

Pelvic pain in patients with lower urinary tract symptoms: Challenges in diagnosis and treatment

W16, 29 August 2011 14:00 - 17:00

Start	End	Topic	Speakers
14:00	14:10	Introduction	Bernhard Schuessler
14:10	14:15	Questions	All
14:15	14:25	Definitions	 Tilemachos Kavvadias
14:25	14:30	Questions	All
14:30	14:45	Diagnostics	 Kaven Baessler
14:45	14:50	Questions	All
14:50	15:20	Treatment	All
15:20	15:30	Questions	All
15:30	16:00	Break	None
16:00	16:40	Hands-on practice on pelvic models	All
16:40	17:00	Discussion	All

Aims of course/workshop

The aim of this Workshop is to make the audience familiar with the various clinical aspects of pelvic pain, specifically in the patient with lower urinary tract symptoms (LUTS). Current definitions and diagnostic tools along with pitfalls during the assessment of pelvic pain will be discussed. Furthermore, currently available treatment options will be presented together with an up to date review of the literature. Ultimate goal is to help physicians build a consistent concept in the assessment and treatment of pelvic pain in the patient with LUTS. In a hands-on session, vaginal and rectal palpation will be practiced using pelvic models to ensure understanding of the anatomy and function

Educational Objectives

The evaluation and treatment of pelvic pain in patients with lower urinary tract symptoms (LUTS) is often performed empirically and provisionally. Published studies have shown an inconsistency and lack of consensus in its evaluation patterns but also an effort to standardize and establish an internationally accepted terminology and treatment approach. This workshop will offer to the delegates:

- 1. An up-to-date literature review of the definitions and diagnostic procedures of pelvic pain,
- 2. An understanding of the clinical importance of its relation with LUTS,
- 3. An overview of the available treatment options and
- 4. A proposal for a consistent concept in the assessment and multimodal treatment of pelvic pain in the patient with LUTS
- 5. A hands-on session on pelvic models to demonstrate and practice vaginal and rectal palpation and trigger point assessment.

Since there has not been a similar Workshop in the last years, we believe that a thorough discussion of the above mentioned topics will be of great benefit for the delegates.

W16 Pelvic pain in patients with lower urinary tract symptoms: challenges in diagnosis and treatment'

INTRODUCTION

Approximately 39% of the female population reports always, often or sometimes having pelvic pain. 15-20% of women have experienced pelvic pain of longer than one year's duration and 61% of them report that the cause of their pain is unknown. In a large telephone survey of Mathias et al. (1996) 14.7% of 5263 women aged 18-50 reported having pelvic pain within the last 3 months. African American and women with age > 35 years were less likely whereas widowed, divorced or separated women were more likely to report chronic pelvic pain.

Pelvic pain is often associated with lower urinary tract symptoms (LUTS) or vice versa. The Standardisation Sub-committee of the International Continence Society (ICS) describes such situations as 'Genito-Urinary Pain Syndromes' and 'Symptom Syndromes Suggestive of Lower Urinary Tract Dysfunction', such as 'painful bladder syndrome (or interstitial cystitis)', 'vaginal pain syndrome', 'pelvic pain syndrome' and 'urgency'. The diagnosis is often vague, by exclusion and mainly symptom- driven.

Reported pain sites vary in publications in women with LUTS: bladder and bladder neck, vaginal, vulvar, urethral, suprapubic and perineal pain; low back pain, pain in the lower abdomen, muscle pain (levator ani, pubo- and iliococcygeus, piriformis, coccygeus and obturator internus); pain in the anterior thighs, buttocks and posterior thighs.

It has been estimated that up to 43% of women with voiding or storage bladder symptoms also have pain symptoms. But also, 63-93% of women with chronic pelvic pain report concomitant LUTS.

ASSESSMENT

Symptoms assessment with questionnaires

- Interstitial Cystitis Symptom Index (ICSI)
- Interstitial Cystitis Problem Index (ICPI)
 - o two 4-question indices for frequency/urgency, nocturia and pain, specified as 'burning, pain, discomfort or pressure in the bladder'
 - o to be used as a complementary tool and not for screening purposes.
 - o validation with IC/PBS patients
- Pelvic Pain and Urgency/Frequency (PUF) Symptom Scale
 - o 12-item index on urgency, frequency, sexual function and pain 'associated with the bladder or in the pelvis' (vagina, lower abdomen, urethra, perineum)
 - o validation using the intravesical potassium sensitivity test (PST).
- McGill Pain Questionnaire (MPQ)
 - o validated scale of rating pain for quantitative measurements of pain
 - o use of specific word-descriptors, such as 'pricking', 'pulling', 'sharp', 'dull', 'heavy', 'squeezing' and others
- Visual analogue scales

According to the terminology of ICS, pain of IC/PBS is isolated suprabupic pain, related to bladder filling; bladder pain is defined by ICS as felt suprapubically or retropubically, it usually increases with bladder filling and it may persist after voiding.

