



# **ESSIC 2023**

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**The many faces of Bladder Pain:  
Implication for a better management**

**Lenox Health Greenwich Village**

**Robert Moldwin**

ESSIC 2023 Meeting Chair & ESSIC Vice-President

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ESSIC President

# **ABSTRACT BOOK**

# 1. LONG-TERM EFFECT OF INTRATRIGONAL BOTULINUM TOXIN IN PATIENTS WITH BLADDER PAIN SYNDROME/INTERSTITIAL CYSTITIS.

**Presenter: Rui Pinto**

Pedro Abreu-Mendes (1) - Paulo Dinis (1) - Francisco Botelho (1) - Francisco Cruz (1) - Rui Pinto (1)

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## INTRODUCTION AND AIM OF THE STUDY

Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC) is associated with a high percentage of failure in long-term treatment. Surgical treatment can be used in refractory patients (1). Botulinum toxin-A (OnaBotA) treatment previously revealed good short and mid-term effectiveness and safety, with a duration of effect of 9 to 12 months(2). We aimed to evaluate long-term efficacy of this procedure and determine eventual predictors to long-term response.

## MATERIALS AND METHODS

A retrospective cohort study with 47 female BPS/IC patients treated with 100 units of intratriganal OnaBotA in a university hospital. Patients were divided into three groups based on their treatment response as: responders, non-responders and lost to follow-up. Clinical and surgical individual records, including the results using a 10-point visual analogue scale (VAS) were analyzed.

## RESULTS

A total of 193 procedures were performed. The number of treatments per patient varied between 1 (10 patients) and 14 (one patient). Forty-eight percent of patients received 4 or more treatments. The median interval between the injection and the patient's request for new injection was 500.5 days (P25:350;P75:581). The effect duration of each treatment was stable during the follow-up (p=0.9). Of the 9 patients with a response duration below the 25th percentile for the first injection, only two abandoned the OnabotA program due to a lack of response and the majority become long-term responders. When analysed per group, the age,

basal VAS and time between the injections does not correlate to the treatment response.

## INTERPRETATION OF RESULTS

Treatment effect duration is sustained along all the treatments. First injection effect duration does not predict long-term response. The OnabotA treatment in real-life setting, with oral treatment adjuvancy in the intervals of injection, present a more durable effect than the previously described 9-12 months.

## CONCLUSIONS

OnabotA injection in BPS/IC patients is effective and safe, as a long-term treatment. When first injection fails, a reinjection should be tried.

## REFERENCES

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2. Pinto R, Lopes T, Silva J, Silva C, Dinis P, Cruz F. Persistent therapeutic effect of repeated injections of onabotulinum toxin A in refractory bladder pain syndrome/interstitial cystitis. *J Urol [Internet].* 2013 Feb;189(2):548-53. Available from: <http://dx.doi.org/10.1016/j.juro.2012.09.027>

# 2. INTRAVESICAL TACROLIMUS IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME:10 YEAR EXPERIENCE.

**Presenter: Nagendra Nath Mishra**

Nagendra Nath Mishra (1) - Toral Gaikwad (1)

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## INTRODUCTION AND AIM OF THE STUDY

Bladder Pain Syndrome/Interstitial cystitis (BPS/IC) is a chronic disease with no cure. Immunosuppressant like cyclosporine have been tried with success but limiting factor is side effect. Tacrolimus is a calcineurin inhibitor as cyclosporin. we have used Tacrolimus intravesically in patients of severe IC/BPS from last 10 years.

## MATERIALS AND METHODS

Tacrolimus in the dose of 0.1 mg per kg body weight was dissolved in sterile water and was instilled in bladder of 71 patients suffering from severe or refractory IC/BPS and the solution was kept in bladder for 30 minutes. The instillation was repeated for 3 dose at the interval of 14 days. In the first 7 patients tacrolimus level was measured 30 minutes post instillation. Procedure was done on out patient basis. Data of 64 patients was available for study and analysed. The patients were contacted on phone and were asked about their present condition as compared to initial presentation before treatment. If the patient responded as marked or moderate improvement they were considered as responders(R) and if they had mild or no improvement they were considered as non responders(NR)

## RESULTS

7 patients out of 64 patients did not complete all 3 instillations due to irritative effect of tacrolimus, which persisted for 24 to 48 hours. No other side effects were observed. Blood tacrolimus level was between safe limit in tested patients. 28 patients had Hunner's Lesion(HL) whereas 36 patients did not have HL(NHL). 32 out of 64 patients were R and 32 were NR. 12 /28 HL patients responded(44%) in comparison to 20/36 of NHL patients(56%)

## INTERPRETATION OF RESULTS

Considering the severity of the disease the instillation was effective in both HL and NHL patients with very less side effect.

## CONCLUSIONS

Intravesical instillation of Tacrolimus is safe and effective. It should be instilled in all the patients not responding to standard oral and intravesical therapy.

