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Non-Controlled Studies or Case Reports

Long-term assessment of effectiveness and quality of life of OnabotulinumtoxinA injections in provoked vestibulodynia.

Pelletier F, Girardin M, Humbert P, Puyraveau M, Aubin F, Parratte B.

J Eur Acad Dermatol Venereol. 2015 Oct 22. doi: 10.1111/jdv.13437.

http://www.ncbi.nlm.nih.gov/pubmed/26491951

BACKGROUND: Provoked vestibulodynia is a relatively common condition that affects sexual activity. Multidisciplinary care is indicated and OnabotulinumtoxinA injections are safe and effective treatment in this indication. **AIMS:** To assess the long-term efficacy of OnabotulinumtoxinA in provoked vestibulodynia. **MATERIALS AND METHODS:** Twenty-one patients treated with OnabotulinumtoxinA injections (50U in each bulbospongiosus muscle) 24 months prior to the study were included. Data on pain [assessed using a visual analogue scale (VAS)], quality of life [measured by the Dermatology Life Quality Index (DLQI)] and quality of sex life [assessed using the Female Sexual Function Index (FSFI)] were collected before treatment, and 3 and 24 months after injection. **RESULTS:** Nineteen patients participated in the study and 37% had no pain after 24 months. Significant improvements were noted in the VAS, DLQI and FSFI scores between baseline and 24 months post treatment ($P < 0.0001$). After 24 months, 18 patients (95%) were able to have sexual intercourse. This study was open and non-controlled. **DISCUSSION AND CONCLUSION:** 100U OnabotulinumtoxinA injections constitute an effective treatment in provoked vestibulodynia with results maintained after 2 years. They significantly improve pain, and have a positive impact on patient quality of life and sex life. Beneficial effects continue in the long-term, allowing patients to resume sexual activity.

"Will I Ever Be a True Woman?" An Exploration of the Experiences of Women With Vestibulodynia.

Groven KS, Råheim M, Håkonsen E, Haugstad GK.

Health Care Women Int. 2015 Oct 16:0.

http://www.ncbi.nlm.nih.gov/pubmed/26473661

In this study we explored the experiences of Norwegian women living with vestibulodynia, a chronic disease affecting young women all over the world. Using a phenomenological approach we conducted in-depth interviews with eight women who had struggled with vestibulodynia for several years. Our findings reveal that their efforts to fulfil their partners' sexual desires as well as their own represented an encompassing ongoing process. In addition, we highlight the interrelationship between the intensity of vulvar pain experienced by individual women and decisions women make about prioritizing their own sexual needs.

Daily Associations Among Male Partner Responses, Pain During Intercourse, and Anxiety in Women With Vulvodynia and Their Partners.

Rosen NO, Bergeron S, Sadikaj G, Delisle I.

J Pain. 2015 Sep 25. pii: S1526-5900(15)00869-X. doi: 10.1016/j.jpain.2015.09.003.
http://www.ncbi.nlm.nih.gov/pubmed/26409115

Vulvodynia is a prevalent vulvovaginal pain condition that disrupts the sexual and psychological health of affected women and their partners. Cross-sectional and daily experience studies suggest that partner responses to this pain influence the psychological and sexual sequelae of affected couples. However, their daily impact on pain and anxiety remain unknown. Using a daily diary method, 69 women (M age = 28.12, SD = 6.68) diagnosed with vulvodynia and their cohabiting partners (M age = 29.67, SD = 8.10) reported on male partner responses to women's pain and anxiety symptoms on sexual intercourse days (M = 6.54, SD = 4.99) over 8 weeks. Women also reported their pain during intercourse. Results indicated that women reported greater pain on days when they perceived higher solicitous and negative male partner responses, and on days when their male partner reported greater solicitous and lower facilitative responses. Women indicated higher anxiety symptoms on days when they perceived more negative male partner responses; men's anxiety symptoms were greater on days when they reported higher negative male partner responses. Targeting partner responses may enhance the quality and efficacy of interventions aimed at reducing pain in women with vulvodynia and couples' psychological distress. **PERSPECTIVE:** This article examines the daily associations among male partner responses, women's pain during intercourse, and anxiety in couples coping with vulvodynia. Targeting male partner responses may enhance the quality of interventions aimed at reducing women's pain and the psychological distress of couples coping with vulvodynia.

