

## A REVIEW OF THE ANNUAL SCIENTIFIC MEETING OF THE INTERNATIONAL CONTINENCE SOCIETY (ICS), 26-30 AUGUST 2013, BARCELONA, SPAIN

*Jane Meijlink*

It was perhaps not so surprising to find that this year's ICS annual scientific meeting held in Spain was well attended by Spanish and Latin American health professionals. Since the ICS is a multi-disciplinary society, this meeting is attended by nurses, physiotherapists, doctors and specialists with an interest in urinary and faecal incontinence and pelvic floor dysfunction and pain from around the world.

The International Painful Bladder Foundation (IPBF) once again had an exceptionally busy booth at this meeting and distributed huge piles of brochures, leaflets, flyers and CDs on IC/BPS and associated disorders, with a new (pilot) fact sheet on ketamine abuse and the urinary tract, linking in well with the many presentations and posters on this increasingly widespread party-drug phenomenon, particularly among young people. This fact sheet is available on the IPBF website. [Click here...](#)



Our newly updated 57 page IPBF brochure – which was very popular in Barcelona – can be found at: [http://www.painful-bladder.org/pdf/Diagnosis&Treatment\\_IPBF.pdf](http://www.painful-bladder.org/pdf/Diagnosis&Treatment_IPBF.pdf)

The IPBF also displayed a poster on its booth with clear images of Hunner lesion (courtesy of Professor Andrey Zaitcev from Moscow and ESSIC). This generated great interest and it was evident that many urologists felt a lack of confidence with regard to identifying lesions in clinical practice. It would be useful to have a workshop dedicated specifically to this topic.

**The images used for the IPBF's Barcelona Hunner lesion poster can be found on the ESSIC website at: <http://www.essic.eu/videomenu.html> along with a large number of videos showing lesions on cystoscopy with hydrodistension.**

Despite the fact that urology societies are tending to focus mainly on urologic cancer these days, interest in IC/BPS and chronic pelvic pain at the ICS and among its members fortunately continues. This year many abstracts on IC/BPS were submitted from all parts of the world and particularly from East Asia where much research is taking place. However, it was regrettably evident that many of the best abstracts submitted were accepted as Posters only or even Read as Title, and not selected for Podium Presentation. Once again, everyone was using different terminology and studies presented included patients diagnosed on the basis of a wide variety of criteria, often with no distinction between patients with or without lesions, leading to some confusion. This underlined how vital it is for agreement to be reached worldwide on diagnostic criteria, terminology and definitions. Similar terminology confusion could be seen this year in the ketamine-associated cystitis studies, with many different terms in use.

We have included a brief overview of abstracts presented in Barcelona related to our field. Some were basic science, some on treatment including a number of trials with hyaluronic acid, chondroitin sulphate, botox, triamcinolone and mirabegron, while one interesting abstract from Leuven, Belgium reported that the study team had identified BK polyoma virus (BKPyV) in the urine of virtually all their patients with the classic lesion form of PBS/IC, suggesting that it might be a potential new therapeutic target. One abstract looks at the controversial issue of glomerulations.

The abstract summaries have been divided into two sections, first IC/BPS and secondly abstracts on ketamine including studies comparing ketamine and IC/BPS.

Further information about the ICS Barcelona meeting can be found on the ICS website: [www.ICS.org](http://www.ICS.org).

By going to <http://www.ics.org/2013/programme>, you can click on the sessions and read the full abstracts from each session. There is also an author index and search available.

## INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME

### Abstract 51

#### **THE ANTIMICROBIAL PEPTIDE AND MAST CELL ACTIVATOR, BETA DEFENSIN 2 (BD2) IS PERSISTENTLY EXPRESSED IN THE BLADDER OF WOMEN WITH INTERSTITIAL CYSTITIS**

*Ali A, Lanz M, Townes C, Robson W, Hall J, Pickard R.*

The authors from Newcastle, UK note that while there is increasing evidence that individuals with IC may have a defect in the protective function of the bladder Glycosaminoglycan (GAG) mucous layer, the aetiology of this defect is not known. However, one proposed mechanism is that an inherited or acquired defect in the innate host epithelial defence mechanisms results in an abnormal response to infection causing injury to the epithelial GAG layer and leading to an on-going permeability defect with lasting damage to the barrier function of urothelium. Within the human urinary tract, the innate immune response is characterised by the constitutive or inducible expression of antimicrobial peptides (AMPs). These small cationic peptides are critical to host anti-microbial defence. In Crohn's disease, which like IC is also thought to involve a defect in the GAG layer, altered expression of AMPs has been demonstrated in the gut. Ali and colleagues therefore proposed that a similar defect in the expression of AMPs within the bladder may be implicated in IC. They hypothesised that women with IC have altered expression of endogenous AMPs resulting in an aberrant immune response which leads to a breakdown in the epithelial GAG layer. They recruited 10 female patients with IC defined by the European Society for the Study of Interstitial Cystitis (ESSIC) criterion and compared bladder biopsies and overnight urine collections with samples collected from a similar population of 8 women with active UTI and 31 control patients with no disease. The resulting data suggest that secretion of BD2, a potent anti-microbial, is significantly increased in IC patients and that this response has similarities to that seen during urinary tract infection. This indicates that despite the absence of infection in IC, the bladder is still mounting a response akin to that seen during cystitis with appreciable amounts of BD2 released in the bladder and expression of BD2 appears to correlate with the magnitude of the inflammation. As well as acting as an antimicrobial, BD2 is recognised as a mast cell activator and chemotractant which may provide clues to the origin of the mastocytosis commonly seen in IC urothelium and the damage caused by their activation. The authors conclude that antimicrobial peptide, BD2 appears to play a key role in an aberrant chronic innate immune

response similar to that seen acutely during infection – this may be an important underlying mechanism for the urothelial pathology seen in IC.

Poster: [http://www.ics.org/Abstracts/Publish/180/000051\\_poster.pdf](http://www.ics.org/Abstracts/Publish/180/000051_poster.pdf)

#### Abstract 52

##### **REDUCED EXPRESSION OF STEM CELL MARKER CD44V9 IN UROTHELIAL BASAL CELLS IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME**

*Furuta A, Suzuki Y, Koike Y, Egawa S, Yoshimura N.*

Furuta and colleagues from Japan and Pittsburgh report that although the aetiology of interstitial cystitis/bladder pain syndrome (IC/BPS) is still not known, one of the most consistently found histopathological changes is erosion or thinning of the bladder epithelium, which may contribute to urothelial dysfunction in IC/BPS patients. However, the mechanism inducing urothelial dysfunction in IC/BPS is still not fully clarified, although the antiproliferative factor (APF) identified in the bladder epithelial cells from IC/BPS patients may be a contributing factor. CD44, a major adhesion molecule for the extracellular matrix, has reportedly been increased in the bladder from IC/BPS patients. Recent studies also showed that the CD44 variant isoform 9 (CD44v9) is identified as a marker of epithelial cells with stem cell-like activity. Here, Furuta and colleagues examined the expression of CD44v9 as well as other epithelium-related markers such as E-cadherin and cytokeratin in the bladder epithelium from patients with IC/BPS. Their results suggest that histological findings in the bladder epithelium such as erosion, thinning or vacuolation are associated with decreased expression of CD44v9 in urothelial basal cells in IC/BPS patients. Because CD44v9 is one of the markers of epithelial cell with stem cell-like activity, the reduction of CD44v9 expression may contribute to decreased regenerative function of the bladder epithelium in IC/BPS. The authors concluded that reduced expression of CD44v9 in the bladder epithelial basal cells may be an important pathophysiological basis for urothelial dysfunction in IC/BPS.

