

A REVIEW OF THE ANNUAL MEETING OF THE AMERICAN UROLOGICAL ASSOCIATION (AUA)

17-22 May 2008, Orlando, Florida, USA

Scientific Highlights at the AUA in the field of Interstitial Cystitis/Painful Bladder Syndrome/Chronic Pelvic Pain

Jane Meijlink



Health professionals – and IC/PBS patient representatives - from the USA and around the world descended on the vast Orange County Convention Center in a tropically hot and humid Orlando, Florida to attend the AUA annual meeting 2008. Coping with the sizzling temperature outdoors and the ice-cold air-conditioning indoors was an art in itself!

IC/PBS/ CPP a hot topic at the AUA

With the innovative NIH/NIDDK Multidisciplinary Approach to the Study of Chronic Pelvic Pain (MAPP) research programme about to be launched, every attention was paid to Interstitial Cystitis/Painful Bladder Syndrome and Chronic Pelvic Pain this year at the AUA, with research varying from the most complex basic science to clinical studies of every description presented in several different sessions, along with no fewer than three educational courses on IC/PBS/ CPP and a state-of-the-art plenary lecture by Dr Philippe Zimmern on the urologist's approach to pelvic pain syndrome in women.

Diagnosis (but not over-diagnosis) and locating source of the pain

It was repeatedly stressed in Orlando that while it is important to ensure that all patients with IC/PBS/ CPP are correctly diagnosed, it is equally important to avoid over-diagnosis due to inadequate exclusion of other possible causes of the symptoms. With greater awareness of IC/PBS worldwide, doctors must not fall into the trap of automatically assuming that all patients with pain, urgency and frequency symptoms most likely have IC/PBS. They may have other (curable) diseases or disorders. Success in diagnosing IC/PBS/ CPP patients is based very strongly on thorough history taking and physical examination. Locating the source of the pain plays an essential role in correct diagnosis. This was emphasized time and time again at the AUA.

A new method of cystoscopy from Japan using narrow band imaging attracted considerable attention.

A study on urgency focused on differentiating between urgency in IC/PBS and urgency in OAB.

Treatment

As many presenters here stated, over the years we have seen innumerable drugs rise and fall: some work in some patients and not in others and some patients never find any adequate treatment. Some trials may produce positive results, while other trials with the same drug in another centre or country appear negative. It is therefore to be hoped that the NIH/NIDDK MAPP project will ultimately lead to better sub-categorization of these greatly differing patients - at present bundled together - and consequently to more tailored treatment and studies.

- Intravesical alkalized lidocaine hot topic

New treatments are in the development pipeline (although it should be emphasized that drug development is a very long pipeline spanning many years) and attention at the AUA this year was particularly focused on the use of intravesical alkalized lidocaine – with or without the addition of heparin - which is likely to play an increasingly important role in the future for the treatment of flares (so-called rescue therapy), with further studies aimed at examining longer term effects on pain and its potential use as a diagnostic tool to ascertain whether the pain is actually in the bladder or not.

- Myofascial physical therapy in the headlines

The potentially beneficial role of myofascial physical therapy for treating chronic pelvic pain was also highlighted at this meeting and hit the headlines of AUA Daily News during the congress.

Further details can be found below per study and presentation.

Below is an overview of a selection of the lectures, posters, presentations and courses related to IC/PBS/ CPP at the AUA annual meeting. The numbers given per study are the AUA abstract numbers.

Plenary Session: State-of-the-art lecture

THE UROLOGIST'S APPROACH TO PELVIC PAIN SYNDROME IN WOMEN

Presented by Philippe Zimmern MD



Dr Philippe Zimmern opened his state-of-the-art lecture on management of pelvic pain syndromes by stressing that pelvic pain is a very extensive topic indeed. He outlined the history of definitions of pelvic pain syndromes, saying that in recent years pain has become the key feature, with frequency, urgency and sensation as optional features.

Dr Zimmern explained to delegates that the upcoming NIH/NIDDK International Symposium in June 2008 on Defining the Urologic Chronic Pelvic Pain Syndromes aims to develop definitions, markers and phenotypes for research purposes and particularly for the upcoming MAPP project.

On the topic of diagnosis, Dr Zimmern emphasized that the main question is: where is the pain coming from? Is this pain coming from the bladder or from elsewhere? In order to ascertain this, history-taking and listening to the patient play a vital role. He particularly stressed that IC patients require far more time than any other patients. They are not standard patients and every patient is different. A good doctor/patient relationship is essential and it is critical to take the time to establish this relationship.