Presenting Symptoms Among Black and White Women with Provoked Vulvodynia.

Brown CS, Foster DC, Bachour CC, Rawlinson LA, Wan JY, Bachmann GA.

J Womens Health (Larchmt). 2015 Oct;24(10):831-6. doi: 10.1089/jwh.2014.5164. Epub 2015 Aug 20.
http://www.ncbi.nlm.nih.gov/pubmed/26291682

BACKGROUND: The prevalence of vulvodynia has been reported to be lower in black compared to white and Latina women. Use of different terminology to describe vulvar pain symptoms may play a role in lower prevalence. The objectives were to compare pain descriptors used by black and white women with provoked vulvodynia (PVD) to determine the effect of race on symptom reporting. **METHODS:** Ninety-two women, self-identified as black (n = 55) and white (n = 37) with clinically confirmed PVD completed a questionnaire containing demographic information and vulvar pain characteristics. Variables that were significant with race retained in the logistic regression model were included in multivariate analysis to determine the effect of race on reporting of vulvar pain symptoms. **RESULTS:** Of statistical significance, white women more often described their pain as burning as compared with black women (84% vs. 22%, $p \leq 0.0001$). White women more frequently reported their pain as stinging (51% vs. 29%, $p = 0.03$) and itching (32% vs. 15%, $p = 0.04$) as well, whereas there was a trend for black women to more often describe their pain as aching (67% vs. 49%, $p = 0.07$). Overall, white women were 19 times as likely to report their pain as burning (adjusted odds ratio [aOR] 18.51, 99% confidence interval [CI] 4.46-76.86). **CONCLUSIONS:** These data suggest that black women are less likely to self-report their vulvar pain as burning, the classic symptom of PVD. Cultural influences and different underlying pain mechanisms may contribute to differences in symptom reporting by race.

Botulinum Toxin A Injections Into Pelvic Floor Muscles Under Electromyographic Guidance for Women With Refractory High-Tone Pelvic Floor Dysfunction: A 6-Month Prospective Pilot Study.

Morrissey D, El-Khawand D, Ginzburg N, Wehbe S, O'Hare P 3rd, Whitmore K.

Female Pelvic Med Reconstr Surg. 2015 Sep-Oct;21(5):277-82. doi: 10.1097/SPV.0000000000000177.
http://www.ncbi.nlm.nih.gov/pubmed/25900057