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## 3. THE LEARNING TO THRIVE PROGRAM: A BEHAVIORAL INTERVENTION FOR PEOPLE WITH IC/BPS.

**Presenter: Laura Santurri**

Laura Santurri (1) - Renee Hetzler (1) - Tony Buffington (2)

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## INTRODUCTION AND AIM OF THE STUDY

Interstitial cystitis/bladder pain syndrome (IC/BPS) is classified as a chronic overlapping pain condition (COPC).<sup>1</sup> The pathophysiology of COPCs is thought to include central nervous system sensitization.<sup>1</sup> Treatment of COPCs remains disappointing,<sup>1</sup> but interventions based on psychosocial models have shown promise in relieving pain and improving daily function.<sup>2,3</sup> This study aims to test the feasibility of a psychosocially-informed behavioral intervention.

## MATERIALS AND METHODS

This is a feasibility study with a non-experimental design. Approval from an institutional review board will be obtained before study activities begin. Sixteen women who self-report an IC/BPS diagnosis will be recruited through national patient support organizations. Participants will engage in a group-based, six-week behavioral intervention, the Learning to THRIVE Program. The program has been designed using principles of instructional design and adult learning theory. It will be delivered primarily online and asynchronously, with a once-per-week virtual synchronous session led by trained facilitators with a background in the care and treatment of people with COPCs. Content will focus on the neuroscience of pain, factors that influence chronic pain, and health literacy, with built-in reflection on how participants can implement evidence-based strategies to manage their individual symptoms.

## RESULTS

The primary outcome will be a determination of study feasibility, with a focus on recruitment



and retention rates, participant adherence to the intervention, and participant satisfaction. Of secondary focus will be perceptions of self-efficacy and readiness to change.

### INTERPRETATION OF RESULTS

The results of this feasibility study will be shared via peer-reviewed mechanisms, used to refine the intervention, and as preliminary data to support a clinical trial.

### CONCLUSIONS

This pilot program will help determine the feasibility of a unique behavioral intervention to improve outcomes in those with IC/BPS who currently have few reliably effective biomedical treatment options.

### REFERENCES

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## 4. DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL EVALUATING EFFICACY AND SAFETY OF THE ALOE VERA IN TREATMENT OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME (IC/BPS).

**Presenter: Mauro Cervigni**

Mauro Cervigni <sup>(1)</sup> - Michele Carlo Schiavi <sup>(2)</sup> - Alessia Martoccia <sup>(3)</sup> - Andrea Fuschi <sup>(3)</sup> - Antonio Carbone <sup>(3)</sup> - Loredana Nasta <sup>(4)</sup>

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### INTRODUCTION AND AIM OF THE STUDY

Aloe Vera is an herbal remedy with antimicrobial, anti-inflammatory and immunomodulating properties that is considered a complementary and alternative therapy to treat Interstitial Cystitis/Bladder Pain Syndrome (IC/BPS). The aim of our study is to prove efficacy and safety of highly concentrated form of the *Aloe vera* plant in the treatment of IC/BPS (1).

### MATERIALS AND METHODS

In a prospective double-blind, placebo-controlled clinical trial we enrolled 30 female patients affected by IC/BPS treated with oral Aloe Vera assumption (6 tablets per day - each tablet containing 600 mg) for four months. Urinary symptoms, Pelvic pain and Quality of Life (QoL) were evaluated through the evaluation of bladder diary in 24 hours, urgent micturition events in 24 hours, urge urinary incontinence in 24 hours, mean number of nocturia events and through the administration of questionnaires: Short Form Health Survey 36 (SF-36), Interstitial Cystitis Symptom Index (ICSI), Interstitial Cystitis Problem Index (ICPI), Genito-Urinary Pain Index Questionnaire (GUPI Questionnaire), McGill Quality of Life (MQOL). Sexual function was evaluated with Promis Sexual Function and Satisfaction questionnaire.

## RESULTS

At four months follow-up mean number of voids and mean number of nocturia events in 24 hours were significantly lower ( $13.72 \pm 2.51$  vs.  $8.57 \pm 2.13$ ,  $p=0.04$ ;  $3.54 \pm 0.75$  vs.  $1.89 \pm 0.81$ ,  $p=0.02$ ). Urgent micturition events and urge urinary incontinence in 24 h did not show a significant change before and after the assumption of Aloe Vera ( $6.34 \pm 1.74$  vs.  $4.12 \pm 1.54$ ,  $p > 0.05$ ;  $0.82 \pm 1.01$  vs.  $0.69 \pm 0.43$ ,  $p > 0.05$ ). Urinary symptoms evaluated with questionnaires improved significantly: ICSI value changed from  $13.23 \pm 2.76$  to  $8.34 \pm 3.76$  ( $p = 0.03$ ), ICPI from  $12.56 \pm 2.99$  to  $7.12 \pm 1.59$  ( $p = 0.02$ ), GUPI Questionnaire from  $18.11 \pm 3.84$  to  $12.43 \pm 2.12$  ( $p = 0.01$ ).