External examination

- Examination for vulvodynia (cotton swab)
- Scars, distorsion, infection/inflammation,
- Position of perineum in relation to ischial spines
- Perineal movement on contraction and Valsalva
- Sensitivity tests

Vaginal examination

- Urethra, bladder, (uterus)
- Levator ani muscle with all parts plus piriformis and obturator internus
- Anterior and posterior vaginal wall
- bladder neck
- Exam at rest, during pelvic floor contraction and Valsalva and/or coughing

Interstitial cystitis / painful bladder syndrome

NIDDK criteria for the diagnosis of IC/PBS: a) suprapubic, pelvic, urethral, vaginal or perineal pain on bladder filling relieved by emptying; b) glomerulations on endoscopy, c) decreased compliance on cystometrogram and/or d) Hunner's ulcers.

The definition of ICS includes: suprapubic pain related to bladder filling, accompanied by symptoms such as frequency, in the absence of other obvious pathology

Chronic pelvic pain - Pelvic pain syndrome

There is no generally accepted definition of chronic pelvic pain. Many accept a duration of 6 or more as the major criterion for chronic pelvic pain. The ICS describes the pelvic pain syndrome as the occurrence of persistent or recurrent episodic pelvic pain associated with symptoms suggestive of lower urinary tract, sexual, bowel or gynaecological dysfunction, with the absence of proven infection or obvious pathology.

Dyspareunia

Peters et al. (2008) reported that 77% of women with IC/PBS have deep dyspareunia

Urethral syndrome

Weiss (2001) mentioned the urethral syndrome as a cause of CPP in patients with urgency/frequency and pelvic pain trigger points. Parsons et al. (2001) found that patient with clinical urethral syndrome had a positive PST, but at a lower rate than patients with IC/PBS, implying a mutually existing dysfunction of the urothelium [68].

Urgency

According to the definitions of the ICS, urgency is the complaint of a sudden compelling desire to pass urine which is difficult to defer. According to Driscoll et al. (2001) 41% of patients with IC/PBS present with urgency, frequency or nocturia as first symptom before the diagnosis of IC/PBS is made. Van Os-Bossagh et al. found that 37% of CPP patients had serious urinary urgency, whereas in 18% urge was triggered or increased by lower abdominal pain and in 20% lower abdominal pain was triggered by urge.

Trigger points

- Are important in the evaluation of pelvic pain
- Tu et al.: women with CPP have levator ani and piriformis muscle trigger points and pain threshold in those sites is lower than in controls
- trigger points often coexist with generalized pelvic pain and irritative LUTS
- Empirical impression: there is an association between overactive bladder symptoms and pain in different sites of the pelvis without any obvious pathology

TREATMENT

The therapy of women with chronic pelvic floor pain aims to treat the underlying pathophysiology of pain or might be simply symptom-driven. Unfortunately, often there is only limited symptom relief.

Nerve Stimulation

Kessler et al. (2007) presented the results of a national registry in Switzerland reporting on 209 patients (181 females and 28 males) who received sacral nerve stimulation for refractory lower urinary tract dysfunction, eleven of whom were diagnosed with chronic pelvic pain syndrome. After a first follow up (median 7 days) and evaluation of the test phase, seven patients underwent permanent implantation. The authors report a decrease of the median pain score from 8 at baseline at the first follow up and 2 (IQR 1-4) at the last follow up (median 10 months, IQR 5-11), as well as a subjective symptom improvement of 100% and 65% respectively. Zabihi et al. report an improvement in the visual analogue pain score of up to 40%, in patients with chronic pelvic pain who were treated with bilateral S2-S4-sacral neuromodulation. Patients with interstitial cystitis also seem to benefit from sacral neuromodulation. Maher et al. report on 15 women with intractable interstitial cystitis who received percutaneous stimulation of the S3 sacral root. Mean bladder pain score decreased from 8.9 to 2.4, average voided volume increased significantly and quality of life variables improved at a follow up of 7 to 10 days after stimulation. Peters and Konstandt also showed that patients with interstitial cystitis reduced their narcotic requirements from 81.6mg/day to 52.0mg/day morphine dose equivalents, which corresponds to a decrease of 36% (p=0.015), after a sacral neuromodulation therapy of 15.4 (range 7.4-23.1) months.

Van Balken et al. presented the results of a prospective multicenter trial testing the percutaneous tibial nerve stimulation as a treatment of chronic pelvic pain. They included 11 women. After 12 weeks of treatment, 42 % of the patients were considered subjective responders. Of those, 43% reported a decrease of mean pain score of >50%. Patients with deep pain (perineal, perianal and vaginal) and shorter period of symptoms seemed to respond better to therapy than patients who report superficial pain (suprapubic, groin). Congregado et al. also report on a cohort of 51 females with lower urinary tract irritative symptoms who received tibial nerve stimulation, 21 of whom had hypogastric pain. At a mean follow up of 21 months, 7 patients (33%) reported still having hypogastric pain. In another report on tibial nerve stimulation of Vandoninck et al., responders with urge incontinence report higher scores in the pain domain of the SF-36 questionnaire, after a twelve week treatment.