He believes that the doctor needs to discover the type of pain, its intensity, its location, duration and evolution, its impact on the patient's quality of life, and the status of bowel and sexual functions. His personal approach is to try to establish the relationship between the pain and the "bladder cycle". Does the pain worsen with filling, does the patient have pain on urination, is the pain relieved by voiding? Or does the pain appear to be unrelated to the bladder storage and voiding cycle? Is the pain urological or is it non-urological? Could the pain be gynaecological (e.g. endometriosis or ovary disorders), gastrointestinal (irritable bowel syndrome, diverticulitis), vaginal (vulvodynia, pelvic muscles) or urethral (urethritis, diverticulitis). Referring to confusable disorders, he illustrated cases involving trigonitis, urethral obstruction, urethral diverticuli, infection of Skene's gland, urethritis and stricture which presented with symptoms characteristic of IC.

A thorough physical examination is important, but the physician should be aware that the patient may be very anxious that this may provoke or intensify the pain. "Look for triggerpoints", said Dr Zimmern, "and think about non-urological organs." If the pain does not seem to be urological, refer the patient to other disciplines. A multidisciplinary approach is essential with delegation of aspects that lie outside the field of urology.

On the subject of diagnostic tests, there is a wide variety of tests currently in use around the world, but he stressed that it is difficult to find the right test when no-one knows how to define the disease. Cystoscopy remains controversial and he believes that IC is still a diagnosis of exclusion.

Dr Zimmern warned about the risks of over-diagnosis and told delegates that there is nothing worse than diagnosing and treating someone for IC who does not in fact have that disease. This can cause a patient unnecessary pain and distress until someone eventually re-assesses the patient and rectifies the situation. He therefore emphasized the need for re-assessment from scratch when taking over a patient from another physician so as not to take over any possible errors in diagnosis.

Regarding surgery and last resort cystectomy, Dr Zimmern stressed that it is more vital than ever to be absolutely sure that the bladder is the source of the pain when considering cystectomy.

Plenary Session: Late breaking news
RANDOMIZED MULTICENTER PILOT TRIAL SHOWS BENEFIT OF MANUAL
PHYSICAL THERAPIES IN TREATMENT OF CHRONIC PELVIC PAIN
Presented by Kenneth Peters MD



While patients with chronic pelvic pain syndromes, including IC/PBS, are often treated by physical therapists specialized in myofascial therapy techniques, there have until now been no randomized control trials or prospective control trials to support this form of therapy.

Dr Kenneth Peters from the William Beaumont Hospital in Detroit hit the AUA News headlines with the results of this first randomized, multi-centre pilot study to evaluate manual physical therapy (MPT) with targeted internal and external connective tissue manipulation and global therapeutic massage (GTM), a non-specific somatic treatment with full body Western massage, in the treatment of chronic pelvic pain and to assess the feasibility of conducting a larger trial in the future.

8 patients were recruited from each of 6 centres participating in the Urological Pelvic Pain Collaborative Research Network (UPPCRN) and ultimately 47 were randomized to either MPT or GTM and two withdrew during the study. Certified physical therapists from all centres were given instruction and training at a weekend workshop to ensure that they performed their therapy in a standard fashion.

The participating patients all had chronic pelvic pain for a maximum of three years and during a pelvic examination by the investigator were shown to have some tenderness and/or the presence of a muscular trigger point. This was also confirmed by a physical examination by the therapist. Ten weekly 1 hour sessions were given. Adverse effects were mainly pain with 3 patients experiencing severe pain. The low study withdrawal rate and low rate of severe adverse events indicated that the patients considered the physical therapy to be acceptable, according to Dr Peters. 57% of patients receiving physical therapy responded positively compared to a 21% response for GTM. An interesting aspect was that while 45% of the men responded to global therapeutic massage, none of the women did. Possible explanations for this striking difference are:

- different response by gender to therapeutic touch
- different disease states (CP/CPPS and IC/PBS) respond differently to therapeutic touch.

The limitations of this study were:

- the number of study participants randomized into the study was insufficient to conclusively evaluate the efficacy of the MPT therapy;
- GTM was not performed by a certified massage therapist;
- it was not possible to blind the subjects to the treatment arm.

So these first positive results from this pilot study indicate that myofascial physical therapy could have clinically meaningful benefit for patients with chronic pelvic pain and that a further study with larger numbers of patients is warranted.