Quality of Life and Sexual quality of life, evaluated respectively with SF-36 and Promis sexual function and satisfaction, improved significantly ( $64.23 \pm 11.76$  vs.  $82.21 \pm 10.24$ ,  $p < 0.0001$ ;  $22.11 \pm 5.24$  vs.  $56.78 \pm 4.88$ ,  $p = 0.001$ ). There was no significant change in values of MQOL at four months follow-up ( $8.76 \pm 1.88$  vs.  $7.91 \pm 1.22$ ,  $p > 0.05$ ).

## INTERPRETATION OF RESULTS

These findings confirm that Aloe Vera is safe and effective treatment for patients with IC/BPS and

it could be considered a valid option for conservative treatment of such group of pats.

## CONCLUSIONS

Usually, IC/PBS symptoms management is made of several treatment options. Oral assumption of Aloe Vera seems to be an effective choice to improve symptoms and QoL in patients affected by IC/BPS.

## REFERENCES

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## 5. MICROGENDXNGS URINE TEST MAY PROVIDE ADDED BENEFIT FOR THE DIAGNOSIS AND TREATMENT OF UTI IN INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PATIENTS EXPERIENCING A SYMPTOM.

**Presenter: Robert J. Evans**

Robert J. Evans <sup>(1)</sup> - Wyatt Whitman <sup>(1)</sup> - ALEX GORDON <sup>(2)</sup> - Maxwell Sandberg <sup>(1)</sup> - Gopal Badlani <sup>(3)</sup> - Catherine Matthews <sup>(1)</sup> - Stephen Walker <sup>(3)</sup>

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## INTRODUCTION AND AIM OF THE STUDY

Patients with interstitial cystitis/bladder pain syndrome (IC/BPS) often experience symptom flares resembling resemble a urinary tract infection (UTI); however, their urine cultures are often negative. Next generation sequencing (NGS) with Microgen<sup>Dx</sup> has the potential to provide a more rapid (~1 day) and comprehensive identification of pathogens that evade detection by standard culture, thereby providing rationale for antibiotic treatment in these patients.<sup>1</sup> The aim of this study was to examine outcomes in IC/BPS patients presenting with a symptom flare who received both standard urine culture and Microgen<sup>Dx</sup>.

## MATERIALS AND METHODS

A retrospective review was performed on outcomes in 28 female IC/BPS patients presenting with a symptom flare who received both a standard urine culture and a Microgen<sup>Dx</sup> urine test.

## RESULTS

Twenty-eight IC/BPS patients presented to the urology clinic experiencing a flare, with symptoms suggestive of a urinary tract infection (UTI). Urine culture was positive in 3/28 (10.7%) of the patients, while Microgen<sup>Dx</sup> found that 18/28 (64.3%) patients were positive for infectious genitourinary pathogens (IGUP). A total of 23/28 patients (82%; including 5 patients who were negative both by culture and NGS tests) opted to pursue treatment with

antibiotics. In the 3 patients with a positive urine culture, 1/3 had resolution of symptoms (ROS) following antibiotic treatment. An additional 8 patients who were culture negative, NGS-test positive and who opted to receive antibiotics, also experienced ROS.

## INTERPRETATION OF RESULTS

Compared to urine culture (n=3), Microgen<sup>Dx</sup> identified 6x more positive urine samples (n=18) containing IGUP. This likely resulted in more patients opting for antibiotic therapy, and experiencing ROS, than would have occurred with the urine culture test results alone.

## CONCLUSIONS

Identifying a UTI as the cause for a symptom flare in IC/BPS patients can be challenging. Microgen<sup>Dx</sup> may be a more rapid and sensitive tool for diagnosing a UTI that is potentially treatable, but not captured by a standard urine culture.

## REFERENCES

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## 6. INTERIM RESEARCH RESULTS OF POSTOPERATIVE FOLLOW-UP PATIENTS WITH ULCERATIVE INTERSTITIAL CYSTITIS.

**Presenter: Alexander Karasev**

Alexander Karasev (1) - Olga Markova (1) - George Kasyan (1)

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## INTRODUCTION AND AIM OF THE STUDY

Interstitial cystitis/bladder pain syndrome (IC/BPS) is still one of frequent causes of

chronic pelvic pain. Despite a long and active study of this nosology, the definition, approaches to diagnostic and the treatment are still imperfect. Purpose of the study: creation and validation of questionnaire for patients with ulcerative IC.