#### Abstract 53

##### **DEVELOPMENT AND EVALUATION OF E-HEALTH SYSTEM FOR CARING PATIENTS WITH INTERSTITIAL CYSTITIS / BLADDER PAIN SYNDROME (IC/BPS)**

*Wu H C, Lee M H, Chen Y, Lin J, Chen W C.*

Wu and colleagues from Taiwan note that the controversies surrounding management of the IC/BPS are fuelled by the heterogeneity of urological and non-urological symptoms leading to poor quality of life and the need for a multidisciplinary care team. In a previous study, it was demonstrated that an Internet information and communication technology (ICT) system to monitor physiological signs, scheduling and reminders about medication, and healthcare education. It was demonstrated to be effective in early identification of adverse events to avoid hospital readmission or to reduce the length of stay in hospital. It was hypothesized that applying this system to take care of IC/BPS patients could improve urological symptoms and quality of life. So the aim of this prospective case control study from Taiwan was to apply information and communication technology (ICT) to improve the quality of life for IC/BPS patients. The E-health system, supporting health education and providing SMS (short message service) for self-management, was demonstrated to be effective in improving urological symptoms, measured by VAS pain score and urgent score and quality of life, measured by SF-36 of IC/BPS patients during the 8 weeks observation period. It was concluded that Internet healthcare education is useful to consolidate patients' healthy dietary habits and lifestyles, as well as to self-manage their symptoms.

#### Abstract 54

**REVISIT BLADDER GLOMERULATIONS AFTER HYDRODISTENTION- ARE GLOMERULATIONS A PATHOGNOMONIC SIGN FOR INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME? A PROSPECTIVELY SYSTEMATIC STUDY**

*Kuo Y, Kuo H.*

Glomerulations after cystoscopic hydrodistention (CHD) have been used in the past in the diagnosis of interstitial cystitis/bladder pain syndrome (IC/BPS). However, the characteristic cystoscopic findings of patients with urological diseases other than IC/BPS have not been fully investigated yet. The aim of this study from Taiwan was to systematically evaluate the rate of glomerulations developed after CHD in patients with common urological diseases. Patients with urological conditions requiring cystoscopy or transurethral procedures were prospectively enrolled in this study. All patients received CHD under general or spinal anesthesia before elective endoscopic operations. Patients with urinary tract infection, gross hematuria or bladder stones were excluded. The presence of glomerulations after CHD was not only found in patients with IC/BPS but also in those with other common urological diseases. A mild degree of chronic inflammation involving the urothelium might account for the development of glomerulations.

**Abstract 55**

**THE IMPORTANCE OF BIO-PSYCHOLOGICAL CARE IN WOMEN WITH INTERSTITIAL CYSTITIS / BLADDER PAIN SYNDROME (IC/BPS) WHO HAVE CHILD ABUSE EXPERIENCE AND PSYCHIATRIC DYSFUNCTION**

*Chen W C, Lee M H, Chiu C, Wu H C.*

According to Chen and colleagues, early stressful experience has been considered as an environment risk factor for IC/PBS. However, some reported higher incidence of child sexual abuse; others observed higher incidence of physical and emotional abuse. The results of this study indicated that women with IC/PBS endorsed higher incidences on various traumatic experiences except for sexual maltreatment in childhood. Moreover, positive correlation between female patients with interstitial cystitis with a history of abuse and depression was also noted. From this they concluded that a multidisciplinary approach and multimodal therapy should be considered for holistic care in IC/PBS patients.

**Abstract 56**

**IMPACT OF INTRAVESICAL HYALURONIC ACID ON SEXUAL FUNCTION OF WOMEN WITH INTERSTITIAL CYSTITIS: A PROSPECTIVE MULTICENTER STUDY ON 103 PATIENTS**

*Hung M, Tsai C, Su T*

While intravesical therapy with hyaluronic acid (HA) is a standard treatment for interstitial cystitis (IC), little is known about its impact on sexual function of patients. This study aimed to evaluate the changes in sexual functioning in women undergoing intravesical therapy with HA for IC. A total of 103 women with cystoscopically diagnosed IC were enrolled in this prospective, multi-centre, observational database study. The authors concluded that many factors affect sexual functioning in women; however, sexual function may improve along with improvement in bladder symptoms after intravesical therapy with HA for IC.

Poster: [http://www.ics.org/Abstracts/Publish/180/000056\\_poster.pdf](http://www.ics.org/Abstracts/Publish/180/000056_poster.pdf)

**Abstract 58**

**THE THERAPEUTIC RESPONSE OF HYDRODISTENSION FOR INTERSTITIAL CYSTITIS PATIENTS**

*Kim J J, Chung J W, Park J S, You H W, Cho W J, Lee K.*

The aim of this study by Kim and colleagues was to determine the therapeutic efficacy of hydrodistension of the bladder for interstitial cystitis(IC) and identify predictive factors of the

presence and duration of the therapeutic response. The study included 117 consecutive patients (22 male, 95 female) treated by hydrodistension of the bladder for IC diagnosed by urodynamic study, cystoscopy, history taking, physical exam, voiding diary, O'Leary-Sant IC Symptom Index (ICS), O'Leary-Sant IC Problem Index (ICPI). Hydrodistension was performed under general anaesthesia. 45.2% of patients demonstrated a therapeutic response at 1 month after treatment. More daytime frequency and nocturia predicted the lower therapeutic response and shorter response duration of hydrodistension for IC diagnosed by detailed examination including urodynamic study and cystoscopy. The smaller MCC $\leq$ 150cc independently predicted the shorter sustentation of therapeutic efficacy in the response group.

#### Abstract 60

##### **INTRAVESICAL ONABOTULINUMTOXINA INJECTIONS DO NOT BENEFIT PATIENTS WITH ULCER TYPE INTERSTITIAL CYSTITIS**

*Jhang J, Jiang Y, Kuo H.*

Jhang and colleagues from Taiwan report that ulcer type and non-ulcer type interstitial cystitis/bladder pain syndromes (IC/BPS) are considered different disease entities. In clinical experience, patients with ulcer type IC/BPS often suffer from intractable lower abdominal pain, and the pain usually does not respond to medical treatment. Previous study suggested botulinum toxin type A (BoNT-A) injections seemed promising for treating symptoms of IC/BPS, including reducing bladder pain and increasing bladder capacity. This study evaluated and compared the treatment outcomes of BoNT-A injections for treatment of ulcer and non-ulcer type IC/BPS. Forty consecutive patients with IC/BPS for whom conventional treatments failed were prospectively enrolled in this study. Patients were classified as having ulcer or non-ulcer IC/BPS by cystoscopic findings. All patients received four sets of intravesical BoNT-A 100U injections every six months for two years regardless of whether or not symptoms improved. The result of their study showed patients with ulcer IC/BPS had smaller bladder capacity and more severe symptoms at baseline. The repeated intravesical BoNT-A injections improved IC/BPS symptoms scores, increased FBC and cystometric bladder capacity, and relieved pain in patients with non-ulcer IC/BPS. But repeat BoNT-A injections did not benefit patients with ulcer IC/BPS. These results implied patients with ulcer IC/BPS have more severe and localized inflammation which could not be relieved after intravesical BoNT-A injections. It was therefore concluded that repeated intravesical BoNT-A injections did not benefit any patient with ulcer type IC/BPS.