Podium Session 5: INFECTIONS/INFLAMMATION OF THE GENITOURINARY TRACT: INTERSTITIAL CYSTITIS

This first ever podium session at the AUA dedicated to IC included the following presentations:

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EFFECTS OF DIFFERENT ENKEPHALIN TREATMENTS ON BLADDER PAIN.

Hitoshi Yokoyama, Chikashi Saitoh, Minoru Miyazato, Osamu Nishizawa, Michael B Chancellor, William F Goins, James R Goss, Joseph C Glorioso, Naoki Yoshimura. Pittsburgh USA and Matsumoto, Japan.

Using female rats with induced bladder pain, Yokoyama and colleagues examined the antinociceptive effects of systemically administered enkephalin, a δ -opioid receptor agonist as well as gene therapy using herpes simplex virus vectors expressing preproenkephalin, the precursor of enkephalin. Their results indicate that both types of enkephalin treatment via systemic administration or HSV-mediated gene transfer are effective in suppressing bladder pain induced by bladder irritation. They conclude that enkephalin gene therapy, which can target bladder afferent pathways and avoid systemic effects, could be a potential treatment for bladder pain in IC/PBS patients.

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NEUROGENIC CYSTITIS INDUCED BY COLONIC IRRIGATION RESULTS IN INCREASED UROTHELIAL PERMEABILITY THAT PARALLELS BLADDER MASTOCYTOSIS AND HYPERACTIVITY.

Elena E Ustinova, Dimitriy W Gutkin, Matthew O Fraser, Michael A Pezzone. Pittsburgh and Durham, USA

Irritable bowel syndrome and interstitial cystitis often overlap and occur concomitantly (as do other chronic pelvic pain disorders).

This study in an animal model hypothesized that chronic mast cell infiltration of pelvic organs following an acute pelvic organ insult plays a role in chronic pelvic organ sensitization and cross-sensitization:

- pelvic organ mastocytosis leads to increased epithelial permeability in the uninsulted organ
- increased permeability results in direct afferent activation in the uninsulted organ by physiologic stimuli.

The study involved irritation of the colon induced with trinitrobenzenesulfonic acid (TNBS), while nothing was done to the urinary bladder. This caused increased bladder permeability (measured by sodium fluorescein) and mast cells (quantified using Giemsa-stained sections under 100x power field).

The results of this study indicate that C-fiber activation in the uninsulted organ results in mastocytosis in 4 days. While damage was seen in the colon, no damage was observed in the bladder, only mastocytosis.

The neurogenic sensitization of bladder afferents by colonic irritation of divergent afferents that innervate both organs and dorsal root reflexes results in simultaneous mast cell attraction and urothelial barrier breakdown, leading to a progressive disease state.

The data suggest that these changes in pelvic organ permeability may predispose the affected organ to chronic irritation from normal luminal contents, resulting in sustained epithelial leak and self-perpetuating irritation and afferent sensitization. These are the first good clinical data that help to explain that the possible link between IBS and IC may be due to the activity of migrating mast cells.

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FEMALE SEXUAL FUNCTION IMPROVES IN TREATED INTERSTITIAL CYSTITIS PATIENTS

Blayne K Welk, Joel Teichman. Vancouver Canada

Poor sexual function is a key factor in determining a poor quality of life in IC/PBS patients. This study aimed to show that successful treatment of IC/PBS patients can lead to an improvement in various domains of sexual function. 32 sexually active female IC/PBS patients with dyspareunia were treated with intravesical lidocaine, heparin and bicarbonate instillations 3x/wk x 3 wk. Symptoms were assessed before and 4 weeks after with several instruments and the female sexual function index (FSFI). The results showed good improvement in several areas of sexual dysfunction. Those with less severe symptoms and less diffuse pain. This is the first prospective study to show that sexual function in IC/PBS patients improves with therapy.

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EFFECTS OF BOTULINUM TOXIN A ON SNAP25 LEVEL AND BLADDER FUNCTION IN A CYCLOPHOSPHAMIDE INDUCED CYSTITIS MODEL IN RATS

Yao-Chi Chuang, Chou-Cheng Huang, Naoki Yoshimura, Pradeep Tyagi, Michael B Chancellor, Po-Hui Chiang, Kaohsiung Hsien. Taiwan and Pittsburgh USA.