Peters et al. in a prospective, single-blind, randomized, cross-over trial, compared the results of sacral versus pudendal nerve stimulation on thirty subjects with voiding dysfunction and reported that the pudendal method was superior to sacral for pelvic pain on a 7-point pain scale(p=0.024).

Local treatments

Local treatments include hydrodistension and intravesical injections and instillations. They are mainly used in patients with interstitial cystitis/painful bladder syndrome (IC/PBS). Riedl et al. presented a cohort of 126 females with IC/PBS, who were treated with a mean of 12.2 weekly intravesical instillations of 40mg hyaluronan (a derivative from hyaluronic acid). They reported a symptom improvement in 85% of the patients. The mean VAS pain score decreased from 8.5 ± 1.7 at baseline to 3.5 ± 2.7 (p=0.0001) after a mean follow up of 6.5 months (range 0-23). Cervigni et al. treated 23 IC/PBS female patients with a combination of hyaluronic acid 1.6% and chondroitin 2.0%, weekly for 20 weeks and then every 2 weeks for 3 months. They report a decrease of the mean VAS pain score from 5.65 (range 1-9) at baseline to 3.83 (range 0-9) at a mean follow up of 5 (range 3-8) months (27). Leppilahti et al. combined 4 weekly hyaluronic acid instillations with hydrodistension and reported a 75% decrease in pain among responders. Shao et al. showed that the combination of hydrodistention with hyaluronic acid instillations has a significant effect on pain score up to nine months after treatment.

Hydrodistention alone seems to only have a short term effect. Cole et al. reported subjective improvement at 1 and 6 months follow up in 61% and 0% respectively in group 1 and 54% and 7% respectively in group 2.

Aghamir et al. performed a 6-week treatment with weekly intravesical instillations with Bacillus Calmette-Guerin (BCG) and reported a decrease in VAS pain score from 4.2 ± 0.7 at baseline to 2.4 ± 0.7 at 24 months follow up, which corresponds to a 43.1% decrease of pain (p=0.001). Peters et al., also after a 6 week treatment with BCG in 12 females with IC/PBS, report a decrease of VAS pelvic pain score of up to 81% (p=0.02, mean pain score decreased from 4.3 ± 0.9 at baseline to 0.8 ± 0.3 at a 27 months follow up) (21).

One placebo controlled, double blind study, comparing intravesical alkalinized lidocaine versus placebo in patients with IC/PBS found a decrease in pain score which was not significant, both in the lidocaine and in the control group, although overall bladder symptoms improved more patients of the lidocaine group (30% versus 9%, p=0.012).

Oral agents

Burkhard et. al treated 103 women with urgency/frequency and chronic urethra and/or pelvic pain with 100mg doxycycline twice daily for two weeks and 100mg once daily for another two weeks. After treatment 30% of the patients considered themselves cured and 41% reported subjective improvement.

Theocharides et al. report on the use of CystoProtek (a dietary supplement designed to improve glycosaminoglycans of the urothelium) in 227 women with IC/PBS. Treatment included four capsules / day (120mg glycosamine sulfate, 150mg chondroitin sulfate, 10mg

hyaluronate sodium, 150mg quercetin and 20mg rutin / capsule). Patients experienced a 48.8% reduction in the mean VAS pain score (p=0.0001) after 11.2±8.7 months.

Pentosan polysulfate sodium (PPS) seems not to be an effective treatment in patient with IC/PBS. Davis et al. present the results of a randomized, double-blind clinical trial, which included 20 patients, who received 200mg PPS twice daily during 18 weeks and intravesical PPS twice a week for the first 6 weeks (treatment group), and 19 patients who received 200mg PPS twice daily during 18 weeks and intravesical placebo also twice a week for the first 6 weeks (placebo group). In both groups there were no significant changes in pain scores at 6-, 12- and 19-week follow up, although subjective improvement and Health Related Quality of Life scores were higher in the treatment group. Nickel et al., also in a randomized trial with 103 subjects receiving oral pentosan polysulfate sodium for interstitial cystitis, reported that patients could benefit from an early initiation of the treatment (within 6 months of establishing the diagnosis of IC/PBS).

In patients without IC/PBS but with vague, nonspecific urinary and pelvic or genital complaints, amitryptiline (25-100mg daily) could be therapeutically useful, as shown in a case series from Pranikoff and Constantino.