#### Abstract 120

##### **A PROSPECTIVE RANDOMISED CONTROLLED MULTICENTRE TRIAL COMPARING INTRAVESICAL DMSO AND CHONDROITIN SULPHATE 2 FOR PAINFUL BLADDER SYNDROME /INTERSTITIAL CYSTITIS**

*De Ridder D, Klockaerts K, Plancke H, Ost D, Van der Aa F.*

In a subgroup of PBS/IC patients, typical cystoscopic findings can be noted and this defines this subgroup as interstitial cystitis. The treatment of PBS/IC is empirical. Bladder hydrodistension under anesthesia, tricyclic antidepressants, antihistaminics and intravesical DMSO instillations are the only treatments for which some evidence exists. Intravesical treatment with DMSO has stood the test of time and is the only FDA approved intravesical treatment of PBS/IC. DMSO however is also used as a solvent in the chemical industry and is in fact used 'off label' in this indication. One of the theories on which intravesical treatment is based, claims that the glycosaminoglycan layer, which protects the urothelial cells is damaged. DMSO, Chondroitin sulphate, hyaluronic acid and heparin have been used to repair the GAG layer with variable clinical success. Chondroitin sulphate seems to be promising, but comparative data are lacking. Assessing the outcome of such treatments is difficult. Objective parameters such as daytime and nighttime frequency may not always reflect the impact of the condition on the life of the patient. In total 36 women consented and were included with a mean

age of 57 (range 27-75y). 22 were allocated to the chondroitin group, 14 to the DMSO group. In the DMSO group 57% withdrew consent during the trial and only 6 patients concluded the trial. Major reasons for withdrawal were pain during and after instillation, intolerable garlic odour and lack of efficacy. In the chondroitin group 27% withdrew consent because of insufficient effect or side effects such as pain at instillations. De Ridder and colleagues report that the major finding of this study was the high drop-out in the DMSO group. DMSO is considered to be the gold standard in intravesical therapy for PBS/IC. This is based on one crossover study where the DMSO arm showed improvement in 53% and the placebo arm in 18% of 33 patients. Other studies are non-randomised and often only show a responder analysis and not an ITT analysis. The chondroitin group performed significantly better in pain reduction and nocturia and in subjective outcome. Chondroitin was also better tolerated than DMSO. Based on this interim analysis the clinical evaluation committee proposed to stop the trial due to the high number of drop-outs in the DMSO arm. It was therefore concluded that intravesical chondroitin sulphate 2% (Uracyst™) is a viable treatment for BPS/IC with minimal side effects. DMSO, while being considered the gold standard should be used with caution and with active monitoring of side effects. More randomised controlled studies are needed on intravesical treatments for BPS/IC.

Poster: [http://www.ics.org/Abstracts/Publish/180/000120\\_poster.pdf](http://www.ics.org/Abstracts/Publish/180/000120_poster.pdf)

#### Abstract 148

##### **ANTISENSE OLIGONUCLEOTIDE TARGETING NGF ATTENUATES BLADDER PAIN BEHAVIOR IN RAT WITH EXPERIMENTAL COLITIS**

*Kawamorita N, Yoshikawa S, Pradeep T, Mb C, Yoshimura N.*

Pelvic organ “cross sensitization” is suspected to contribute to clinically overlapping symptoms in patients with chronic pelvic pain syndrome (CPPS) such as irritable bowel syndrome (IBS) and bladder pain syndrome/interstitial cystitis (BPS/IC). Previous animal studies demonstrated that experimental colitis evoked bladder overactivity associated with hyperexcitability of afferent neurons innervating the bladder although it has not been investigated whether this colitis model exhibits bladder pain. On the other hand, overexpression of nerve growth factor (NGF) in the bladder has been shown to play an important role in the symptom development in BPS/IC patients. The authors, from Pittsburgh and Oakland, recently reported that instillation of liposome conjugated with antisense oligonucleotide (OND) targeting NGF into the bladder suppressed bladder overactivity in a rat model of acute cystitis. This study was performed to explore whether pain behaviour induced by bladder irritation and NGF expression in the bladder are increased after colitis and whether instillation of liposomal-ODN conjugates into the bladder can suppress pain behaviour and NGF expression in a rat model of experimental colitis. This study shows that the rat model of experimental colitis is useful to study the mechanism inducing bladder pain behaviour in addition to bladder overactivity that has previously been shown. The liposomal antisense treatment targeting NGF in the bladder could be a new, effective modality for the treatment of bladder pain in CPPS patients including those with BPS/IC and IBS, in whom the cross-sensitization mechanism is involved in the emergence of overlapping symptoms from different pelvic organs.

#### Abstract 150

##### **INHIBITION OF BLADDER HYPERSENSITIVITY BY INTERLEUKIN 4 (IL-4) GENE THERAPY USING HERPES SIMPLEX VIRUS (HSV) VECTORS IN RATS WITH CYCLOPHOSPHAMIDE INDUCED CYSTITIS**

*Oguchi T, Yokoyama H, Funahashi Y, Yoshikawa S, Nishizawa O, Goins W F, Goss J R, Glorioso J C, Chancellor M, Tyagi P, Yoshimura N.*

Oguchi and colleagues first examined whether chemical cystitis induced by cyclophosphamide (CYP) enhances pain behaviour elicited by bladder irritation using resiniferatoxin (RTx). Furthermore, they

investigated effects of gene therapy using replication-deficient HSV vectors expressing anti-inflammatory cytokine IL-4 (S4IL4) on pain behaviour and bladder overactivity induced by intravesical application of RTx in this cystitis rat model. They conclude that bladder inflammation evokes bladder hypersensitivity and overactivity, which are suppressed by anti-inflammatory cytokine therapy mediated by replication-deficient HSV vectors. Thus, IL-4 gene therapy could be a new strategy for treating bladder pain and/or urinary frequency in patients with PBS/IC.

#### Abstract 151

### **ACTIVATION OF TRANSCRIPTION FACTOR CAMP RESPONSE ELEMENT-BINDING PROTEIN (CREB) SIGNALLING IN AFFERENT PATHWAYS UNDERLIES NEUROGENIC BLADDER DYSFUNCTION AND CHRONIC PELVIC PAIN IN IC/BPS.**

*Pan X, Lei Q, Villamor A, McMillan M, Malykhina A.*

Chronic pelvic pain is a common symptom of many functional pelvic disorders including interstitial cystitis/bladder pain syndrome (IC/BPS). Recent studies suggest that bladder pain in IC/BPS could result from long-lasting sensitization in neural pathways induced by pathophysiological changes in neighbouring pelvic organs. Previous work by these researchers established that transient colitis triggers the development of a neurogenic bladder and chronic pelvic pain via release of pro-inflammatory neuropeptides such as calcitonin gene-related neuropeptide (CGRP) in the urinary bladder. CGRP gene expression is controlled by a transcription factor cAMP response element-binding protein (CREB), a critical modulator of neuronal plasticity. The goal of this work in rats was to clarify the role of CREB in cross-sensitization in the pelvis and associated bladder pain. The authors report that their data suggest that activation of CREB signalling in bladder sensory and spinal neurons by noxious peripheral stimulation is important in programming the molecular changes underlying bladder discomfort and pain in neurogenic IC/BPS. They conclude that identification of the cellular and molecular mechanisms responsible for the functional interplay between the nervous and urological systems provides a scientific basis for the advancement of novel pharmacological therapies for the treatment of IC/BPS and chronic pelvic pain.

#### Abstract 333

### **MODELING THE EFFECT OF NITRIC OXIDE UPON INFLAMMATION IN THE RAT URINARY BLADDER**

*Winder M, Aronsson P, Johnsson M, Tobin G.*

Winder and colleagues from Gothenburg note that painful bladder syndrome is somewhat of an umbrella term for chronic inflammatory diseases characterized by urgency, urinary frequency and pain. One of these diseases is interstitial cystitis. Many of the symptoms of interstitial cystitis are directly associated to changes occurring in the bladder contractile response. A common way to induce a syndrome similar to interstitial cystitis is by injection with the alkylating agent cyclophosphamide, a drug often used in cancer treatment. In the current study, the aim was to study the effect of nitric oxide upon cholinergic and purinergic contraction during cyclophosphamide-induced inflammation in the rat urinary bladder. Further, the data were modelled in order to detect minute changes which would otherwise be indiscernible. It was concluded that the current study gives rise to the possibility that nitric oxide can act in both a facilitatory and inhibitory fashion in the rat urinary bladder during inflammation, affecting both cholinergic and purinergic contraction.