This study investigated the effect of intravesical botulinum toxin A (BoNT-A) on the level of SNAP-25 and bladder function in cyclophosphamide (CYP)-induced cystitis in rats. The results led the researchers to conclude that BoNT-A treatment decreased SNAP-25 level in the bladder, but not in the spinal cord, and inhibits CYP-induced bladder inflammation and hyperactive bladder. This finding suggests a local neuromodulation of BoNT-A on the bladder without compromising central neurotransmission.

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ALTERED URINARY BLADDER FUNCTION AND IMPAIRED NOCICEPTION IN MICE LACKING ESTROGEN RECEPTOR- α

Zunyi Wang, Peiqing Wang, Dale E Bjorling. Madison USA

Since painful bladder disorders affect more women than men, it has been suggested that estrogen and its receptors may play a role in inflammation and pain. In this study bladder function and pain sensation in chemically-induced cystitis were studied in ER- α and ER- β knock-out and wild-type mice. They found that absence of ER- α prevented increased peripheral pain perception associated with cystitis. This is novel and the researchers believe that this may help explain patient differences in perception of pain associated with cystitis.

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FLEXIBLE TELESCOPE WITH NARROW BAND IMAGING SYSTEM FOR INTERSTITIAL CYSTITIS

Tomohiro Ueda, Masayuki Nakagawa, Hideki Tanoue, Motohiro Okamura, Hiroshi Yoshida, Naoki Yoshimura. Kyoto, Japan and Pittsburgh USA

Bearing in mind that diagnostic investigations for IC/PBS are highly invasive and costly, Ueda and colleagues aimed to develop an IC/PBS method of diagnosis using a flexible cystoscope with a narrow band imaging (NBI) system that can detect mucosal angiogenic lesions. In this study of 49 females and 3 males (total 52), ulcers found in 37 patients found using conventional cystoscopy were also identified using NBI without hydrodistension. Furthermore, 6 cases of carcinoma in situ (CIS) were identified from biopsies obtained from the ulcerative lesions positively identified by NBI cystoscopy. The lesions detected by NBI cystoscopy

are also associated with overexpression of platelet-derived endothelial growth factor. It was concluded that examining the bladder mucosa with an NBI system flexible cystoscope makes it possible to easily detect ulcers in the bladder mucosa and areas with angiogenesis. This means diagnosis can be made simply, less invasively and at lower cost in outpatients and makes cystoscopy with anaesthesia unnecessary. Furthermore, the diagnostic accuracy of IC/PBS is enhanced by the fact that the NBI system can clearly identify the area for biopsy in the case of ulcerative lesions which are difficult to distinguish from CIS. It was therefore concluded that the NBI system appears to be a revolutionary method to detect bladder lesions associated with IC/PBS without hydrodistension in outpatients who complain of pelvic pain, urinary frequency and a persistent urge to void.

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DIAGNOSIS OF INTERSTITIAL CYSTITIS USING INFRARED MICROSCOPY

Charles A Buffington. Columbus USA

Infrared microspectroscopy involved collecting serum IR spectrum using an integrated microscope. This study assessed the feasibility of using serum infrared spectra to improve the diagnosis of IC in humans and domestic cats. Buffington discovered that specific infrared bands distinguished IC from healthy subjects in both humans and cats. The data from this study suggests that intermediate compounds in the metabolism of tryptophan might be associated with the pathophysiology of IC. Conclusions were:

- IR spectroscopy may be a rapid and useful method to help diagnose IC;
- serum from humans and cats contains chemical information that can be used to discriminate affected from healthy subjects;
- IR spectroscopy and multivariate analysis combined with LC-MS provides a powerful tool to look for biomarkers.

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MAST CELL-DERIVED HISTAMINE MEDIATES CYSTITIS PAIN

Charles N Rudick, Paul J Bryce, Laura A Guichelaar, David J Klumpp. Chicago USA

In a mouse model, this study from Chicago looked into mast cell-derived histamine in relation to pain. Although mast cells and neural involvement have been implicated in the pathogenesis of IC, the molecular mechanisms underlying pelvic pain in IC patients are unknown. These investigators used a neurogenic cystitis model induced by pseudorabies virus (PRV) that recapitulates key aspects of IC such as pelvic pain and mast cell-mediated bladder pathophysiology to take a look at the molecular basis of pelvic pain. Their data from this study suggest that mast cells cause cystitis pain and bladder inflammation through the separable actions of histamine and TNF respectively. They are consequently of the opinion that histamine receptors could be useful targets for pelvic pain treatment. While both hydroxyzine and cimetidine have been used as part of multimodal treatment for some years, they have not always been that effective and then only in certain patients. It is hoped that newer generations of specific antihistamine drugs will be more effective than older ones.