OBJECTIVES: High-tone pelvic floor dysfunction (HTPFD) is a debilitating chronic pain disorder for many women with significant impact on their quality of life (QoL). Our objective was to determine the efficacy of electromyography-guided onabotulinumtoxinA (Botox; Allergan, Irvine, Calif) injections in treating patient's perception of pelvic pain and improving QoL measurement scores. **METHODS:** This is a prospective pilot open-label study of women with chronic pelvic pain and HTPFD who have failed conventional therapy between January 2011 and August 2013. Botox injections (up to 300 U) were done using needle electromyography guidance, from a transperineal approach, to localize spastic pelvic floor muscles (PFMs). Data were collected at baseline, 4, 8, 12, and 24 weeks after injections. This included demographics; Visual Analog Scale (VAS) scores for pain and dyspareunia; validated questionnaires for symptoms, QoL, and sexual function; Global Response Assessment scale for pelvic pain; digital examination of PFM for tone and tenderness; and vaginal manometry. Side effects were also recorded. **RESULTS:** Out of 28 women who enrolled in the study, 21 completed the 6-month follow-up and qualified for analysis. The mean (SD) age was 35.1 (9.4) years (range, 22-50 years), and the mean (SD) body mass index was 25 (4.4). Comorbidities included interstitial cystitis/bladder pain syndrome (42.9%) and vulvodynia (66.7%). Overall, 61.9% of subjects reported improvement on Global Response Assessment at 4 weeks and 80.9% at 8, 12, and 24 weeks post injection, compared with baseline. Of the subjects who were sexually active at baseline, 58.8% (10/17), 68.8% (11/16), 80% (12/15), and 83.3% (15/18) reported less dyspareunia at 4, 8, 12, and 24 weeks, respectively. Dyspareunia Visual Analog Scale score significantly improved at weeks 12 (5.6, $P = 0.011$) and 24 (5.4, $P = 0.004$) compared with baseline (7.8). Two of the 4 patients who avoided sexual activity at baseline secondary to dyspareunia resumed and tolerated intercourse after Botox. Sexual dysfunction as measured by the Female Sexual Distress Scale significantly improved at 8 weeks (27.6, $P = 0.005$), 12 weeks (27.9, $P = 0.006$), and 24 weeks (22.6, $P < 0.001$) compared with baseline (34.5). The Short-Form 12 Health Survey (SF-12) showed improved QoL in the physical composite score at all post injections visits (42.9, 44, 43.1, and 45.5 vs 40 at baseline; $P < 0.05$), and in the mental composite score at both 12 and 24 weeks (44.3 and 47.8 vs 38.5, $P = 0.012$). Vaginal manometry demonstrated significant decrease in resting pressures and in maximum contraction pressures at all follow-up visits ($P < 0.05$). Digital assessment of PFM (on a scale from 0 to 4) showed decreased tenderness on all visits (mean of 1.9, 1.7, 1.8, 1.9; $P < 0.001$) compared with baseline (2.8). Reported postinjection adverse effects included worsening of the following preexisting conditions: constipation (28.6%), stress urinary incontinence (4.8%), fecal incontinence (4.8%), and new onset stress urinary incontinence (4.8%). **CONCLUSIONS:** Electromyography-guided Botox injection into PFM could be beneficial for women with refractory HTPFD who have failed conservative therapy

Retrospective Studies

Hormonal contraception and pelvic floor function: a systematic review.
Champaneria R, D'Andrea RM, Latthe PM.
Int Urogynecol J. 2015 Sep 25.
http://www.ncbi.nlm.nih.gov/pubmed/26407563

INTRODUCTION AND HYPOTHESIS: Hormonal contraceptive use is common practice worldwide. Although the effects of hormone treatments in the pelvic region are well established, there is no clear evidence regarding their effects on incontinence, bladder, bowel, vaginal and sexual symptoms in premenopausal women. We hypothesized that hormonal contraceptives affect pelvic floor function. We therefore performed a comprehensive systematic review of published studies to determine the influence of hormonal contraception on pelvic floor functions. **METHODS:** Electronic literature databases were searched from database inception to March 2015. Keywords and medical subject headings searched for included terms and word variations for 'contraception', and 'bowel', 'vaginal', 'sexual' and 'urinary' symptoms. Studies were eligible if they looked at these symptoms in women taking hormonal contraception. Two reviewers independently screened studies for inclusion, and extracted data on study characteristics, quality and results. Data were combined where possible. **RESULTS:** Of the 429 citations identified, 13 studies were included in the review. Data were meta-analysed where possible and presented as prevalence. The results indicate statistically significant links between interstitial cystitis and oral contraceptive use at any point (ever) (OR 2.31, 95 % CI 1.03 - 5.16; p = 0.04) and vulvar vestibulitis and current oral contraceptive use (OR 2.10, 95 % CI 1.26 - 3.49; p = 0.004). The evidence is unclear in other areas. **CONCLUSIONS:** Our results indicate that oral contraceptives may have an effect on pelvic floor function. They could increase the risk of painful bladder and vulvar vestibulitis, but their effect on dyspareunia is inconsistent. However, robustly collected prospective data to establish causal associations are needed.