#### Abstract 453

### **POSSIBLE INVOLVEMENT OF PROSTAGLANDIN E2 IN THE PATHOPHYSIOLOGY OF INTERSTITIAL CYSTITIS**

*Wada N, Ameda K, Okada H, Date I, Hashizume K, Kita M, Iwata T, Matsumoto S, Kakizaki H.*

Interstitial cystitis (IC), non-specific inflammatory disease of the bladder, presents with a constellation of symptoms including urinary frequency, urgency and bladder pain. Prostaglandin E2

(PGE2) is known to be associated with inflammation or pain. There have been controversies about the involvement of PGE2 in the pathophysiology of IC. Urinary PGE2 in patients with IC was elevated in some reports, but not in other reports. Therefore the aim of this study was to examine the precise role of PGE2 in the pathophysiology of IC. Study patients were those with IC who were diagnosed based on the presence of characteristic symptoms such as bladder pain or discomfort and cystoscopic findings including Hunner lesions or glomerulations. The authors report that overproduction of PGE2 in the bladder seems to have a significant role in the pathophysiology of IC. Blockade of the action of PGE2 may lead to relieving symptoms in IC patients.

**Abstract 549**

**SUPRASPINAL PROJECTION OF SEROTONERGIC AND ADRENERGIC PATHWAYS MODULATES NOCICEPTIVE TRANSMISSION IN THE LOWER URINARY TRACT OF RATS**

*Mitsui T, Kannno Y, Kitata T, Moriya K, Nonomura K.*

Since the etiology of bladder pain syndrome (BPS) / interstitial cystitis (IC), which cause persistent pelvic pain, pressure, or discomfort perceived to be related to the lower urinary tract (LUT), is unknown, BPS/IC management is currently focused on pain relief. Although 5-hydroxytryptamine (5-HT) and norepinephrine have been implicated as mediators of endogenous analgesic mechanisms in the descending pain pathways, the effect of these supraspinal projection has been still unknown in the LUT. In the present study from Japan, Mitsui and colleagues investigated the effect of descending serotonergic and adrenergic pathways on nociception in the LUT in female Sprague-Dawley rats. It was concluded that supraspinal projections of descending serotonergic and adrenergic pathways into the lumbosacral spinal cord modulate nociceptive transmission in the LUT. Administration of a SNRI attenuates nociceptive transmission in the LUT, which could result from enhancement of descending serotonergic and adrenergic pathways.

**Abstract 551**

**DIFFERENTLY INCREASED MRNA EXPRESSION PATTERN OF GENES INVOLVED IN PRONOCICEPTIVE INFLAMMATORY REACTIONS IN BLADDER TISSUE OF CLASSIC AND NON-CLASSIC INTERSTITIAL CYSTITIS.**

*Nomiya A, Homma Y, Tagaya M, Oyama T, Takagaki K, Niimi A, Nishimatsu H, Igawa Y.*

Although the pathogenesis of interstitial cystitis (IC) is still unknown, recent studies suggest the difference in pathogenesis of classic and non-classic IC. In this study from Tokyo, mRNA expression of transient receptor potential (TRP) family of channels and acid-sensing ion channel 1 (ASIC1) was assayed in bladder tissue of classic and non-classic IC, and compared with that in controls. Patients with IC scheduled for hydrodistension or those with non-invasive bladder cancer undergoing transurethral resection (as controls) were enrolled. Diagnosis of IC was based on the clinical guidelines for IC. 50 subjects (non-classic IC, 17; classic IC, 22; control, 11) were enrolled and all the IC patients were compatible with NIDDK criteria. The present study demonstrated increased expression of genes involved in pronociceptive inflammatory reactions in classic IC, including TRPM2, and TRPV1, TRPV2, TRPV4, ASIC1, NGF and CXCL9, whereas overexpression was limited only for TRPV2 and NGF mRNA in non-classic IC. Overexpression of TRPM2 mRNA demonstrated in the bladder of classic IC, which was the most pronounced among TRP family, has not been reported previously. It was concluded that different expression pattern suggests distinct pathophysiology for classic and non-classic IC. The genes and their products are potential candidates for biomarkers or novel therapy targets for IC.

**Abstract 553**

**CYTOKINE RESPONSES IN BPS/IC ESSIC TYPE 3C**

*Logadottir Y, Lindholm C, Jirholt P, Gjertsson I, Fall M, Delbro D, Peeker R.*

Bladder Pain Syndrome (BPS), previously denominated Interstitial Cystitis (IC), is a heterogeneous syndrome of unknown etiology. BPS/IC Type 3C (classic IC) is characterized by Hunner lesions and characteristic inflammatory infiltrates in the bladder wall, whereas non-Hunner BPS/IC (nonulcer IC) has no circumscribed lesions and no inflammatory changes. The authors note that they have previously shown large amounts of nitric oxide (NO) evaporation from the bladder wall in patients with BPS Type 3C compared to undetectable NO in non-Hunner BPS bladders or healthy controls. However, the factors, responsible for the increased NO production are not fully known. The aim of the present study was to analyse the local cytokine response in relation to inducible Nitric Oxide Synthase (iNOS) expression and mast cell infiltration in BPS/IC ESSIC Type 3C. The authors concluded that their results support the notion that activation of iNOS, with high production of NO, is an important mechanism behind the inflammation seen in BPS/IC Type 3C.

**Abstract 555**

**TRIAMCINOLONE INJECTION VS. FULGURATION FOR TREATMENT OF HUNNER'S ULCER-TYPE INTERSTITIAL CYSTITIS: PRELIMINARY RESULTS OF A PROSPECTIVE RANDOMIZED TRIAL**

*Oliver J, Klutke C.*

Classic interstitial cystitis (IC) is characterized by Hunner's ulcers and affects 5-10% of all IC patients. While both fulguration and steroid injection of Hunner's ulcers have been described as successful treatments, to date no studies have compared these options. Oliver and Klutke from Washington sought to compare treatment response and duration between these two therapies for Hunner's ulcers. Patients presenting with Hunner's ulcer-type IC were recruited for the study beginning in January 2012. They included patients with urgency, frequency, and chronic pelvic pain consistent with IC as well as a cystoscopy and biopsy confirming the presence of Hunner's ulcers. Patients were excluded if they had an active urinary tract infection, history of bladder malignancy, recent bladder surgery, allergy to triamcinolone, were pregnant or unable to undergo anesthesia. While the number of patients evaluated thus far limits any definitive conclusions, their preliminary results agree with prior studies that submucosal injection of triamcinolone for Hunner's ulcer-type IC offers improvement in patient symptoms and quality of life. The authors conclude that preliminary results of a prospective randomized trial comparing triamcinolone injection vs. fulguration for the treatment of Hunner's ulcer-type IC suggest that triamcinolone injection of Hunner's ulcers results in improvement in symptoms and quality of life for patients and may offer a more durable response when compared with fulguration. They further note that this study is ongoing and future results including more patients and longer follow-up will be helpful in directly comparing these treatment options

**Abstract 556**

**CAN ULTRASOUND ESTIMATED BLADDER WEIGHT PREDICT THE SEVERITY OF GLOMERULATION, AND BLADDER CAPACITY IN WOMEN WITH INTERSTITIAL CYSTITIS / BLADDER PAIN SYNDROME (IC/BPS)**

