patients in Beijing Hospital, classified into early (n = 7) and late VLS (n = 8) groups according to pathological manifestations. Melanocyte density and full epidermal and cell-layer (from the bottom of the stratum corneum to that of the basal layer) thickness were calculated using an image analysis software. The control group was normal vulvar skin tissues from 15 females after plastic surgery. **Results:** The early VLS ($0.170 \pm 0.071 \mu\text{m}$) and late VLS ($0.110 \pm 0.035 \mu\text{m}$) groups had significantly lower densities of epidermal melanocytes than the control group (0.275 ± 0.036) ($F = 36.426$, $P < 0.001$). The cell-layer thickness did not differ between the early VLS ($154.603 \pm 121.984 \mu\text{m}$) and control ($176.974 \pm 80.296 \mu\text{m}$) groups ($P = 0.899$) but significantly decreased in the late VLS group ($83.455 \pm 37.129 \mu\text{m}$) compared to the control group ($P = 0.003$). **Conclusions:** Melanocyte density decreased in early and late VLS. The

full epidermal and cell-layer thickness did not significantly change in early VLS, but the cell-layer thickness decreased in late VLS.

Erosive Lichen Sclerosus-A Clinicopathologic Subtype

Tania Day, Geoffrey Otton, Graeme Dennerstein, Hong Tran, James Scurry
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Objective: The aim of the study was to identify whether erosive lichen sclerosus (LS) is a distinct clinicopathologic subtype. **Materials and methods:** The pathology database was searched for "erosion," "erosive," "ulcer," and "lichen sclerosus." Inclusion criteria were histopathologic diagnosis of LS and erosion or ulcer overlying a band of hyalinization and/or fibrosis. Exclusions were concurrent neoplasia and insufficient tissue. Histopathologic review documented site, epithelial thickness, adjacent epidermal characteristics, infiltrate, and dermal collagen abnormality. Clinical data included demographics, comorbidities, examination findings, microbiologic results, treatment, and response. **Results:** Ten examples of erosive LS and 15 of ulcerated LS occurred in 24 women with a mean age of 67 years. Ulcerated LS was associated with diabetes and nontreatment at time of biopsy. Clinicians identified red patches in all but 1 case of erosive LS. Ulcerated LS was documented as fissure, ulcer, or white plaque, with 8 (53%) described as lichenified LS with epidermal breaches. Erosive LS favored hairless skin with normal adjacent stratum corneum sloping gently into erosion, whereas most ulcers in LS had an abrupt slope from hair-bearing skin. All cases were treated with topical steroids; 2 patients with erosive LS and 10 with ulcerated LS also had oral antifungals, topical estrogen, antibiotics, and/or lesional excision. Treatment yielded complete resolution in 50%. **Conclusions:** Erosive LS is an unusual clinicopathologic subtype characterized by red patches on hairless skin seen microscopically as eroded epithelium overlying a band of hyalinized or fibrotic collagen. In contrast, ulcerated LS is usually a traumatic secondary effect in an uncontrolled dermatosis.

Applying limiting entropy to quantify the alignment of collagen fibers by polarized light imaging

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Collagen alignment has shown clinical significance in a variety of diseases. For instance, vulvar lichen sclerosus (VLS) is characterized by homogenization of collagen fibers with increasing risk of malignant transformation. To date, a variety of imaging techniques have been developed to visualize collagen fibers. However, few works focused on quantifying the alignment quality of collagen fiber. To assess the level of disorder of local fiber orientation, the homogeneity index (HI) based on limiting entropy is proposed as an indicator of disorder. Our proposed methods are validated by verification experiments on Poly Lactic Acid (PLA) filament phantoms with controlled alignment quality of fibers. A case study on 20 VLS tissue biopsies and 14 normal tissue biopsies shows that HI can effectively characterize VLS tissue from normal tissue ($P < 0.01$). The classification results are very promising with a sensitivity of 93% and a specificity of 95%, which indicated that our method can provide quantitative assessment for the alignment quality of collagen fibers in VLS tissue and aid in improving histopathological examination of VLS.

Pediatric Vulvar Lichen Sclerosus: A Survey of Disease Course

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Study objective: To assess long-term outcomes of Lichen Sclerosus (LS) in the female pediatric population, specifically in relation to patient age, treatment type and duration, and remission.

Design: Retrospective chart review was conducted to identify female pediatric patients (0-18 years of age) who were diagnosed with LS between 1/1/2015 and 1/1/2020 at the University of North Carolina Dermatology and/or OB/GYN Departments. Patients were contacted via telephone for follow-up interviews consisting of a series of questions regarding patient age, symptom onset, time of diagnosis, treatment, and current symptoms. **Results:** Out of the 128 patients identified, 61 patients consented and participated in follow-up interviews. At the time of study follow-up, 90% of participants reported their symptoms were improved. Patients reported using a variety of treatments, with medium- to high-potency topical steroids being the most common. At the time of follow-up, 87% of patients reported being asymptomatic, 70% of which were not using any form of maintenance therapy. Those who achieved symptom resolution did so at an average of 8.4 years of age. There was no significant difference in ages between asymptomatic patients on maintenance therapy and off maintenance therapy. There was a positive correlation found between the duration of LS treatment and time in remission ($p < 0.001$). Increased patient age at time of follow-up also correlated positively with time in remission ($p < 0.001$). **Conclusion:** In our cohort, the need for continued maintenance therapy was not correlated with age or, by proxy, pubertal status. Thus, LS remission may be determined more by early and successful pharmacological interventions.