Sexual pain disorders.
Cabello-Santamaría F, Río-Olvera FJ, Cabello-García MA.
Curr Opin Psychiatry. 2015 Nov;28(6):412-7. doi: 10.1097/YCO.0000000000000200.
http://www.ncbi.nlm.nih.gov/pubmed/26382162

PURPOSE OF REVIEW: The purpose of this review was to assess recent research (the last 18 months) and its impact on understanding sexual pain disorders relevant to daily clinical practice. **RECENT FINDINGS:** It has been highlighted that sexual pain is related to the number of tender points, pressure pain threshold, more deliberate fear and less global positive affective associations with sexual stimuli, episiotomy, attachment styles, drug abuse and the influence of ambivalence over emotional expression in couples. The efficacy of a multidisciplinary vulvodynia programme of treatment, another type of therapy based on the fear-avoidance and pain self-efficacy model and a novel cognitive-behavioral couple therapy has been stated. **SUMMARY:** There is a gradual advance in the knowledge of sexual pain disorder etiology. At the same time different therapeutics strategies have been increasing, but it is necessary to introduce guidelines on the basis of the evidence to approach with efficacy this severe disorder.

Basic Science

Neonatal vaginal irritation results in long-term visceral and somatic hypersensitivity and increased hypothalamic-pituitary-adrenal axis output in female mice.
Pierce AN, Zhang Z, Fuentes IM, Wang R, Ryals JM, Christianson JA.
Pain. 2015 Oct;156(10):2021-31. doi: 10.1097/j.pain.0000000000000264.
http://www.ncbi.nlm.nih.gov/pubmed/26098441

Experiencing early life stress or injury increases a woman's likelihood of developing vulvodynia and concomitant dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis. To investigate the outcome of neonatal vaginal irritation (NVI), female mouse pups were administered intravaginal zymosan on postnatal days 8 and 10 and were assessed as adults for vaginal hypersensitivity by measuring the visceromotor response to vaginal balloon distension (VBD). Western blotting and calcium imaging were performed to measure transient receptor potential ankyrin 1 (TRPA1) and vanilloid 1 (TRPV1) in the vagina and innervating primary sensory neurons. Serum corticosterone (CORT), mast cell degranulation, and corticotropin-releasing factor receptor 1 (CRF1) expression were measured as indicators of peripheral HPA axis activation. Colorectal and hind paw sensitivity were measured to determine cross-sensitization resulting from NVI. Adult NVI mice had significantly larger visceromotor response during VBD than naive mice. TRPA1 protein expression was significantly elevated in the vagina, and calcium transients evoked by mustard oil (TRPA1 ligand) or capsaicin (TRPV1 ligand) were significantly decreased in dorsal root ganglion from NVI mice, despite displaying increased depolarization-evoked calcium transients. Serum CORT, vaginal mast cell degranulation, and CRF1 protein expression were all significantly increased in NVI mice, as were colorectal and hind paw mechanical and thermal sensitivity. Neonatal treatment with a CRF1 antagonist, NBI 35965, immediately before zymosan administration largely attenuated many of the effects of NVI. These results suggest that NVI produces chronic hypersensitivity of the vagina, as well as of adjacent visceral and distant somatic structures, driven in part by increased HPA axis activation.

Lower Anogenital Tract Disease Therapy Outcomes, COMET, and CROWN: Call for Research Submissions.
Andrews J.
J Low Genit Tract Dis. 2015 Oct;19(4):275-7. doi: 10.1097/LGT.0000000000000141.
http://www.ncbi.nlm.nih.gov/pubmed/26247259