*Lee M H, Wu H C, Chen W C.*

Recently, the clinical diagnosis of Interstitial Cystitis / Bladder Pain Syndrome (IC/BPS) has been based on the Society for Urodynamics and Female Urology (SUFU) and ESSIC definition as an unpleasant sensation perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than 6 weeks or 6 months duration, in the absence of infection or other identifiable causes. Cystoscopic hydrodistension with different severity of glomerulations which was observed after hydrodistension had become primary cystoscopic features in IC/BPS. However, the anesthetized cystoscopic hydrodistension may have the complication of bladder perforation. Recent studies demonstrated that a non-invasive ultrasound method of estimating bladder weight (UEBW) has been proposed as diagnostic for outflow tract obstruction and detrusor overactivity in men and

women. The aim of our study is to investigate that the connection between IC/BPS groups and non-IC/BPS groups and the relativity of IC/PBS patients and their bladder muscle thickness, bladder weight and the severity of glomerulation to evaluate a simple, reliable, safe and economical approach by using noninvasive, highly accurate and highly consistent three-dimensional(3D) ultrasound imaging. The bladder wall thickness and ultrasound estimated bladder weight of IC/BPS patients are higher than controls; however, no statistic difference could be found. Therefore, these two could not be used as the clinical measure tools. No obvious differences are found among IC/BPS patients' bladder thickness, weight, the severity of glomerulation and bladder capacity.

**Abstract 557**

**STABILITY AND DISCRIMINANT VALIDITY OF BRAZILIAN VERSION OF THE QUESTIONNAIRE "PELVIC PAIN AND URGENCY/FREQUENCY (PUF) PATIENT SYMPTOM SCALE"**

*Fernandes M, Lopes M H, D'Ancona C.*

Despite the still small number of patients diagnosed with interstitial cystitis in Brazil, the test-retest reliability and discriminant validity of the instrument "Pelvic Pain and Urgency/Frequency (PUF) Patient Symptom Scale" was carried out satisfactorily. In future studies the intention is to carry out further assessments of psychometric measures with larger number of patients.

**Abstract 558**

**POLYOMAVIRUS BK – A POTENTIAL NEW THERAPEUTIC TARGET FOR PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS?**

*Van der Aa F, Beckley I, De Ridder D.*

The purpose of this particularly interesting study from Leuven in Belgium was to correlate the level of urinary BK polyoma virus (BKPyV) with clinical findings and treatment outcomes, in patients with painful bladder syndrome/interstitial cystitis (PBS/IC). Urine samples were collected from 15 patients with PBS/IC and 8 control patients (with other pelvic pain syndromes, urolithiasis, overactive bladder and benign prostatic hyperplasia). BKPyV titres were quantitatively determined using real time PCR. The PBS/IC patients subsequently underwent cystoscopy, hydrodistension and bladder biopsy. Finally, a chart review was performed in order to correlate PBS/IC subtype and treatment outcomes with BKPyV status. Positive BKPyV titres were found in 11 out of 15 PBS/IC patients but in none of the controls. Cystoscopy was performed in 13 of the 15 PBS/IC patients (in 2 BKPyV positive patients, cystoscopy was not performed). Bladder ulceration and glomerulations were observed in all 9 BKPyV positive PBS/IC patients but only 1 out of 4 BKPyV negative patients (Figure 1). None of the non-ulcerative PBS/IC patients had BKPyV positive urine. Viral titres were not predictive of the clinical course however, 3 patients with the highest viral titres eventually underwent cystectomy. The authors report that they identified BKPyV in the urine of virtually all their patients with ulcerative PBS/IC. This finding suggests there may be a pathophysiological association between the virus and the haemorrhagic manifestations of PBS/IC. Classifying PBS/IC patients into BKPyV positive or negative groups may prove useful in future research on markers of disease prognosis and the subtypes of PBS/IC. The authors conclude that BKPyV may therefore have a role as a potential therapeutic target in PBS/IC.

*Editor's Note: The **BK virus** is a member of the [polyomavirus](http://en.wikipedia.org/wiki/BK_virus) family. Past infection with the BK virus is widespread, but significant consequences of infection are uncommon, with the exception of the immunocompromised and the immunosuppressed.*

[http://en.wikipedia.org/wiki/BK\\_virus](http://en.wikipedia.org/wiki/BK_virus)

**Abstract 559**

**EXPRESSION OF AND LOCALIZATION OF ESTROGEN RECEPTOR BETA IN IC/PBS BLADDER**

*Niimi A, Nomiya A, Matsuzawa Y, Yamada Y, Fukuhara H, Nishimatsu H, Homma Y*

Since interstitial cystitis/ painful bladder syndrome (IC/PBS) is a female-dominant disease and the prevalence in postmenopausal woman is relatively high, the involvement of estrogen in the pathogenesis of IC/PBS has been concerned. Estrogen receptor beta (ER beta) is identified as a dominant estrogen receptor in human bladder and recently there have been two reports that the expression of ER beta was decreased in rat chemical cystitis model and ER beta KO murine model showed the similar histological findings resembling IC/PBS, such as infiltration of inflammatory cells and erosion of epithelium. The aim of this study from Japan was to investigate the expression and localization of ER beta in the bladder of IC/PBS patients. IC/PBS patients compatible with the NIDDK criteria were included. They completed O'Leary and Sant's indices and underwent cystoscopy followed by biopsy and hydrodistension under spinal anesthesia. Bladder biopsies were collected from 11 patients with Hunner lesion, 10 patients of non-ulcer type and 12 controls. Unlike previous reports on animal models, immunohistochemical staining showed the elevated expression of ER beta positive cells in erosive epithelium of ulcer-type IC/PBS. The authors conclude that the results of this study suggest that expression of ER beta might not be related to IC/PBS pathophysiology.

**Abstract 560**

**DECREASE OF URINARY NERVE GROWTH FACTOR BUT NOT BRAIN-DERIVED NEUROTROPHIC FACTOR IN PATIENTS WITH INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME SUCCESSFULLY TREATED WITH INTRAVESICAL HYALURONIC ACID**

*Jiang Y, Lee C, Liu H, Kuo H.*

Jiang and colleagues from Taiwan report that some studies on intravesical hyaluronic acid (HA) treatment for IC/BPS patients showed symptom improvement in a broad range between 30% and 85%. However, they lacked strong evidence to prove the anti-inflammatory effects of HA treatment for IC/BPS. Urinary neurotrophins including nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) increased in IC/BPS patients, and could potentially be used as urinary biomarkers in the diagnosis and treatment prognosis of lower urinary tract diseases. This study was designed to investigate the changes of urinary NGF and BDNF levels in IC/PBS patients after HA treatment, and try to discover potentially reliable biomarkers of IC/BPS. From January 2009 to December 2010, thirty-three consecutive patients with IC/BPS were prospectively enrolled in this study, and a group of 45 age-matched normal subjects served as controls. All IC/BPS patients received 9 times of intravesical HA instillations in a 6-month treatment course, including 4 weekly intravesical instillations of 40 mg of HA (50 mL, 0.08%) followed by 5 monthly HA instillations. Urine samples were collected for measuring urinary NGF and BDNF levels at baseline and 2 weeks after the last HA treatment. Patients were also assessed for the VAS of pain, daily frequency and nocturia episodes, functional bladder capacity (FBC) and global response assessment (GRA). Patients with a GRA decrease of 2 after HA treatment was considered as responders. The urinary NGF and BDNF levels were compared between IC/BPS patients and the controls, and between the responders and nonresponders to HA treatment. They found that urinary NGF and BDNF levels were significantly higher in IC/BPS patients compared to the controls. Urinary NGF, but not BDNF, levels decreased significantly after intravesical HA therapy. The reduction in urinary NGF levels was significant in responders with VAS reduction and GRA improvement. These results suggest that inflammation in IC/BPS bladders can be improved following HA therapy.