Fractionated Carbon Dioxide Laser for the Treatment of Vulvar Lichen Sclerosus

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No abstract available

Lasers as an adjuvant for vulvar lichen sclerosus: A systematic review and meta-analysis

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Vulvar lichen sclerosus (VLS) is a chronic inflammatory dermatosis that can result in significant psychosocial and sexual impairment. VLS is associated with 4%-6% risk of malignant transformation if left untreated. The effective management of VLS can be challenging as some patients can be recalcitrant to first-line ultrapotent topical corticosteroids (TCS) despite appropriate use. Off-label use of lasers has shown good results in VLS, suggesting its usefulness as an adjunct to medical therapy. This combined systematic review and meta-analysis synthesizes the available evidence for ablative and nonablative lasers for VLS.

Treatment Options in Vulvar Lichen Sclerosus: A Scoping Review

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Vulvar lichen sclerosus (VLS) is a chronic inflammatory disorder, which affects women of all ages. The aim of this review is to focus on first-line, second-line, and maintenance therapies as well as follow-up of women with VLS. With numerous controversies, we decided to conduct a scoping review on this subject. A review protocol was developed, and the Knowledge Resource Services website was used to run a search of articles pertaining to VLS with keywords "Vulvar," "Vulval," and "Lichen Sclerosus." The search was limited to published data from the last 10 years, i.e., July 2009 onward, and researches published in English language. A total of 338 articles pertaining to VLS were obtained. Out of this, 62 were original articles related to management of VLS. Effective treatments such as high-potency topical steroids are now the standard of care and first-line treatment. Follow-up may be done every three to six months for the first two years and then at least yearly to ensure adequacy of treatment and encourage compliance. Long-term follow-up in specialist clinics is recommended for women who have persistent complaints, thickened skin, or history of neoplastic lesion. Monitoring young patients yearly is recommended as there are chances of recurrence.

Diagnosis and management of cutaneous and anogenital lichen sclerosus: recommendations from the Italian Society of Dermatology (SIDeMaST)

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Ital J Dermatol Venerol. 2021 Apr 29. doi: 10.23736/S2784-8671.21.06764-X.

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Lichen sclerosus (LS) is a disabling chronic inflammatory disease of skin and genital mucous membrane causing itch, pain, dysuria and restriction of micturition, and significant sexual dysfunction and dyspareunia both in women and men. If left untreated, LS is associated with a high degree of sclerosis and scarring, as well as with an elevated risk of cancer in the genital area. Although a central role of autoimmunity is suggested, the pathogenesis of LS is still not clearly understood and the disease remains difficult to treat. The goals of treatment of LS are to alleviate symptoms and discomfort, prevent anatomical changes and prevent malignant transformation. This guideline has been developed by an Italian group of experts. It summarizes evidence-based and expert-based recommendations. The highest level of evidence favors the use of topical high potency corticosteroids; second and third lines' treatments include topical calcineurin inhibitors and topical retinoids, respectively. Surgical treatment has become the treatment of choice in male genital LS with persistent phimosis not responsive to medical treatment. The aim of this paper is to offer evidencebased and easily applicable recommendations for the management of LS.

Vulvar lichen sclerosus in women of reproductive age

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Vulvar lichen sclerosus (vLS) is an inflammatory skin condition that predominantly affects the vulvar and perianal regions. Approximately 50% of cases present prior to menopause; however, there is a paucity of data on vLS in women of reproductive age as well as during their pregnancies. A retrospective review was performed at two tertiary referral centers to better describe cases of vLS in women of reproductive age. Thirty-three patients with a mean age of 40 years met inclusion criteria. In this group, vulvar pruritus was the most common presenting symptom (52%); 61% had biopsy-proven vLS, 42% had at least one autoimmune condition, 21% had comorbid depression or anxiety, 33% were given an incorrect diagnosis prior to vLS, and 42% had documented nonadherence to topical steroids. Among the eight patients who became pregnant, four had cesarean deliveries and 63% were symptomatic during pregnancy. When treating a woman who presents with vulvar pruritus or skin changes, vLS should be considered.

Vulvar Pruritus: A Review of Clinical Associations, Pathophysiology and Therapeutic Management

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Vulvar pruritus is an unpleasant sensation and frequent symptom associated with many dermatologic conditions, including infectious, inflammatory and neoplastic dermatoses affecting the female genitalia. It can lead to serious impairment of quality of life, impacting sexual function, relationships, sleep and self-esteem. In this review, common conditions associated with vulvar itch are discussed including atopic and contact dermatitis, lichen sclerosus, psoriasis and infectious vulvovaginitis. We review the potential physiologic, environmental and infectious factors that contribute to the development of vulvar itch and emphasize the importance of addressing their complex interplay when managing this disruptive and challenging symptom.