OBJECTIVES: There is a problem of inconsistent and inappropriate outcome selection for research studies. We can improve the relevance of research results for women and for their physicians and clinicians by encouraging researchers to critically evaluate outcome measures, and use valid, appropriate, standardized measures. To this purpose, and to facilitate synthesis of the evidence, outcomes reported by clinical studies should be standardized for different disease conditions through the development of core outcome sets (COS). **METHODS:** There is an international effort for reaching consensus on outcome measures and establishing COS that represent agreed-upon standardized collections of outcome measures that will be reported in all studies within a clinical area. Across clinical specialties, the Core Outcome Measures in Effectiveness Trials (COMET) initiative launched in 2010. In 2014, the editors of women's health journals answered the challenge of COMET and formed the Core Outcomes in Women's Health initiative. The Journal of Lower Genital Tract Diseases is a participating member of the Core Outcomes in Women's Health consortium. **RESULTS:** There is broad inconsistency in

outcome measures and reporting in the field of lower anogenital tract diseases. No core outcome sets currently exist. Suggested target conditions in anogenital disease are vulvar dermatoses, cervical intraepithelial neoplasia, and vulvodynia. **CONCLUSIONS:** Investigators are encouraged to conduct secondary systematic research to determine previously reported primary outcome measures and suggest domains for COS. Core Outcomes in Women's health initiative and COMET encourage the formation of consensus panels of stakeholders (researchers, health care providers, patients, and others) to recommend outcome domains and COS and then publish their report.

Co-morbid Disorders

New perineal injection technique for pudendal nerve infiltration in diagnostic and therapeutic procedures.
Weinschenk S, Hollmann MW, Strowitzki T.
Arch Gynecol Obstet. 2015 Sep 15.
http://www.ncbi.nlm.nih.gov/pubmed/26374644

PURPOSE: Pudendal nerve injection is used as a diagnostic procedure in the vulvar region and for therapeutic purposes, such as in vulvodynia. Here, we provide a new, easy-to-perform perineal injection technique. **PATIENTS AND METHODS:** We analyzed 105 perineal injections into the pudendal nerve with a local anesthetic (LA), procaine in 20 patients. A 0.4 × 40 mm needle was handled using a stop-and-go technique while monitoring the patient's discomfort. The needle was placed 1-2 cm laterally to the dorsal introitus. After aspiration, a small amount of LA was applied. After subcutaneous anesthesia, the needle was further advanced step-by-step. Thus, 5 ml could be applied with little discomfort to the patient. Anesthesia in the pudendal target region was the primary endpoint of our analysis. **RESULTS:** In 93 of 105 injections (88.6 %), complete perineal anesthesia was achieved with a single injection. 12 injections were repeated. These injections were excluded from the analysis. Severity of injection pain, on visual analog scale (VAS) from 0 to 100, was 26.8 (95 % CI 7.2-46.4). Age ($\beta = 0.33$, $p < 0.01$) and the number of previous injections ($\beta = 0.35$, $p < 0.01$) inversely correlated with injection pain. Injection pain and anesthesia were not affected by BMI, the number and the side of previous injections, or order of injection. A reversible vasovagal reaction was common, but no serious adverse effects occurred. **CONCLUSION:** Perineal pudendal injection is an effective and safe technique for anesthesia in diagnostic (vulva biopsy) and therapeutic indications (pudendal neuralgia), and regional anesthesia in perinatal settings.

Effect of local estrogen therapy (LET) on urinary and sexual symptoms in premenopausal women with interstitial cystitis/bladder pain syndrome (IC/BPS).
Gardella B, Iacobone AD, Porru D, Musacchi V, Dominoni M, Tinelli C, Spinillo A, Nappi RE.
Gynecol Endocrinol. 2015 Oct;31(10):828-32. doi: 10.3109/09513590.2015.1063119. Epub 2015 Jul 31.
http://www.ncbi.nlm.nih.gov/pubmed/26291799