Lentz et al. presented a case series with 15 women with chronic, cyclic irritable bladder symptoms and pelvic pain who underwent diagnostic and / or therapeutic laparoscopy and cystoscopy with hydrodistention for the above mentioned symptoms. 67% of the patients had findings of both interstitial cystitis and endometriosis. Subjective improvement was reported in 8 out of 9 patients after a treatment with oral contraceptives and in 5 out of 6 in women who received leuprolide acetate.

Physical therapy

Oyama et al. present a manual therapeutic approach for females with interstitial cystitis and high-tone pelvic floor dysfunction. Twenty-one symptomatic women underwent transvaginal massage using the Thiele technique twice a week for 5 weeks. The authors report a decrease of pain score from a mean of 5.4 at baseline to 3.5 (p=0.005) at short-term follow up (2 weeks after treatment) and to 2.6 (p=0.005) at long-term follow (4.5 months after treatment). Improvement of pelvic floor tone was also statistically significant both at short and long-term follow up. Manual therapy of pelvic floor myofascial trigger points also seems to reduce pain of interstitial cystitis. Weiss reports a decrease of average 3.74 units on a zero to ten pain score scale after an eight to twelve week manual trigger point treatment with one to two visits/week.

According to two reports of Skilling and Petros, a combination of electrotherapy and pelvic floor exercises seems to have high subjective success rates (up to 76%) in patients with chronic pelvic pain, but also a high dropout rate (up to 47%).

Other treatment options

Gottsch et al. present data from a randomized, double-blind, placebo controlled trial, comparing botulinum toxin A and placebo (saline) periurethral injection for IC/PBS. Both cases and controls did not report any improvement after treatment.

Magnet stimulation therapy does not appear to be useful in non specific pelvic pain according to a report of Kirschner-Hermanns and Jakse.

Rofeim et al. reported on 24 patients with interstitial cystitis who were treated with YAG Laser under cystoscopic control to ablate the Hunner's ulcers of the bladder mucosa. The authors report a decrease in pain score from 9.1 preoperatively to 1.2 (p=0.003) 1 week after treatment.

One prospective randomized controlled study used guided imagery as treatment of interstitial cystitis. Cases (25-minute guided imagery twice daily for 8 weeks) showed significantly lower pain scores compared with controls (25-minute rest twice daily for 8 weeks).

CASE PRESENTATIONS

- Dypareunia on penetration and overactive bladder
- Pelvic pain and pelvic organ prolapse
- Pelvic pain after implantation of non-absorbable vaginal mesh for pelvic organ prolapse
- Buttock pain and suprapubic cramps
- Dyspareunia and trigger points

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References

Aboseif S, Tamaddon K, Chalfin S, Freedman S, Kaptein J (2002) Sacral neuromodulation as an effective treatment for refractory pelvic floor dysfunction. Urology 60:52-56

Aboseif S, Tamaddon K, Chalfin S, Freedman S, Kaptein J. Sacral neuromodulation as an effective treatment for refractory pelvic floor dysfunction. Urology 2002;60:52-56

Abrams P, Cardozo L, Fall M, et al (2002) The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodynam 21:167–178

Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. (2003) The standardisation of terminology in lower urinary tract dysfunction: report from the standardisation sub-committee of the International Continence Society. Urology 61:37-49

ACOG practice bulletin (2004) Chronic pelvic pain. Obstet Gynecol 103:589-605

Aghamir S, Mohseni M, Arasteh S. (2007) Intravesical Bacillus Calmette-Guerin for treatment of refractory interstitial cystitis. Urol J 4:18-23

Berry S, Bogart L, Pham C, Liu K, Nyberg, Stoto M et al. (2010) Development, Validation and Testing of an Epidemiological Case Definition of Interstitial Cystitis / Painful Bladder Syndrome. J Urol 183:1848-1852 Brewer M, White W, Klein F, Klein L, Waters W (2007) Validity of pelvic pain, urgency and frequency questionnaire in patients with interstitial cystitis/painful bladder syndromes. Urology 70:646-49

Burkhard F, Blick N, Hochreiter W, Studer U (2004) Urinary urgency and frequency and chronic urethral and/or pelvic pain in females. Can Doxycycline help? J Urol 172:232-235

Carrico D, Peters K, Diokno A (2008) Guided imagery for Women with interstitial cystitis: results of a prospective, randomized controlled pilot study. J Altern Complement Med 14:53-60

Cervigni M, Natale E, Nasta L, Padoa A, Lo Voi R, Porru D. (2008) A combined intravesical therapy with hyaluronic acid and chondroitin for refractory painful bladder syndrome / interstitial cystitis. Int Urogynecol J 19:943-947

Chu P, Ma W, Wong C, Chu R, Cheng C, Tse J, et al. (2008) The destruction of the lower urinary tract by ketamine abuse: a new syndrome BJU Int 102:1616-22