## MATERIALS AND METHODS

Interim results of the postoperative observation of patients with a confirmed diagnosis of ulcerative IC are presented. Respondents were asked 15 questions both online and fill out a questionnaire. Only 34 out of 80 patients met the inclusion criteria and agreed to participate in the survey. The most important inclusion criteria were the absence of the surgical treatment in the last three months and previously confirmed Hunner's lesions by endoscopic technique.

## RESULTS

Thirty-four patients participated in the survey, including 1 man and 33 women. The average score of patients according to the visual analog scale for pain (VAS) was 4.7. Urinary tract infection (UTI) was noted in 53% of respondents. Relief of symptoms with taking antibiotics was noted in 50% of respondents. 79% of respondents also experienced pain in the urethra and perineum. For the treatment, most patients use oral Pentosan Polysulfate (PPS), Amitriptyline, and nitrofurantoin antibiotics. The average time from onset symptom to diagnosis was about 6 years.

## INTERPRETATION OF RESULTS

UTI is a criterion for ruling out the diagnosis of IC but more than 50% of patients have a positive urine culture. Despite the standard treatment approaches, patients experience constant pain. PPS and amitriptyline continue to be the most effective drugs for IC.

## CONCLUSIONS

UTI does not rule out IC. Despite the existing effective drugs, they cannot completely eliminate the clinical symptoms. It requires of the development of new approaches to the management of patients in the interictal period.

## 7. INTRAVESICAL USE OF BACTERIOPHAGE IN PATIENTS WITH BPS COMPLICATED BY UTIs.

**Presenter: Dmitri Lysachev**

Authors: Alexander Karasev<sup>(1)</sup>, Andrew Zaitsev<sup>(1)</sup>, Dmitry Pushkar<sup>(1)</sup>, Fedor Zurabov<sup>(1)</sup>, Alexander Zurabov<sup>(1)</sup>, Gurkova Marina<sup>(1)</sup>, Oksana Arefieva<sup>(1)</sup>, Dmitri Lysachev<sup>(1)</sup>

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### INTRODUCTION AND AIM OF THE STUDY

Patients with bladder pain syndrome/interstitial cystitis (BPS/IC) may be dealing with recurrent lower urinary tract infection (UTIs). Phage therapy is an alternative to antibiotics. The aim of our work is to study intravesical bacteriophage application of BPS/IC patients with UTIs.

### MATERIALS AND METHODS

We present the observation of bacteriophage treatment in 4 BPS/IC patients with UTIs. We evaluated the efficacy and safety of the intravesical bacteriophage cocktail based on 26 urophages in complex therapy of BPS/IC patients with UTIs. Patients were treated with intravesical bacteriophages 2 times a week for 12 weeks.

### RESULTS

Before the study, the number of urinations per day was 40, nocturia - up to 12. The IC O'Leary index was 14, the PUF scale was 28, and the Acute Cystitis Symptom Score (typical symptoms) was 10. Bacteriological examination of urine revealed *Escherichia coli* and *Klebsiella pneumoniae*, resistant to cephalosporins and fluoroquinolones. After 3 months of therapy with intravesical bacteriophages, the number of urinations per day was 15, nocturia - up to 3. The IC O'Leary index was 8, the PUF scale was 10, and the Acute Cystitis Symptom Score was 6. The growth of *Escherichia coli* and *Klebsiella pneumoniae* at lower titers than before treatment was observed, but sensitivity to fluoroquinolones was restored.

### INTERPRETATION OF RESULTS

When monitoring patients for 3 months during treatment with intravesical bacteriophages and

showed no adverse effects and no recurrence of UTIs. There was a clinical improvement, a decrease in the titers of uropathogens and a restoration of sensitivity to some antibiotics.

### CONCLUSIONS

The results of the study showed that bacteriophage therapy in patients BPS/IC with UTIs, the number of relapses UTIs became significantly less. The growing threat of antimicrobial resistance has caused renewed interest in bacteriophages as an alternative to the treatment of bacterial infections, which is extremely important in BPS/IC patients.

## 8. PATHOPHYSIOLOGY, CLINICAL PRESENTATION AND MANAGEMENT OF KETAMINE INDUCED CYSTITIS.

**Presenter: Hann-Chorng Kuo**

Hann-Chorng Kuo (1) - Jia-Fong Jhang (2)

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### INTRODUCTION AND AIM OF THE STUDY

Ketamine has been illegally used as a recreational drug in many Asian countries. After using this drug for a longer duration, these ketamine abusers start to have bladder irritative symptoms, which will gradually develop into more severe urinary frequency and urgency symptoms, and finally to an ulcerative painful bladder. The similarity of ketamine cystitis (KC) and interstitial cystitis (IC) has not been reported.

### MATERIALS AND METHODS

We searched for current available literature and reviewed the underlying pathophysiology, clinical characteristics, and management of KC.