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PHARMACOKINETICS OF LIPOSOMES AFTER INTRAVESICAL ADMINISTRATION

Jonathan Kaufman, Pittsburgh, USA

Liposomes are stable self-assembled phospholipid bubbles filled with water which adhere to a surface. Liposomes have a long history of safe clinical use. This investigator has been studying empty liposomes as an intravesical IC treatment. The reason for investigating liposomes is because the most consistent finding in IC is a compromised bladder barrier function. Previous studies have reported the therapeutic effect of empty liposomes on bladder irritation. The investigation team has been working towards drug development of empty liposomes as a coating treatment for lower urinary tract symptoms of bladder irritation. This study reports on the pharmacokinetics after intravesical administration of radiolabelled liposomes in rats. It was concluded that intravesical treatment with liposomes can have a significant advantage when targeting the bladder lining and stays put in the bladder for an estimated 24 hours. These pharmacokinetic studies, taken together with efficacy and toxicity studies, support the use of empty liposomes as a local therapy for PBS/IC and refractory overactive bladder.

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INTERRUPTION OF MAST CELL FUNCTION EFFECTIVELY INHIBITS BLADDER INFLAMMATION IN AN AUTOIMMUNE CYSTITIS MODEL

Wu-Jiang Liu, Yi Luo, Iowa City, USA

While an increased number and activation of mast cells have been seen in interstitial cystitis patients, the role of mast cells in this disease is unclear. The aims of this study were to determine the role of mast cells in T cell-induced bladder inflammation and to provide an animal model for future development of effective therapies for IC/PBS. It was concluded that:

- blockage of mast cell activity effectively alleviates T cell-induced bladder inflammation;
- a mast cell targeting approach may be useful for the treatment of bladder inflammation with an immune/autoimmune component such as IC.

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EFFECT OF INTRAVESICAL LIDOCAINE ON URODYNAMIC PARAMETERS IN PATIENTS WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS)

Arun K Srinivasan, Edan Y Shapiro, Casey A Seideman, Robert M Moldwin, New Hyde Park, NY, USA

Intravesical instillation of alkalized lidocaine has been shown to improve symptoms of pain and urinary urgency in IC/PBS patients. The aim of this study was to quantify changes in urodynamic parameters that might be responsible for this improvement.

8 IC patients (2 male, 6 female) underwent multi-channel urodynamic evaluation (UDS). 20 cc alkalized 2% lidocaine was then instilled into the bladders of these patients for 10 minutes. A second UDS was then performed. The two urodynamic parameters were subsequently compared. Statistically significant changes were observed in relation to bladder capacity, maximum flow rate, first strong sensation to void. No adverse events were reported. This study provides further evidence for the efficacy of this treatment in patients with IC/PBS. Further investigation is underway to correlate urodynamic changes with clinical improvement.

Conclusions:

- Significant improvement in the filling and voiding function of the bladder after intravesical alkalized lidocaine instillation;
- Urodynamic parameters can be an objective means to evaluate progression and response to treatment in IC patients;
- May have potential beyond the IC patient population;
- Limitations: retrospective, absence of controls, small study population.

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INTRAVESICAL ALKALIZED LIDOCAINE (PSD597) OFFERS IMMEDIATE AND SUSTAINED RELIEF FROM THE SYMPTOMS OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME (IC/PBS); RESULTS OF A PHASE II MULTI-CENTRE PLACEBO-CONTROLLED TRIAL

J Curtis Nickel, Michael G Wyllie, Richard A Henry. Kingston Canada and Kent United Kingdom.

Dr Curtis Nickel began by telling AUA delegates that after years of uninspiring results he now had great pleasure in announcing a trial that had actually produced positive results, as he presented results from the PSD597 (intravesical alkalized lidocaine) study group.

There is a clear, unmet need for a safe and effective means of providing relief from acute and chronic symptoms of IC/PBS. Current treatments for many IC/PBS patients have limited efficacy in reducing pain while many local anaesthetics instilled into the bladder failed to take effect due to the acid level of the urine (pH 5-6) which means that most local anesthetic is left ion trapped in the bladder and cannot cross the bladder urothelium. In alkalized lidocaine instillation treatment, the lidocaine solution is instilled into the bladder via a catheter, followed by sodium bicarbonate solution. The lidocaine converts to non-ionic bioavailable form. The catheter is clamped in place, the solution left for about an hour and then drained off via the catheter. The purpose of this study was to assess the immediate and sustained relief of the symptoms and safety following a 5 consecutive day course of treatment with intravesical alkalized lidocaine (PSD597) or placebo.