Clauw D, Schmidt M, Radulovic D, Singer A, Katz P, Bresette J (1997) The relationship between fibromyalgia and interstitial cystitis. J Psychiat Res 31:125-131

Clemens J, Markossian T, Meenan R, O'Keeffe-Rosetti M, Calhoun E (2007) Overlap of voiding symptoms, storage symptoms and pain in men and women. J Urol 178:1354-58

Clemens J, Meenan R, O'Keeffe Rosetti M, Brown S, Gao S, Calhoun E (2005) Prevalence of interstitial cystitis symptoms in a managed care population. J Urol 174:576-580

Clemons J, Arya L, Myers D (2002) Diagnosing interstitial cystitis in women with chronic pelvic pain. Obstet Gynecol 100:337-41

Cole E, Scarpero H, Dmochowski R. (2005) Are patient symptoms predictive of the diagnostic and / or therapeutic value of hydrodistention? Neurourol Urodyn 24:638-642

Congregado Ruiz B, Pena Outeirino X, Campoy Martinez P, Leon Duenas E, Leal Lopez A (2004) Peripheral afferent nerve stimulation for treatment of lower urinary tract irritative symptoms. Eur Urol 45:65-69

Davis E, Khoudary S, Talbott E, Davis J, Regan L (2008) Safety and Efficacy of the use of intravesical and oral pentosan polysulfate sodium for interstitial cystitis: a randomized double blind clinical trial. J Urol 179:177-185

Doggweiler-Wiygul R, Wiygul J (2002) Interstitial cystitis, pelvic pain and the relationship to myofascial pain and dysfunction: a report on four patients. World J Urol 20:310-14

Driscoll A, Teichman J (2001) How do patients with interstitial cystitis present? J Urol 166:2118-20

Dwyer P (2011) Chronic pelvic pain in urogynecological practice. Int Urogynecol J 22:381-382

Everaert K, Devulder J, De Muynck M, Stockman S, Depaepe H, De Looze D, et al. (2001) The pain cycle: implications for the diagnosis and treatment of pelvic pain syndromes. Int Urogynecol J 12:9-14

Fall M, Oberpenning F, Peeker R. (2008) Treatment of interstitial cystitis 2008: Can we make evidence based decisions? European Urology 54:65-78

Fauconnier A, Dallongeville E, Huchon C, Ville Y, Fallisard B (2009) Measurement of acute pelvic pain intensity in gynecology: a comparison of five methods. Obstet Gynecol 113:260-9

FitzGerald M, Koch D, Senka J (2005) Visceral and cutaneous sensory testing in patients with painful bladder syndrome. Neurourol Urodyn 24:627-32

FitzGerald M, Senton K, Brubaker L (2005)Localisation of the urge to void in patients with painful bladder syndrome. Neurourol Urodynam 24:633-37

Forrest J, Mishell D (2009) Breaking the cycle of pain in interstitial cystitis/painful bladder syndrome: toward standardisation of early diagnosis and treatment: consensus panel recommendations. J Reprod Med. 54:2-14

Gardella B, Porru D, Ferdeghini F, Gabellotti E, Napi R, Rovereto B, et al. (2008) Insight into urogynecologic features of women with interstitial cystitis/painful bladder bladder syndrome. Eur Urol 54:1145-53

Giannantoni A, Porena M, Consatntini E, Zucchi A, Mearini L, Mearini E. (2008) Botulinum A toxin

intravesical injection on patients with painful bladder syndrome: 1 year follow up. J Urol 179:1031-1034

Gillenwater J, Wein A (1998) Summary of the NIADDK, Workshop on interstitial cystitis J Urol 140:203

Gillenwater JY, Wein AJ (1988) Summary of the National Institute of Arthritis, Diabetes, Digestive and Kidney Diseases Workshop on Interstitial Cystitis, National Institutes of Health, Bethesda, Maryland, August 28-29, 1987. J Urol 140:203-6

Gottsch H, Miller J, Yang C, Berger R (2011) A Pilot study of Botulinum Toxin for Interstitial cystitis / Painful bladder syndrome Neurourol Urodynam 30:93-96

Hanno P, Dmochowski R (2009) Status of International Consensus on Interstitial Cystitis/Bladder Pain Syndrome/Painful Bladder Syndrome: 2008 Snapshot. Neurourol Urodynam 28:274-286

Hanno P, Lin A, Nording J, Nyberg L, Van Ophoven A, Ueda T, Wein A (2010) Bladder Pain syndrome International Consultation on Incontinence. Neurourol Urodynam 29:191-198

Howard F (2003) Chronic pelvic pain. Obstet Gynecol 101:594-611

Jamieson D, Steege J (1996) The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices. Obstet Gynecol 87:55-8

Kessler T, Buchser E, Meyer S, Engeler D, Al-Khodairy A, Bersch U, Iselin C, Roche B, Schmid D, Schurch B, Zrehen S, Burkhard F. (2007) Sacral neuromodulation for refractory lower urinary tract dysfunction: results of a nationwide registry in Switzerland European Urolology 51:1357-1363