### RESULTS



Patients with long-term ketamine abuse usually have reduced functional bladder capacity, increased bladder sensation, detrusor overactivity, severe urgency, urinary incontinence, and bladder contracture. Ketamine metabolites can cause severe inflammation of the urothelium, urothelial barrier deficits, vascular endothelial fibrinoid change, increase oxidative stress, and fibrosis of the bladder wall. Decrease of bladder compliance, subsequent urinary tract infection, severe bladder pain at a full bladder, miction pain are also frequently encountered if not treated. Finally, hydronephrosis, ureteral stricture, vesicoureteral reflux (VUR), and renal failure may develop in patients with continuous ketamine abuse.

## INTERPRETATION OF RESULTS

In KC, IVP shows stasis of contrast media in ureter, ureteral stricture and dilatation, hydronephrosis, and contracted bladder. CT scan shows thickened bladder wall and marked perivesical lymphatic infiltration. VUDS shows low compliance, terminal DO and high detrusor pressure. Regarding the findings after hydrodistention, KC usually does not develop glomerulations as IC, instead, KC will present with diffuse oozing and fissures of the whole bladder mucosa. Patients with KC also have smaller functional capacity and more contracted bladder after hydrodistention than that of Hunner's IC.

## CONCLUSIONS

In conclusion, KC is a new inflammatory bladder disease which progresses to the end-stage bladder condition and severe bladder pain, contracted bladder and hydronephrosis. The pathophysiology, histopathology, clinical presentation and management are different from those for IC.

## REFERENCES

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2. Lee CL, Jiang YH, Kuo HC. Increased apoptosis and suburothelial inflammation in patients with ketamine-related cystitis: a

comparison with non-ulcerative interstitial cystitis and controls. *BJU Int* 2013;112:1156-62.

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## 9. SURVEY STUDY OF BPS/IC IN THE NETHERLANDS: DEMOGRAPHICS, IMPACT ON QUALITY OF LIFE AND TREATMENT MODALITIES.

**Presenter: Charlotte Van Ginkel**

Charlotte van Ginkel (1) - Cléo Baars (1) - John Heesakkers (2) - Frank Martens (1) - Dick Janssen (1)

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## INTRODUCTION AND AIM OF THE STUDY

The aim of this study was to investigate the demographics, symptoms, impact on quality of life (QoL) and treatments for bladder pain syndrome/interstitial cystitis (BPS/IC) in the Netherlands.

## MATERIALS AND METHODS

A digital questionnaire was administered to BPS/IC patients (n=193).

## RESULTS

The majority being female (89%) and 46% having Hunner Lesions. Many patients had symptoms long before diagnosis. The most common symptoms were pain (93%), frequency (80%), sleep difficulties (77%) and urgency (74%). All patients were affected on their QoL, moreover HL+ patients experienced a significant greater impact than HL- patients. Various therapies were offered, with bladder instillations, pelvic floor physical therapy and medication being the most commonly used therapies, but with some improvement left to be desired.

## INTERPRETATION OF RESULTS

The findings underline the impact of BPS/IC on the patient's QoL, with the notable affect by sleep difficulties. Furthermore, this underscores



the importance of offering a range of treatment options, as recommended by guidelines[1].

**CONCLUSIONS**

This study provides insight into the BPS/IC population in the Netherlands. The significant impact of IC/BPS on patient’s QoL and the variable effectiveness of available treatments emphasize the need for holistic approach in management of this condition.

**REFERENCES**

1. Engeler, D.S., et al., The 2013 EAU guidelines on chronic pelvic pain: is management of chronic pelvic pain a habit, a philosophy, or a science? 10 years of development. Eur Urol, 2013. 64(3): p. 431-9.

**Table 1. Demographic data of study population**

		Study population (n=193)			
		n	% <sup>2</sup> , 95%-CI		
<b>Male/Female</b>		20/166	11/89, 7-16/84-93		
<b>Subtype IC/BPS<sup>1</sup></b>	Type 1	6	3, 1-7		
	Type 2	81	44, 37-52		
	Type 3	84	46, 38-53		
	Unknown	13	7, 4-12		
<b>Main symptoms</b>	Pain	177	92, 87-95		
	Frequency	151	78, 72-84		
	Sleep difficulties	147	76, 70-82		
	Urgency	140	73, 66-79		
<b>Symptoms before diagnosis</b>	0 – 2 year	88	46, 38-53		
	3 – 5 year	45	23, 18-30		
	6 – 10 year	17	9, 5-14		
	11 – 20 year	23	12, 8-17		
	>20 year	17	9, 5-14		
Unknown	3	2, 0-4			
<b>Impact on QoL</b>					
		<b>Mean ± SD</b>	<b>range</b>		
	Hunner lesions	3,75* ± 0,97	(0 - 5)		
	Non-Hunner lesions	3,34 ± 1,26	(0 - 5)		
<b>Treatments offered</b>			<b>Received treatment</b>	<b>Treatment did not help</b>	
		n	% <sup>2</sup> , 95%-CI	n	% <sup>2</sup> , 95%-CI
	Bladder instillation	153	81, 74-86	46	30, 22-38
	Pelvic Floor Physical Therapy	146	77, 70-83	84	58, 50-66
	Medication	144	75, 68-81	66	34, 28-41
	Neuromodulation	75	39, 32-46	42	57, 45-68