**Abstract 561**

**CLINICAL COMPARISON OF INTRAVESICAL HYALURONIC ACID AND HYALURONIC ACID-CHONDROITIN SULPHATE THERAPY FOR PATIENTS WITH PAINFUL BLADDER SYNDROME/INTERSTITIAL CYSTITIS**

*Gulpinar O, Kayis A, Güçlü A G, Süer E, Arıkan N.*

In this Turkish study, patients with a history of painful bladder syndrome/interstitial cystitis (PBS/IC) who had poor response or refractory to previous treatment(s) were compared for clinical efficacy of intravesical hyaluronic acid (HA) or hyaluronic acid-chondroitin sulphate (HA-CS) therapy. Patients were randomised for intravesical therapy with 50 ml sterile sodium hyaluronic acid (HYACYST®) or sodium hyaluronate %1.6- sodium chondroitin sulphate %2 (IALURIL®). Intravesical instillations were done weekly in first month, once in 15 days in the second month and monthly in third and fourth months as a total of 8 intravesical doses. Patients were evaluated with visual analog scale (VAS) of pain, 24 hours frequency, nocturia, Interstitial Cystitis Symptom Index (ICSI), Interstitial Cystitis Problem Index (ICPI), cystometric bladder capacity and median voided volume at the beginning and after 6 months of the therapy. The potassium chloride sensitivity test was administered to all patients initially. In this study, a total of 53 patients were randomised. Thirty patients were randomised for IALURIL® group. Twenty-three patients were randomised for HYACYST® group. Parson's test was positive for 23 patients (60.5%) and 15 patients (39.5%) in IALURIL® and HYACYST® groups respectively. Total positive rate of Parson's test was 71.7% of the patients (38/53). Response of the patients regarding the VAS, ICCS, ICPS, 24 hours frequency, nocturia, cystometric bladder capacity and median voided volume at the initial and post 6 months after the therapy and comparing of two treatments are summarized in Table 1. There were no statistically significant differences between initial findings of the two groups. There were no severe adverse effects noted.

#### Abstract 642

#### **USE OF BOTOX IN THE TREATMENT OF PELVIC FLOOR HYPERTONICIA IN WOMEN WITH CHRONIC PELVIC PAIN: OUR EXPERIENCE**

*Gentile B C, Giulianelli R, Albanesi L, Attisani F, Granata D, Mavilla L, Mirabile G, Pisanti F, Schettini M, Schettini M.*

Vulvodinia, with or without hypertonia of the pelvic floor has a chronic multifactorial etiology. In the history of these patients are often past histories of recurrent infections (especially Candida), previous trauma on the genital area, childhood or puberty stories of sexual abuse. This pathology is often associated with other disorders such as anorexia / bulimia syndromes or anxiety/ depression with an altered and problematic body image. Many studies shown that in these patients vestibular tissues have high concentrations of mast cells that release inflammatory factors with a state of hyperalgesia. This is associated with micro abrasions and edema. In addition to pelvic pain, these women may have other symptoms such as dyspareunia, dysuria and strangury, as well as a pollakiuria day and / or night. In this study, Gentile and colleagues from Italy used injections of botulinum toxin in those patients in whom the muscle hypertonicity component was predominant and who were not responding to common conservative therapies. They found that hypertonus of the pelvic floor responds to the infiltration of botulinum toxin, without side effects and concluded that the treatment is simple, minimally invasive and repeatable over time.

#### Abstract 644

#### **ENDOMETRIOSIS AS A RISK FACTOR OF BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS: A RETROSPECTIVE COHORT STUDY**

*Yii S C, Chung S D, Lin H C.*

In this study from Taipei aimed at exploring the association between endometriosis and bladder pain syndrome/interstitial cystitis (BPS/IC), Yii and colleagues identified 9,191 female patients who had received a diagnosis of endometriosis as the study cohort. They randomly selected 27,573 subjects to be included as the comparison cohort. Each patient in this study was individually tracked for a 3-year period to identify those who subsequently received a diagnosis of BPS/IC. Cox proportional hazards regressions were carried out to estimate the 3-year risk of BPS/IC following a diagnosis of endometriosis. The incidence of BPS/IC following a diagnosis of endometriosis was 0.09% during the

follow-up period for all subjects. The incidence rate of BPS/IC was 0.20% at follow-up period in patients with endometriosis, and 0.05% in controls. They found that patients with endometriosis were at a higher risk than with comparison patients for having been subsequently diagnosed with BPS/IC during longitudinal follow-up.

#### Abstract 650

##### **BETA3-ADRENOCEPTOR AGONIST, MIRABEGRON: A NOVEL MEDICAL THERAPY FOR LOWER URINARY TRACT SYMPTOMS IN PATIENTS WITH INTERSTITIAL CYSTITIS**

*Tsuchida T, Inoue C1, Ohtake Y, Haneda Y, Kobayashi H, Miyamoto T, Takeda M.*

Tsuchida and colleagues from Yamanashi note that the prominent symptoms of interstitial cystitis (IC), such as bladder pain and frequent micturition, are intractable and reduce patient's QOL. Because bladder hydrodistension therapy only provides temporary relief of pain and lower urinary tract symptoms (LUTS), retreatment within a couple of months is usually necessary. Thus, self-bladder training may be crucial for IC patients. According to their previous reports ( The effect of Chinese herbal medicine containing aconitine on the pain relief in interstitial cystitis patients:-a preliminary study, in the 104th AUA annual meeting 2009, The astrocyte-targeted therapy by bushi for the neuropathic pain in mice, *PLoS ONE*. 2011; 6: 8. e23510), chronic pain and bladder pain in patients with IC have become controllable using traditional Chinese medicine containing aconitin tuber, at the Department of Urology, University of Yamanashi Hospital. However, little improvement for LUTS, especially frequent micturition, has been obtained with combination of Chinese medicine containing aconitin tuber, anti-cholinergic, and other possible medications. Mirabegron has just been approved by FDA for the treatment of OAB in 2012, and possesses a unique mechanism of action; beta3-adrenergic agonist. Hence, the objective of this study was to examine the efficacy of Mirabegron in the frequent micturition in patients with IC. At the Department of Urology, University of Yamanashi Hospital, 50 IC patients received a traditional Chinese medicine including bushi, and showed good improvement of pain. Ten patients out of 50 complained of frequent micturition even after bladder hydrodistension therapy, and were administered Mirabegron 50mg/day as add-on therapy with traditional Chinese medicine including bushi. Marked and long-term improvements in micturition volume, frequency of micturition, and nighttime micturition frequency were observed in all 10 patients. Sustained improvement in full bladder pain was also observed. Very interestingly, some patients showed continuous disappearance of bladder pain and LUTS even after discontinuation of Mirabegron. The authors concluded that their results suggest that Mirabegron, with the novel mechanism of action, is useful for alleviating full bladder pain and LUTS in patients with IC.