Kessler T, Buchser E, Meyer S, Engeler D, Al-Khodairy A, Bersch U, et al., on behalf of the Swiss Sacral Neuromodulation Working Group (2007) Sacral neuromodulation for refractory lower urinary tract dysfunction: results of a nationwide registry in Switzerland. Eur Urol 51:1357-63

Kirschner-Hermanns R, Jakse G (2003) Magnet stimulation therapy: a simple solution for the treatment of stress and urge incontinence. Urologe 42:819-822

Lazzeri M, Beneforti P, Spinelli M, Zanollo A, Barbagli G, Turini D (2000) Intravesical resinferatoxin for the treatment of hypersensitive disorder: a randomised placebo controlled study. J Urol 164:676-9

Lazzeri M, Spineli M, Beneforti P, Malaguti S, Giardiello G, Turini D (2004) Intravesical Infusion of

Resiniferatoxine by a temporary in situ drug delivery system to treat interstitial cystitis: a pilot study. European Urology 45:98-102

Lazzeri M, Spinelli M, Beneforti P, Giardiello G, Turini D (2004) Intravesical infusion of Resinferatoxin by a temporary in situ drug delivery system to treat interstitial cystitis: a pilot study. Eur Urol 45:98-102

Lentz G, Bavendam T, Stenchever M, Miller J, Smalldridge J (2002) Hormonal manipulation in women with chronic, cyclic irritable bladder symptoms and pelvic pain. Am J Obstet Gynecol 186:1268-73

Leppilahti M, Hellstrom P, Tammela T. (2002) Effect of diagnostic hydrodistension and four intravesical

hyaluronic acid instillations on bladder ICAM-1 intensity and association of ICAM-1 intensity with clinical response in patients with interstitial cystitis. Urology 60:46-51

Leppilahti M, Sairanen J, Tammela T, Aaltomaa S, Lehtoranta K, Auvinen A (2005) Prevalence of clinically confirmed interstitial cystitis in women: a population based study in Finland. J Urol 174:581-3

Lifford K, Curhan G (2009) Prevalence of painful bladder syndrome in older women. Urology 73:494-8

Maher C, Carey M, Dwyer P, Schluter P (2001) Percutaneous sacral nerve root neuromodulation for intractable interstitial cystitis. J Urol 165:884-6

Mathias S, Kuppermann M, Liberman R, Lipschutz R, Steege J (1996) Chronic pelvic pain: prevalence, health-related quality of life and economic correlates. Obstet Gynecol 87:321-7

Melzack R (1975) The McGill Pain Questionnaire: major properties and scoring methods. Pain 1:277-99

Minaglia S, Ozel B, Bizhang R, Mishell D (2005) Increased prevalence of interstitial cystitis in women with detrusor overactivity refractory to anticholinergic treatment. Urology 66:702-6

Nickel J, Kaufman D, Zhang H, Wan G, Sand P (2007) Time to initiation of pentosan polysulfate sodium treatment after interstitial cystitis diagnosis: effect on symptom improvement Urology 71:57-61

Nickel J, Moldwin R, Lee S, Davis E, Henry R, Wyllie M. (2008) Intravesical alkalinized lidocaine (PSD597) offers sustained relief from symptoms of interstitial cystitis and painful bladder syndrome BJU Int 103:910-918

Nickel J, Tripp D, Teal V, Propert K, Burks D, Foster H, et al. (2007) Sexual function is a determinant of poor quality of life for women with treatment refractory interstitial cystitis. J Urol 177:1832-36

Novi J, Jeronis S, Srinivas S, Srinivasan R, Morgan M, Arya L (2005) Risk of irritable bowel syndrome and depression in women with interstitial cystitis: a case control study. J Urol 174:937-940

O'Leary M, Sant G, Fowler F, Whitmore K, Sporalich-Kroll J (1997) The interstitial cystitis symptom index and problem index. Urology 49:58-63

Ottem D, Carr L, Perks A, Lee P, Teichman J (2007) Interstitial cystitis and female sexual dysfunction. Urology 69:608-10

Oyama I, Rejba A, Lukban J, Fletcher E, Kellogg-Spadt S, Holzberg A, Whitmore K (2004) Modified Thiele massage as therapeutic intervention for female patients with interstitial cystitis and high-tone pelvic floor dysfunction. Urology 64:862-865

Parsons C, Dell J, Stanford E, Bullen M, Kahn B, Waxwell T, et al. (2002) Increased prevalence of interstitial cystitis: previously unrecognised urologic and gynecologic cases identified using a new symptom questionnaire and intravesical potassium test. Urology 60:573-78