Laser/coagulation	58	30, 24-37	12	21, 11-33
Hydrodistension	58	30, 24-37	33	56, 42-69
Intravesical botulin	40	21, 15-27	19	48, 32-64
Therapy in Pain center	31	16, 11-22	12	39, 22-58

<sup>1</sup> Based on the ESSIC classification of types of bladder pain syndrome

<sup>2</sup> Percent of the cases

\*statistical significant p=0,020

# 10. THE BURDEN OF URINARY TRACT INFECTIONS IN BLADDER PAIN SYNDROME ON PATIENTS AND THE HEALTHCARE SYSTEM

**Presenter: Cléo Baars**

Cléo Baars (1) - Charlotte van Ginkel (1) - John Heesakkers (2) - Frank Martens (1) - Dick Janssen (1)

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**INTRODUCTION AND AIM OF THE STUDY**

Bladder pain syndrome/ interstitial cystitis(BPS/IC) patients are more susceptible to urinary tract infections(UTI) [1, 2], likely worsening pre-existing symptoms. However little attention is given. This study aimed to explore the burden of UTIs on BPS/IC patients.

**MATERIALS AND METHODS**

Two studies were conducted in cystoscopic proven BPS/IC patients: patient-file-study (n=100) and survey-study(n=217).

**RESULTS**

UTIs were prevalent in over 50% of BPS/IC patients, with high proportions of these patients experiencing anxiety for a new UTI (70%) and worsening of BPS/IC symptoms afterwards (60%). Additionally, for these patients healthcare consumption was significantly increased (survey and patient-files). In 70% a delay in diagnosis was seen, due to doctors confusing BPS/IC symptoms with UTIs. There was much antibiotic resistance (80% of positive urine cultures) and prophylactic antibiotic use in BPS/IC patients, especially those with UTIs (75%) versus without UTIs (still 38%).

**INTERPRETATION OF RESULTS**

UTIs have significant negative impact on BPS/IC patient lives and the healthcare system, causing delay in diagnosis, increased symptom severity, patient anxiety, increased healthcare consumption and antibiotic resistance.

**CONCLUSIONS**

These findings emphasize the need for improved UTI guidelines concerning diagnosis, management and prevention for BPS/IC patients to enhance quality of life and improve care.

**REFERENCES**

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Patient file	All patients (n=100)		UTI group (N=53)		No UTI (N=47)		
	(%)	95%-CI	(%)	95%-CI	(%)	95%-CI	
UTI(s) since 01-2020	53	[43 – 63]	-	-	-	-	
	Median	IQR [range]	Median	IQR [range]	Median	IQR [range]	
Nr of UTIs since 01-2020	1	2 [0 – 9]	2	2 [1 – 9]	-	-	
Nr of digital contacts	0	0 [0 – 7]	0*	0 [0 – 2]	0*	0 [0 – 7]	
Nr of telephonic contacts	2	5 [0 – 36]	3*	7 [0 – 36]	1*	3 [0 – 23]	
Nr of physical contacts	10	15 [0 – 65]	15*	17 [1 – 65]	9*	12 [0 – 43]	
Total nr of contacts	15	19 [1 – 65]	18*	24 [4 – 65]	11*	15 [1 – 46]	
	(%)	95%-CI	(%)	95%-CI	(%)	95%-CI	
Resistance <sup>c</sup>	-	-	80	[56 – 94]	-	-	
Use of antibiotic prophylaxis <sup>b</sup>	58	[48 – 68]	75**	[62 – 86]	38**	[25 – 54]	
	37		51		21%		
Survey	All patients (N=198)	UTI group (N=108)		No UTI (N=83)			
	(%)	95%-CI	(%)	95%-CI	(%)	95%-CI	
GP confusing BPS/IC for UTI	70	[63 – 77]	84**	[76 – 91]	54**	[43 – 65]	
Delay because GP confuses BPS/IC for UTI	0 – 2yr	60	[51 – 68]	55	[43 – 66]	69	[53 – 82]
	3 – 5yr	18	[12 – 26]	18	[10 – 28]	18	[8 – 32]
	6 – 10yr	10	[6 – 17]	13	[6 – 22]	7	[1 – 18]
	>10yr	12	[7 – 19]	15	[8 – 25]	7	[1 – 18]
Regular UTIs	Total	55	[48 – 62]	-	-	-	-
	Now	21					
	In the past	34					
Fear of new a UTI	Yes	53	[46 – 60]	70**	[61 – 79]	31**	[21 – 42]
	Unclear	12	[8 – 18]	8	[3 – 14]	15	[8 – 25]
Worsening of BPS/IC symptoms after a UTI	Yes	42	[35 – 49]	60**	[50 – 69]	17**	[9 – 27]
	Unclear	30	[23 – 37]	26	[18 – 36]	35	[24 – 46]
Increased healthcare (for BPS/IC) consumption during or after UTI	Yes	32	[26 – 40]	47**	[37 – 57]	13**	[6 – 22]
	Unclear	29	[23 – 36]	28	[20 – 38]	29	[20 – 41]