#### Abstract 666

##### **EXPERIENCE OF ENDOVESICAL HYALURONIC ACID IN THE TREATMENT OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME**

*Favre G, Tejerizo J C, Gonzalez M, Zubieta M E, Britez L, Tirapegui F, Damia O.*

A total of 11 women with a mean age of 44 years old (29-60) with IC/PBS diagnosis refractory to medical treatment were included in this study from Buenos Aires to evaluate the effectiveness of endovesical hyaluronic acid in the treatment of Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS). The IC/PBS diagnosis was based on the patient's symptoms, excluding other possible bladder pathologies. A cystoscopy under general anaesthesia with hydrodistention was performed in every patient. They all completed the visual analogue scale (VAS) questionnaire (0=no pain-10=highest intensity) and a micturition time chart. All patients included in this study had had multiple previous treatments, such as Non-Steroidal Anti-Inflammatory Drugs, Pentosan Polysulfate, Amitriptyline, Dimethyl Sulfoxide (DMSO), Botulinum toxin, Anticholinergics and Hydroxyzine, without any clinical improvement. Patients were administered 40 mg of hyaluronic acid in 50 mL of

saline, intravesically, once a week for 4 weeks and then once a month for 6 months. Normal cystoscopy was observed in all patients after the 6 months of treatment. After the third endovesical administration (week 3), 100% (11) of the patients showed an improvement of pelvic pain which was maintained in 54.5% of patients (6) until the end of the follow-up, in 36.4% (4) there was a minor degree of pelvic pain recurrence during the period of follow-up, and in 1 (9%) patient there was a complete symptom recurrence at the end of the study. The average number of voidings was reduced after the 6 months treatment period, from 13.4 (10-20) daily voidings to 6.4 (5-11). After 6 months of treatment, nocturia was improved, with a significant reduction, from 6.5 (4-12) to 2.3 (1-6). No adverse effects were notified. They found a positive response with success evaluated as the improvement of the three primary endpoints: pelvic pain, increased daytime frequency and nocturia. They found that a weekly administration for 4 weeks and then a monthly administration for 6 months to be an acceptable administration scheme with significant symptoms improvement. They are of the opinion that a chronic maintenance therapy should be considered in future studies with longer follow-ups, as well as whether it should be on a weekly or monthly basis. They concluded that endovesical hyaluronic acid appears to be safe and efficient in the treatment of IC/PBS.

#### Abstract 710

##### **THE EFFICACY OF INTRAVESICAL AGENTS**

*Chaudry M, Ramage C, Bates A.*

Hyaluronic acid (Cystistat®) and chondroitin sulphate (Uracyst®) are two intravesical agents used at Bradford Royal Infirmary to treat interstitial cystitis unresponsive to initial medical management. These treatments are believed to replace the deficient Glycosaminoglycan (GAG) layer of the bladder wall. The aim was to assess and compare the efficacy of these treatments. Patients referred for intravesical therapy were randomly assigned to Cystistat® or Uracyst®. After 6 months they were asked about changes in bladder pain, urinary frequency, urgency and nocturia face to face or by telephone interview. Any changes in treatment during this time were noted. 30 patients commenced intravesical therapy - 15 with Cystistat®, 15 with Uracyst®. Six (40 %) patients who commenced Cystistat® discontinued therapy – 2 wanted no further treatment and four changed to Uracyst®. Twelve (80 %) patients started on Uracyst® changed therapy to Cystistat®. At the end of the six-month period, 22 patients continued on Cystistat®, 7 on Uracyst® and 2 patients had discontinued therapy completely. Overall 77% of patients had decreased bladder pain, 73 % had decreased urgency, 53% had decreased urinary frequency, 50 % had decreased nocturia. Five of the seven patients continuing on Uracyst® (16.7% of the total group) were satisfied with their treatment as were 19 (63%) of the patients on Cystistat®. Six patients (20%) had failed to get any relief from the treatments offered to them. The authors concluded that intravesical agents improve bladder related symptoms especially pain. There were also significant improvements in frequency and urgency. They note that it was difficult to evaluate each therapy individually as many patients changed between therapies. Patients who were started on Uracyst were less likely to report an improvement in symptoms and more likely to require a change in their intravesical agent. As a result Uracyst® is no longer used first-line in this department.

#### Abstract 734

##### **THE CONTROL STUDY BETWEEN AMITRIPTYLINE AND PREGABALIN FOR BLADDER PAIN**

*Sekiguchi Y, Azekoshi Y, Kinjyo M, Maeda Y, Kubota Y.*

Pregabalin is one of standard medicines for chronic pain. There have been a few papers on pregabalin for bladder pain syndrome (BPS). Amitriptyline is one of the standard medicines for BPS. Therefore, Azekoshi and colleagues from Yokohama carried out this control study between amitriptyline and pregabalin for bladder pain syndrome. The subjects were 57 patients who suffered from BPS. The Patients with BPS were defined by lower abdominal discomfort after treatment with

both antibacterial agents and antimuscarinic agents. They had amitriptyline or pregabalin alternatively. The dose of pregabalin was increased from 25mg to 150mg over 2 months. The dose of amitriptyline was increased from 10mg to 30mg over 2 months. The number of patients who did not come to the clinic after the first consultation were 3 in the pregabalin group and 4 in the amitriptyline group. The number of patients who did not continue to have drugs due to side effects were 6 in the pregabalin group (continuation rate 77%) and 8 in the amitriptyline group (continuation rate 65%). The change pre and post treatment by pregabalin was from  $4.81 \pm 2.52$  to  $3.25 \pm 2.88$  and by amitriptyline  $4.87 \pm 2.45$  to  $2.2 \pm 2.30$  by pain scale. There was no statistically significant difference between them. There was however a statistical significance for reduction of pain, urgency and pollakisuria between pregabalin and amitriptyline with O'Leary Sant IC questionnaire. (Table.1) Regarding side effects, dizziness, drowsiness, nausea, loss of concentration, palpitation and weight gain occurred in the pregabalin group. There were 4 with drowsiness, continuing pain, dizziness, disturbance of taste and constipation in the amitriptyline group. The rate of continuing pregabalin may be better than that of amitriptyline. On the other hand, if the patients can tolerate the drugs, amitriptyline may be effective more than pregabalin for BPS symptoms. It was concluded that BPS patients can have pregabalin more than amitriptyline at initial treatment stage.

#### Abstract 791

#### **THE EFFICACY AND SAFETY OF INTRAVESICAL HYALURONIC ACID IN PATIENTS WITH INTERSTITIAL CYSTITIS/ PAINFUL BLADDER SYNDROME: PRACTICE EXPERIENCE**

*Sambandan N, Kebbe Y, Briggs K, Sutherland S, Hammadeh M.*

The purpose of this study from Queen Elizabeth Hospital Woolwich was to assess the efficacy and safety of intravesical hyaluronic acid (HA) in the management of patients with Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS). Also to perform a literature review about the use of Glycosaminoglycan (GAGs) such as Hyaluronic acid (HA) and Chondroitin sulphate (CS) in the management of IC/PBS and compare their findings with the published evidence available. They reviewed retrospectively the outcomes of 23 patients treated at this district general hospital for IC/PBS with a full course of HA using subjective urinary symptoms assessment and a bladder diary before and at 3, 6, and 12 months after completion of the course of HA. Patients were investigated with urine microscopy, urine cytology, ultrasound scan of the renal tract, and conventional urodynamic studies. They also performed a literature review of studies using HA or CS for the management of IC/PBS and compared their experience of using this treatment with the recently published literature. We identified 23 patients (21 female and 2 male) aged between 26-83 years with a clinical diagnosis of IC/PBS. Of the 23 patients reviewed, 70% had bladder pain, 96% had frequency, 78% had urgency, and 35% urge incontinence. Following treatment with a full course of HA, 74% reported improvement in bladder pain, 78% reported improvement in urinary frequency, 44% improvement in urgency and 65% had an improvement in bladder capacity. This treatment was tolerated well by the patients with minimal side effects. Only 2 patients had bladder pain during the treatment course, one subsequently discontinued HA treatment. It was concluded that HA offers a safe and effective management option for patients with IC/PBS. However, the authors note that further randomized controlled trials with a larger sample size are required to further investigate the long-term efficacy and safety.