The association between vulvodynia and interstitial cystitis/bladder pain syndrome (IC/BPS), a chronic, debilitating disease of unknown etiology, may involve sex hormone-dependent mechanisms regulating vulvo-vaginal health. We aimed to prospectively investigate the effects of 12 weeks of local estrogen therapy (LET) on urinary/bladder and sexual symptoms in premenopausal women with IC/BPS. Thirty-four women (mean age: 36.1 ± 8.4) diagnosed with IC/BPS were treated vulvo-vaginally three-

times/week with estriol 0.5 mg cream and tested by validated questionnaires (ICSI/ICPI, pain urgency frequency [PUF], female sexual function index [FSFI]) and by cotton swab testing, vaginal health index (VHI) and maturation index (MI) before and after treatment. Vulvodynia was present in 94.1% of IC/BPS women. A significant positive effect of LET was evident on urinary and sexual function ($p < 0.001$, for both) following 12 weeks, as well as an improvement of the VHI ($p < 0.001$) and the MI ($p < 0.04$). The results of this open study indicate that 12 weeks of local estriol cream at vaginal and vestibular level may ameliorate urinary/bladder pain symptoms, as well as may improve domains of sexual function. The association between vulvar pain and bladder pain could, therefore, be related to a vaginal environment carrying signs of hypoestrogenism, but further studies are needed to clarify this issue.

Central and peripheral pain generators in women with chronic pelvic pain: patient centered assessment and treatment.
Hoffman D.
Curr Rheumatol Rev. 2015;11(2):146-66.
http://www.ncbi.nlm.nih.gov/pubmed/26088216

Women with chronic pelvic pain (CPP) often present without obvious cause on imaging studies, laboratory values or physical exam. Dysfunctional sensory processing in the central nervous system (CNS) may explain pain of unclear origin. Central sensitization (CS), a mechanism of centrally mediated pain, describes this abnormal processing of sensory information. Women with CPP often present with several seemingly unrelated symptoms. This can be explained by co-existing chronic pain syndromes occurring in the same patient. Central sensitization occurs in all of these pain syndromes, also described as dysfunctional pain syndromes, and thus may explain why several often occur in the same patient. Six of the most common pain disorders that co-exist in CPP include endometriosis, painful bladder syndrome/interstitial cysitis, vulvodynia, myofascial pain/ pelvic floor hypertonus, irritable bowel syndrome, and primary dysmenorrhea. Central pain generators, (pain originating from CS) and peripheral pain generators, (pain from local tissue damage), can both occur in each of these six conditions. These pain generators will be described. Chronic pain, specifically dysfunctional sensory processing, is recognized as a systemic disease process like diabetes to be managed as opposed to a local problem to be "fixed" or cured. A multi-disciplinary approach to assessment and treatment with a focus on improving emotional, physical and social functioning instead of focusing strictly on pain reduction is more effective in decreasing disability. This is best achieved by determining the patient's needs and perspective through a patient-centered approach. Algorithms for such an approach to assessment and treatment are outlined.

"How-To" Guide to Pelvic Floor Muscle Dysfunction.
Albrecht KB.
Clin Obstet Gynecol. 2015 Sep;58(3):546-50. doi: 10.1097/GRF.0000000000000135.
http://www.ncbi.nlm.nih.gov/pubmed/26125960

The purpose of this paper is to assist the clinician in recognizing pelvic floor muscle dysfunction in women with vulvar symptoms, to provide general treatment algorithms, and to facilitate understanding of the scientific rationale behind appropriate treatment. In short, this paper is meant to provide a "how-to" guide to pelvic floor pain management for the Ob/Gyn.

Dermatological Disorders

Vulvar Dermatoses: A Review and Update.
Simonetta C, Burns EK, Guo MA.
Mo Med. 2015 Jul-Aug;112(4):301-7.
http://www.ncbi.nlm.nih.gov/pubmed/26455062

The purpose of this article is to review six important inflammatory dermatoses of the vulva and to update readers on the new advancements in treatment of these mucosal conditions. Psoriasis, lichen sclerosis, lichen simplex chronicus and lichen planus are common vulvar conditions that cause pruritis and/or pain. PIasma cell vulvitis and desquamative inflammatory vaginitis are rare and challenging to be recognized, which often remain undiagnosed.