Parsons C, Dell J, Stanford E, Bullen M, Kahn B, Willems J (2002) The prevalence of interstial cystitis in gynecological patients with pelvic pain, as detected by intravesical potassium sensitivity. Am J Obstet Gynecol 187:1395-400

Parsons C, Tatsis V (2004) Prevalence of interstitial cystitis in young women. Urology 64:866-70

Parsons C, Zupkas P, Kellogg Parsons J (2001) Intravesical potassium sensitivity in patients with interstitial cystitis and urethral syndrome. Urology 57:428-33

Peters K, Carey J, Konstandt D. (2003) Sacral neuromodulation for the treatment of refractory interstitial cystitis: outcomes based on technique Int Urogynecol J 14:223-228

Peters K, Carrico D, Ibrahin I, Diokno A (2008) Characterisation of a clinical cohort of 87 women with interstitial cystitis/painful bladder syndrome. Urology 71:634-40

Peters K, Carrico D, Kallinowski S, Ibrahim I, Diokno A (2007) Prevalence of pelvic floor dysfunction in patients with interstitial cystitis. Urology 70:16-18

Peters K, Diokno A, Steinwert B, Gonzalez J. (1998) The efficacy of intravesical Bacillus Calmette-Guerrin in the treatment of interstitial cystitis: long-term follow up. J Urol 159:1483-87

Peters K, Feber K, Bennett R. (2005) Sacral versus pudental nerve stimulation for voiding dysfunction: a prospective, single-blinded, randomised control trial Neurourol Urodyn 24:643-647

Peters K, Girdler B, Carrico D, Ibrahim I, Diokno A (2008) Painful bladder syndrome/interstitial cystitis and vulvodynia: a clinical correlation. Int Urogynecol J 19:665-9

Peters K, Killinger K, Carrico D, Ibrahim I, Diokno A, Grazziotin A (2007) Sexual function and sexual distress in women with interstitial cystitis: a case-control study. Urology 70:543-47

Peters K, Killinger K, Ibrahim I, Villalba P (2008) The relationship between subjective and objective assessments of sacral neuromodulation effectiveness in patients with urgency-frequency. Neurourol Urodynam 27:775-8

Peters K, Konstandt D. (2004) Sacral Neuromodulation decreases narcotic requirements in refractory interstitial cystitis BJU Int 93:777-779

Petros P, Skilling P (2001) Pelvic floor rehabilitation in the female according to the integral theory of female urinary incontinence. First report. Obstet Gynecol 94:264-269

Pitts M, Ferris J, Smith A, Shelley J, Richters J (2008) Prevalence and correlates of three types of pelvic pain in a nationally representative sample of Australian women. MJA 189:138-143

Porru D, Politano R, Gerardini M, Giliberto G, Stancati S, Pasini L, et al. (2004) Different clinical presentation of interstitial cystitis syndrome. Int Urogynecol J 15:198-202

Pranikoff K, Constantino G (1998) The use of Amitriptiline in patients with urinary frequency and pain. Urology 51 (Suppl 5A):179-181

Price D, McGrath P, Rafii A, Buckingham B (1983) The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 17:45-56

Reiter R (1990) Occult somatic pathology in women with chronic pelvic pain. Clin Obstet Gynecol 33:154-160 Riedl C, Engelhardt P, Daha K, Morakis N, Pflueger H. (2008) Hyaluronan treatment of interstitial cystitis / painful bladder syndrome Int Urogynecol J 19:717-721

Rofeim O, Hom D, Freid R, Moldwin R (2001) Use of the Neodymium: YAG Laser for interstitial cystitis: A prospective study. J Urol 166:134-136

Rosenberg M, Hazzard M (2005) Prevalence of interstitial cystitis symptoms in women: a population based study in the primary care office. J Urol 174:2231-34

Rosenberg M, Page S, Hazzard M (2007) Prevalence of interstitial cystitis in a primary care setting. Urology 69:48-52

Seth A, Teichman J (2008) Differences in the clinical presentation of interstitial cystitis/painful bladder syndrome in patients with or without sexual abuse history. J Urol 180:2029-33

Shaker H, Hassouna M (1998) Sacral nerve neuromodulation: an effective treatment for refractory urge incontinence. J Urol 159:1516-19

Shaker H, Hassouna M (1998) Sacral root neuromodulation in idiopathic nonobstructive chronic urinary retention J Urol 159:1476-1578

Shao Y, Shen Z, Rui W, Zhou W (2009) Intravesical istillation of hyaluronic acid prolonged the effect of bladder hydrodistention in patients with severe interstitial cystitis. Urology 75:547-551

Sibert L, Rigaud J, Delavierre D, Labat J. Chronic pelvic pain: epidemiology and economic impact. Prog Urol 2010 Nov;20(12):872-85

Sidman J, Lechtman M, Lyster E (2009) A unique hypnotherapeutic approach to interstitial cystitis: a case report. J Reprod Med 54:523-4