#### **KETAMINE INDUCED CYSTITIS**

#### Abstract 57

**COMBINATION WITH CYSTOSCOPIC HYDRODISTENSION AND DIAGNOSTIC LAPAROSCOPY CAN GIVE MORE CLUES ABOUT OUTER AND INNER BLADDER CONDITION IN PATIENTS WITH KETAMINE INDUCED CYSTITIS**

*Lee M H, Chen W C, Wu H C.*

Lee and colleagues note that the symptoms of ketamine-induced cystitis (KIC) include a range of lower urinary tract symptoms (LUTS) mainly irritative in nature and the patients will complain of intense urgency, extreme frequency and intractable dysuria. Studies have suggested that cystoscopy shows ketamine-induced cystitis with bladder mucosa lesions similar to cystoscopic findings in patients with interstitial cystitis(IC). However, the authors did not find any publications that reported laparoscopic findings and correlations with cystoscopic hydrodistension in patients with KIC. The aim of this study from Taiwan was therefore to investigate the inner and outer findings of bladder using hydrodistension and laparoscopy. Their study revealed that the patients with KIC have a significant decrease in bladder capacity and constrictive bladder shape by laparoscopy. They conclude that there is not only urothelial inflammation with contact bleeding in cystoscopy but also constrictive bladder shape with some fluid accumulation over the cul-de-sac when performing cystoscopic hydrodistension in KIC bladders. The patients with ketamine-induced cystitis not only have denuded bladder mucosa, but also constrictive bladder. These findings may explain why poor therapeutic effect of intravesical therapy was noted.

**Abstract 331**

**KETAMINE-INDUCED ULCERATIVE CYSTITIS IS ASSOCIATED WITH INCREASED EXPRESSION OF TRANSFORMING GROWTH FACTOR-B AND ENHANCED INTERSTITIAL FIBROSIS IN RAT**

*Juan Y, Li Y, Long C, Jang M, Wu W, Huang C, Levin R M, Chuang S.*

This study from Taiwan investigated whether the expression of transforming growth factor- $\beta$  (TGF- $\beta$ ) is up-regulated and evaluated the progression of interstitial fibrosis after long-term ketamine treatment by using a ketamine addiction rat model. Chronic ketamine treatment resulted in bladder hyperactivity with a significant increase in micturition frequency and a decrease in bladder compliance. These alterations in micturition pattern were accompanied by increases in the expressions of inflammatory and fibrosis markers, TGF- $\beta$ , fibronectin and type I collagen after long-term ketamine treatment. Mason trichrome's stain showed ketamine treatment decreased urothelium thickness while increased collagen to smooth muscle ratio and exacerbated interstitial fibrosis. Ketamine treatment significantly decreased intramural neurofilaments stainings by immunofluorescence study, indicating ketamine resulted in bladder partial denervation. It was concluded that chronic ketamine treatment significantly increased bladder interstitial fibrosis. Increased interstitial fibrosis might result in decreased bladder compliance and increased micturition frequency. The expression of TGF- $\beta$ , which was a potent pro-fibrotic cytokine, also significantly increased. The increased expression of TGF- $\beta$  is capable of stimulating fibroblast collagen and fibronectin biosynthesis. Persistent activation of ERK1/2 may induce oxidative stress with subsequent induction of COX-2 expression. The authors concluded that ketamine administration results in frequent bladder contractions and decreased bladder compliance. These overactive bladder symptoms are associated with an increase in TGF- $\beta$  and enhanced bladder interstitial fibrosis. Ketamine –induced bladder overactivity was also associated with a decrease in intramural nerve densities and ERK1/2 activation.

**Abstract 357**

**SIMILARITY AND DISSIMILARITIES OF KETAMINE CYSTITIS AND INTERSTITIAL CYSTITIS - A PROTEOMICS ANALYSIS AMONG KETAMINE CYSTITIS, INTERSTITIAL CYSTITIS AND NORMAL BLADDERS**

*Yang H, Zhai W, Jiang Y, Kuo H.*

The aim of this study from Taiwan was to identify significantly differentially expressed proteins between (i) patients with interstitial cystitis/painful bladder syndrome (IC/PBS) and asymptomatic control (AC) subjects, (ii) patients with ketamine cystitis (KC) and AC subjects, and (iii) patients with IC/PBS and KC with the use of proteomic techniques. Three patients each with KC and IC/PBS undergoing partial cystectomy and augmentation enterocystoplasty were enrolled consecutively. 3 patients with bladder cancer or prostate cancer undergoing radical surgery who had never had an episode of urinary tract infection or irritative bladder symptoms were also included and serve as controls. The bladder wall specimens obtained during partial cystectomy and augmentation enterocystoplasty (IC/PBS and KC) or radical operations (radical cystectomy or radical prostatectomy, AC) was harvested and sent for pathological examination and urological laboratory for investigations. A proteomic approach was used to study the proteins associated with KC and IC/PBS and bioinformatics was used to construct the protein-protein network. This study demonstrated that the etiology of IC/PBS and KC might be mediated by multiple signalling pathways. The authors concluded that the identified proteins contributing to the spectrum of IC/PBS and KC bladders may be used to elucidate the etiology of IC/PBS and KC and as candidate biomarkers for diagnostic test.

#### Abstract 437

##### **URINARY CYTOKINES/CHEMOKINES IN KETAMINE ABUSERS**

*Cheung R Y K, Lui D W T, Wong C K M, Lee L L, Lee J H S, Chan S S C, Choy R K W*

Urinary cytokines have been investigated as a biomarker for overactive bladder (OAB) syndrome. Lower urinary tract symptoms caused by ketamine abuse shared similar symptomatology of irritative and obstructive symptoms as OAB. Therefore, studying the relationship of urinary cytokines in ketamine abusers may benefit our understanding in the pathophysiology of ketamine cystitis. This study from Hong Kong aimed to study the cytokine and chemokine levels in urine of ketamine abuser compared to age matched controls. In this study, EGF was found to be increased in women with a history of ketamine abuse and with significantly more irritative and obstructive urinary symptoms when compared with age-matched control group. It was concluded that the urine levels of EGF were increased among ketamine abusers. This study demonstrated that urine excreted kidney cytokine EGF may be biomarker of lower urinary tract irritation and obstruction in ketamine abusers. Therefore, it merits a more thorough analysis to determine its role in ketamine abusers.

#### Abstract 476

##### **IS ELECTRON MICROSCOPY USEFUL IT IN THE DIAGNOSIS OF KETAMINE-ASSOCIATED CYSTITIS?**

*Saeb-Parsy K, Gatward G, Warren A, Thiruchelvam N.*

Saeb-Parsy and colleagues from Cambridge report that while ketamine has been historically used as an anaesthetic agent, over the years its use as a recreational drug has gained popularity. The effects of ketamine use on the urogenital tract are being increasingly recognised. Patients with exposure to ketamine may present with severe cystitis (dysuria, frequency, urgency and haematuria). Ketamine cystitis often fails to respond to conventional conservative and antibiotic treatment. Diagnosis of ketamine cystitis presents a significant challenge to the urologist as there are no agreed pathological features. As such its diagnosis often is clinical and based on history of irritative urinary symptoms and previous or current recreational use of ketamine. Here the authors present cystoscopic, histopathological staining and electron microscopic appearance of patients with ketamine-associated cystitis. Ten patients with a history of ketamine use and on-going irritative urinary symptoms underwent cystoscopy and biopsy in our unit between 2009 and 2012. In each patient samples were taken from both normal and abnormal areas when present and examined with light microscopy as well as electron microscopy. Slides were reviewed by a single uropathologist. Although evidence of inflammation was present in patients with ketamine-associated cystitis, neither light nor electron microscopy revealed any diagnostic abnormalities in patients with ketamine use. Similarly, there

were no key diagnostic features present at the time of cystoscopy. Based on the current data they are unable to comment on any associated specific morphological features as a result of ketamine use, even on high power view. They concluded that further research is required to facilitate a better understanding of the appearance of normal urothelium on electron microscopy and its comparison in patients with ketamine-associated cystitis; this may help with establishment of histopathological criteria to aid with the diagnosis of ketamine-associated cystitis.

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