Table 1: Burden of UTIs in BPS/IC patients, results from survey and patients file study

Percentages are rounded to the nearest whole number (95% confidence interval)

Significance between the groups UTI and no-UTI: \*ps0.05 and \*\*ps0.01

<sup>a</sup> Percentage of all positive urine cultures

<sup>b</sup> Percentage of patients who have used this therapy at some point since 2020 (95% confidence interval), followed by percentage of patients who have used it all three years (2020-2022)

**11. COEXISTENCE OF EBV PERSISTENCE AND REACTIVATION IN THE BLADDERS OF INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME WITH HUNNER LESION AND THE CLINICAL EFFICACY OF VALACYCLOVIR TREATMENT**

**Presenter: Jia-Fong Jhang**

Jia-Fong Jhang (1) - Hann-Chorng Kuo (1)

*Hualien Tzu Chi Hospital, Hualien Tzu Chi Hospital, Hualien, Taiwan, Province Of China (1)*

**INTRODUCTION AND AIM OF THE STUDY**

To identify EBV infection in the bladders of IC/BPS patients with Hunner lesion (HIC) and the efficacy of valacyclovir for IC/BPS.

**MATERIALS AND METHODS**

The bladders from HIC patients were subjected to IHC, flow cytometry, and RNA transcriptome analyses. Patients with IC/BPS were prospectively enrolled for valacyclovir treatment 500 mg twice a day for 4 weeks. Urine samples were analyzed for EBV DNA by qPCR.

**RESULTS**

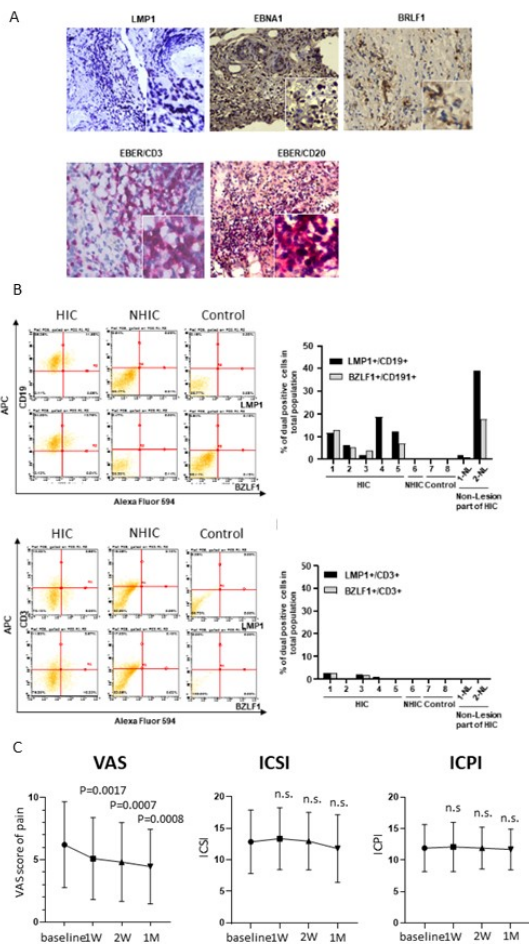
Transcriptomic analysis revealed an elevation of EBV infection KEGG pathway genes in the HIC bladders. The IHC and flow cytometry assays revealed both EBV latent genes (EBNA1 and LMP1) and lytic genes (BZLF1 and BRLF1) in HIC bladders (figure 1A and 1B). Among 28 patients with IC/BPS (4 HIC) who received valacyclovir, urinary EBV was detected in three patients at baseline. The VAS pain score in the patients with IC/BPS was significantly decreased at the end of the study (figure 1C). Urinary EBV was not detected in all samples after valacyclovir treatment

**INTERPRETATION OF RESULTS**

EBV infection can persist and reactivate in the bladder of HIC patients, and valacyclovir could relieve bladder pain.

**CONCLUSIONS**

EBV infection might be the etiology in some of the patients with IC/BPS.



(BC) and non-low BC1,2. Low BC patients tend to be older, with higher symptom scores, and fewer non-urological symptoms<sup>3</sup>. The mechanisms by which patients transition to a low BC remains unknown, therefore the aim of this study was to investigate molecular mechanisms that underlie the low BC IC/BPS phenotype.