102 adult patients (99 female) with a clinical diagnosis of IC/PBS from 19 centres in the USA and Canada were randomized to receive daily instillation of intravesical PSD597 or placebo (double-blind) for 5 consecutive days. 95 patients completed the study. All patients were subsequently offered voluntary open-label treatment for 5 days. 86% of them opted to enter this open-label study and 98% of these completed the open-label study. Adverse events were limited to urinary tract discomfort. There was no systemic lidocaine toxicity. Results included 30% drug effect versus 10% placebo. For IC/PBS this is a good result, according to Dr Nickel..

It was concluded that:

- PSD597 is effective for the treatment of the symptoms of IC/PBS
- Maintenance of the treatment effect extends beyond the end of treatment
- The open-label study suggests that longer or repeated PSD597 treatment may lead to a greater and sustained response rate
- Treatment has an acceptable safety profile.

Since the proprietary combination treatment is not yet available, physicians can currently use generic lidocaine followed by sodium bicarbonate.

The IC experts in avid conversation following the well-attended IC podium session.



Moderated Poster Session 7: BLADDER & URETHRA: ANATOMY, PHYSIOLOGY AND PHARMACOLOGY

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INTRAVESICAL BOTULINUM TOXIN A ADMINISTRATION INHIBITS COX-2 AND EP4 EXPRESSION AND SUPPRESSES BLADDER HYPERACTIVITY IN CYCLOPHOSPHAMIDE INDUCED CYSTITIS IN RATS

Yao-Chi Chuang, Chou-Cheng Huang, Kaohsiung Hsien, Naoki Yoshimura, Pradeep Tyagi, Michael B Chancellor, Po-Hui Chiang. Kaohsiung Hsien, Taiwan and Pittsburgh USA

In a rat model, cyclophosphamide injection activated COX2 and EP4 expression in the bladder and spinal cord and induced bladder inflammation and hyperactivity. These effects were suppressed by botulinum toxin-A (BoNT-A) treatment. This finding suggests a potential clinical benefit of BoNT-A for the treatment of interstitial cystitis or other chronic inflammatory conditions.

Moderated Poster Session 8: INFECTION/INFLAMMATION OF THE GENITOURINARY TRACT: KIDNEY & BLADDER

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LIDOCAINE PREVENTS SOMATIC MECHANICAL HYPERSENSITIVITY ACCOMPANYING EXPERIMENTAL CYSTITIS.

Simone Guerios, Zun-Yi Wang, Wade A Bushman, Dale E Bjorling. Madison, USA

This study was performed to test the hypothesis that lidocaine given prior to or after establishment of cystitis in rats would prevent development of increased sensitivity to mechanical stimuli applied to the hind paw. Lidocaine given before - but not after - establishment of cystitis prevented peripheral mechanical hypersensitivity. Since lidocaine typically alleviates bladder-associated pain in patients with cystitis, the results of this study suggest that processes resulting in somatic hypersensitivity are different to those associated with pain coming from the

bladder, and further suggest that relief of visceral pain may not be accompanied by alleviation of somatic discomfort.

Moderated Poster Session 25: URINARY DIVERSION: BLADDER RECONSTRUCTION, AUGMENTATION, SUBSTITUTION, DIVERSION

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LONG TERM OUTCOMES OF CYSTECTOMY WITH BLADDER SUBSTITUTION IN THE TREATMENT OF ADVANCED INTERSTITIAL CYSTITIS.PAINFUL BLADDER SYNDROME: A TETROSPECTIVE COHORT SERIES.

Nivedita Dhar, Courtney Moore, Amit Bhatt, Adrian V Hernandez, Craig Zippe, Sandip Vasavada, Raymond Rackley. Cleveland USA

While fewer cystectomies are performed today than in the past due to improvements in treatment, surgery is sometimes necessary as a last resort in severe cases. However, according to the investigators there is nothing to be found in the literature on this subject. The purpose of this first retrospective study was to determine whether long-term outcomes of women with refractory interstitial cystitis as measured by two validated questionnaires, the Female Sexual Function Index (FSFI) and the patient global assessment survey (GAS), supports the use of cystectomy with bladder substitution in the treatment of refractory IC. In this group of patients, cystectomy with bladder substitution led to durable improvement in sexual function, pain relief (without recurrence of pain in the diversion), voiding symptoms, sleep and overall quality of life as measured by the FSFI and GAS.