Skilling P, Petros P (2004) Synergistic non-surgical management of pelvic floor dysfunction: second report. Int Urogynecol J 15:106-110

Stanford E, Koziol J, Feng A (2005) The prevalence of interstitial cystitis, endometriosis, adhesions and vulvar pain in women with chronic pain. J Minim Inv Gynecol 12:43-9

Stanford E, Mattox T, Parsons J, McMurphy C (2006) Prevalence of benign microscopic hematuria among women with interstitial cystitis: implications for evaluations of genitourinary malignancy. Urology 67:946-49

Stanford E, McMurphy C (2007) There is a low incidence of recurrent bacteriuria in painful bladder syndrome/interstitial cystitis patients followed longitudinally. Int Urogynecol J 18:551-4

Stones W, Cheong Y, Howard F, Singh S. Interventions for treating chronic pelvic pain in women. Cochrane Database of Systematic Reviews 2005, Issue 2. Art. No.: CD000387.DOI:10.1002/14651858.CD000387

Theocharides T, Kempuraj D, Vakali S, Sant G (2008) Treatment of refractory interstitial cystitis / painful bladder syndrome with CystoProtek, an oral multi-agent natural supplement Can J Urol 15:4410-4

Tu F, As-Sanie S, Steege J (2006) Prevalence of pelvic musculoskeletal disorders in a female chronic pain clinic. J Reprod Med 51:185-9

Tu F, Fitzgerald C, Kuiken T, Farell T, Norman H (2007) Comparative measurement of pelvic floor pain sensitivity in chronic pelvic pain. Obstet Gynecol 110:1244-8

Van Balken M, Vandoninck V, Messelink B, Vergunst H, Heesakkers J, Debruyne F, et al. (2003) Percutaneous tibial nerve stimulation as neuromodulative treatment for chronic pelvic pain. Eur Urol 43:158-63

Van Balken M, Vergunst H, Bemelmans B (2006) Prognostic factors for successful percutaneous tibial nerve stimulation. Eur Urol 49:360-5

Van de Merwe J, Nordling J, Bouchelouche P, Bouchelouche K, Cervigni M, Daha LK, et al. (2007) Diagnostic Criteria, Classification and Nomenclature for Painful Bladder Syndrome/Interstitial Cystitis: An ESSIC proposal. Eur Urol 53:60-67

Van Ophoven A, Rossbach G, Oberpenning F, Herlte L (2004) Hyperbaric oxygen fot the treatment of interstitial cystitis: long term results of a prospective study. Eur Urol 46:108-113

Van Os-Bossagh P, Pols T, Hop W, Bohnen A, Vierhout M, Drogendijk A. Voiding symptoms in chronic pelvic pain. Eur J Obstet Gynecol Rep Biol 2003;107:185-190

Vardoninck V, Van Balken M, Finazzi Agro E, Petta F, Caltagirone C, Heesakkers J, Kiemeney L, Debruyne F, Bemelmans B. (2003) Posterior tibial nerve stimulation in the treatment of urge incontinence Neurourol Urodyn 22:17-23

Warren J, Howard F, Cross R, Good J, Weissman M, Wesselman U, et al. (2009) Antecedent non bladder syndromes in case control study of interstitial cystitis/painful bladder syndrome. Urology 73:52-7

Warren J, Langenberg P, Greenberg P, Diggs C, Jacobs S, Weeselmann U (2008) Sites of pain from interstitial cystitis/painful bladder syndrome. J Urol 180:1373-77

Warren J, Meter W, Greenberg P, Horne L, Diggs C, Tracey J (2006) Using the International Continence Society's definition of painful bladder syndrome Urology 67:1138-43

Weiss J (2001) Pelvic floor myofascial trigger points: manual therapy for interstitial cystitis and the urgency-frequency syndrome. J Urol 166:2226-2231

Weiss J (2001) Pelvic floor myofascial trigger points: manual therapy for interstitial cystitis and the urgency-frequency syndrome. J Urol 166:2226-31

Welk B, Teichman J. (2008) Dyspareunia response in patients with interstitial cystitis treated with intravesical lidocaine, bicarbonate and heparin. Urology 71:67-70

Williams R, Hartmann K, Steege J (2004) Documenting the current definitions of chronic pelvic pain: implications for research. Obstet Gynecol 103:686-91

Zabihi N, Mourtzinos A, Grey Maher M, Shlomo R, Rodriguez L. (2008) Short-term results of bilateral S2-S4 sacral neuromodulation for the treatment of refractory interstitial cystitis, painful bladder syndrome, and chronic pelvic pain Int Urogynecol J 19:553-557

Zondervan K, Yudkin P, Vessey M, Jenkinson C, Dawes M, Barlow D, et al. (2001) Chronic pelvic pain in the community - Symptoms, investigations and diagnoses. Am J Obstet Gynecol 184:1149-55