Moderated Poster Session 49: URODYNAMICS/INCONTINENCE/FEMALE UROLOGY: FEMALE UROLOGY II

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A CROSS-SECTIONAL INVESTIGATION OF THE PREVALENCE OF DEPRESSION AND ABUSE AMONG WOMEN DIAGNOSED WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME

Pegah Safaeian, Howard B Goldstein, Peter Finamore, Kristene E Whitmore. Philadelphia and Voorhees, USA.

The aim of this study on this somewhat controversial topic was to evaluate the prevalence of depression and both physical and sexual abuse among women diagnosed with interstitial cystitis/painful bladder syndrome. 141 women participated in this anonymous study. All of them completed the validated Beck's Depression Inventory II Questionnaire (BDI-II) and the validated Drossman Questionnaire of Physical and Sexual Abuse. 69% scored 10 or higher on the BDI-II which corresponds to depression. Depression is common in all chronic pain disorders. While 36% reported experiencing sexual abuse during their lifetime, the prevalence of physical abuse in this sample group was not statistically different to that of the US average 28%. The prevalence of emotional abuse was 57% which was significantly lower than the US average of 69%. It was emphasized that this does not mean that IC has a psychological cause, but that patients who need

additional support should be referred to the relevant disciplines while at the same time continuing appropriate treatment for the IC.

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DOES THE SYMPTOM OF “URGENCY” DIFFER FOR WOMEN DIAGNOSED WITH INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME AND OVERACTIVE BLADDER?

J Quentin Clemens, Karin Liu, Laura Bogart, Sandra H Berry. Ann Arbor and Santa Monica, USA

The purpose of this study was to compare urgency symptoms in women with interstitial cystitis/painful bladder syndrome and overactive bladder. 236 women with IC/PBS and 125 with OAB participated on the basis of a comprehensive telephone survey about their current symptoms. The questionnaire included 11 questions about urinary urgency.

It was concluded that:

- Urgency is commonly reported by women with both IC/PBS and OAB.
- Although urgency symptoms differed in women diagnosed with IC/PBS versus those diagnosed with OAB, there was a significant overlap.
- Urgency occurred both suddenly and gradually in both conditions.
- Urgency was primarily reported as due to pain, pressure or discomfort in IC/PBS, while in OAB the urgency was more commonly due to fear of leakage. However approximately half the women with OAB also reported urgency due to pain, pressure or discomfort.
- Compared with IC/PBS, urgency in OAB more often resulted in leakage and was perceived to be more of a problem.
- These findings reinforce the clinical observation that it is often challenging to differentiate between these two conditions.

AUA EDUCATIONAL COURSES on IC/PBS:

A few interesting or useful points have been picked out per course.

Course 78 MC Plus

THE COMPREHENSIVE MANAGEMENT OF INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME IN AN INTEGRATED UROLOGIC PRACTICE.

John B Forrest MD, Saundra Seidel RN



Even though this 6 am free course on IC/PBS meant rising long before dawn, it proved to be so popular that it was standing room only for the last arrivals. This is an indication of the rapidly increasing interest in this disorder. Dr Forrest began by saying that IC/PBS is becoming a major discussion topic in the USA, not least due to the surging cost factor. IC is now one of the top urologic diseases on the basis of cost.

In a brief discussion of definitions and nomenclature, he emphasized that changing terminology can have major ramifications. He suspects that urologists may be missing many cases of IC in the early stages. In some patients, urgency and frequency tends to precede pain by several years. However, early diagnosis is very important since nerves undergo change as they get chronically bombarded by pain. Early intervention is the key to preventing development of visceral pain syndromes and all sources of pain should be identified. He recommends treating all sources of pain and dysfunction, using multi-modal treatment - drugs, physical therapy and neuromodulation - with the aim of preventing further up-regulation. He emphasized that the patient needs to be told how to handle flares and to have medication at hand. Patients who do self-care tend to do better. It gives them the feeling that they have some control over the disease and their life. A practical tip: when discussing the use of intravesical alkalized lidocaine, he recommended leaving the catheter in and draining the solution off via the catheter. If the catheter is removed and the patient allowed to void out the solution, it can cause stinging in the urethra. The challenge for the urologist, he said, is to see the patient when the patient needs to be seen.

Course 112 IC

INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME AND RELATED CONDITIONS: PRACTICAL MANAGEMENT STRATEGIES.

Robert Moldwin

Top clinical expert Dr Robert Moldwin – well-known worldwide for his book *The Interstitial Cystitis Survival Guide* – gave an excellent course focused on the practical aspects of diagnosing and treating the patient. This was precisely the kind of information the urologists wanted to know and at the end of the course they were crowding round him with their questions.



On the subject of gender-specific prevalence, Dr Moldwin said that it is likely that males are still being under-diagnosed and that according to Clemens et al (2005) the ratio could be 5:1 female: male rather than the 8/9:1 that is so frequently quoted. In men there appears to be a strong overlap between IC and CPPS.

Dr Moldwin did not dwell on controversial nomenclature issues, but sufficed by saying that whether you use the term IC, PBS, BPS or whatever, they all amount to “allodynia of the bladder” (+/- inflammation). The name is not relevant for clinical purposes. However, the definition is very important. While criteria for research have to be very strict, in a clinical setting they need to be more flexible, but should nevertheless allow the patient to be clearly identified.

Like many other speakers at this AUA meeting, he emphasized the need to identify other possible pain generators when making a diagnosis. Confirmatory testing can be done to establish the bladder as a source of the symptoms. IC exists in a galaxy of other disorders, but concerns the bladder itself.

Patient questionnaires, he said, are not designed for making a diagnosis, but are useful for monitoring progress.

Dr Moldwin explained to attendees that treatment should be started as early as possible since pain can become ingrained in the central nervous system. This also means raising far more awareness at primary care level to ensure that patients get referred to a urologist at the earliest possible stage.

Not every patient is sensitive to food. While many patients will soon know from experience which foods exacerbate their IC, this should not be taken to extremes since it can lead to anorexic patients. Many patients are also under-drinkers and should be encouraged to drink more.

A useful tip for amitriptyline: whereas it is normally recommended to take the daily dose before going to bed, Dr Moldwin recommended taking it a bit earlier, for example at dinner time, otherwise it could lead to a hangover in the morning. It is not advisable for patients who already suffer from constipation to take tricyclic antidepressants as this constipation problem can be further exacerbated.

Course 93 IC

INTERSTITIAL CYSTITIS/PAINFUL BLADDER SYNDROME: A PRIMER AND AN UPDATE

Philip M Hanno MD, David Burks MD



The first part of this course by Dr Philip Hanno was historical and theoretical, while Dr David Burks spoke on the practical management of IC/PBS patients in a clinical setting.

Dr Hanno emphasized that everything he was going to say was hypothetical. He suggested that IC is a bladder problem that can turn into a chronic neuropathic pain disorder. While the pain has traditionally been described as suprapubic, this is only part of the story and the pain may in fact be felt in many different sites. Some patients may simply have burning pain before, during or after urination.

A problem arises in the definition of pain which also includes pressure or discomfort since most patients do not perceive pressure and discomfort to be a pain sensation.

Dr Hanno also warned about the risks of diagnosis: some patients may be diagnosed with IC but in fact have something else. On the other hand, some patients may have both IC and some other disorder, including OAB. In other words, patients may have co-existing problems.

The initial presenting symptoms may be urgency/frequency (including at night) without pain. On the subject of frequency, it was emphasized that it is difficult to attach a number to frequency since the number of voids depends partly on lifestyle, drinking habits etc.

Concerning the controversy surrounding cystoscopy/biopsy: if you see a red spot on the bladder wall, biopsy is mandatory since it is difficult to distinguish between Hunner's ulcer/lesion and carcinoma in situ.

It was emphasized that glomerulations are not specific to IC. The absence of glomerulations does not mean that a patient does not have IC.

On the subject of the potassium sensitivity test: this test has neither the specificity nor the sensitivity to have value as a diagnostic tool.

Regarding pelvic floor physical therapy: the NIH/NIDDK now has a protocol to standardize the technique used and this includes sham control.

Bladder retraining is not considered to be suitable for patients with pain by these speakers.

Both speakers believe that it is essential for the patients to be well educated about their disease and this is where the patient support groups can play an important role. Diet is important for many patients, but not all.

Delegates were warned to be on the alert since IC patients can be the victims of unorthodox providers, untested therapies and unproven surgical procedures. Few treatments have been subjected to placebo-controlled trials.

WEBCASTS

An extensive selection of webcasts from the AUA annual meeting can be found at: <http://webcasts.prous.com/aua2008/>

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