**MATERIALS AND METHODS**

Bladder biopsy tissue samples from 41 female IC/BPS patients (19 low BC; 22 non-low BC) were selected for gene expression profiling using whole-genome microarrays. Results were analyzed using Qluore Omics Explorer and Ingenuity® Pathway Analysis.

**RESULTS**

Figure 1 shows the results of principal component analysis and hierarchical clustering. The comparison between samples from low and non-low BC patients identified 2,360 differentially expressed transcripts as significant ( $q \leq 0.05$ ).

**INTERPRETATION OF RESULTS**

A key theme that emerged was low BC patients had dysregulation and inhibition of apoptosis and cell death.

**CONCLUSIONS**

This initial comparison of differential gene expression in bladder mucosal biopsies provides support for the concept of distinct phenotypic subgroups within IC/BPS based on BC and points to a dysregulation in urothelial cell apoptosis as a contributing factor for the low BC subgroup.

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2. Colaco M, Koslov DS, Keys T, Evans RJ, Badlani GH, Andersson KE, et al. Correlation of gene expression with bladder capacity in interstitial cystitis/bladder pain syndrome. *Journal of Urology*. 2014;192(4).

**12. DYSREGULATE APOPTOSIS IS A FEATURE OF THE LOW BLADDER CAPACITY INTERSTITIAL CYSTITIS/BLADDER PAIN SYNDROME PHENOTYPE**

**Presenter: Robert Evans**

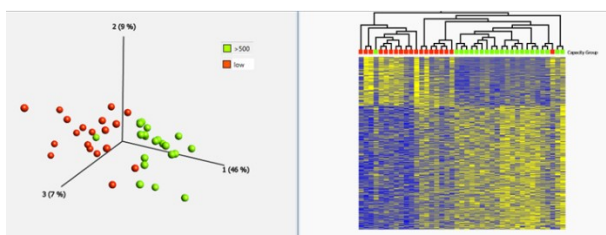
Max Sandberg (1) - Wyatt Whitman (2) - Catherine Matthews (2) - Gopal Badlani (3) - Robert Evans (2) - Stephen J. Walker (2)

Wake Forest Urology (1) - Department of Urology; Wake Forest University School of Medicine (2) - Department of Urology-School of medicine; Wake Forest University - Wake Forest Institute for Regenerative (3)

**INTRODUCTION AND AIM OF THE STUDY**

Interstitial cystitis/bladder pain syndrome (IC/BPS) patients align broadly into two phenotypic subgroups: low bladder capacity

3. Logadottir Y, Fall M, Kåbjörn-Gustafsson C, Peeker R. Clinical characteristics differ considerably between phenotypes of bladder pain syndrome/interstitial cystitis. *Scand J Urol Nephrol.* 2012 Oct 1;46(5):365–70.



**Figure 1.** Principal Component Analysis and Hierarchical Clustering. Left panel: PCA comparing low BC (red) and non-low BC (green) patients. Right panel: Hierarchical clustering of differentially expressed genes (DETs) between samples. Yellow = upregulated genes in low BC group; blue = downregulated genes.

### 13. IN VITRO: THE ROLE OF HYALURONIC ACID IN THE UROTHELIAL BARRIER

**Presenter: Cléo Baars**

Cléo Baars (1) - Charlotte van Ginkel (1) - John Heesakkers (2) - Frank Martens (1) - Dick Janssen (1)

*Radboudumc, Urology, Nijmegen, Netherlands (1) - Maastrichtumc, Urology, Maastricht, Netherlands (2)*

#### INTRODUCTION AND AIM OF THE STUDY

Hyaluronic acid (HA) is one of the glycosaminoglycans (GAGs) found in the GAG-layer of the bladder urothelium, the exact role is unclear. We aimed to examine the function of HA by seeing the effect of its removal in-vitro.

#### MATERIALS AND METHODS

Differentiated primary porcine urothelial cells were treated with hyaluronidase (for 24h) or protaminesulfate (PS, for 3h) or left untreated. At different timepoints the transepithelial electrical resistance (TEER) and mRNA expression GAGs (HAS3, CSGALNACT2), inflammation markers (IL-6, IL-8) and barrier markers (UPK, ZO-1, OCLN) was measured.

#### RESULTS

PS caused a decrease in TEER, which is a known effect [1], whereas hyaluronidase led to a slight increase in TEER. Hyaluronidase increased the expression of HAS3 and IL-8, but no clear effect was seen on CSGALNACT2 and IL-6. Additionally, there was no clear effect of hyaluronidase on barrier markers.

#### INTERPRETATION OF RESULTS

The results suggests that removal of HA starts a fast-acting positive feedback loop for new production of HA with HAS3. Hyaluronidase seems to be less inflammatory than PS, leaving the barrier function intact and only affecting one inflammation marker

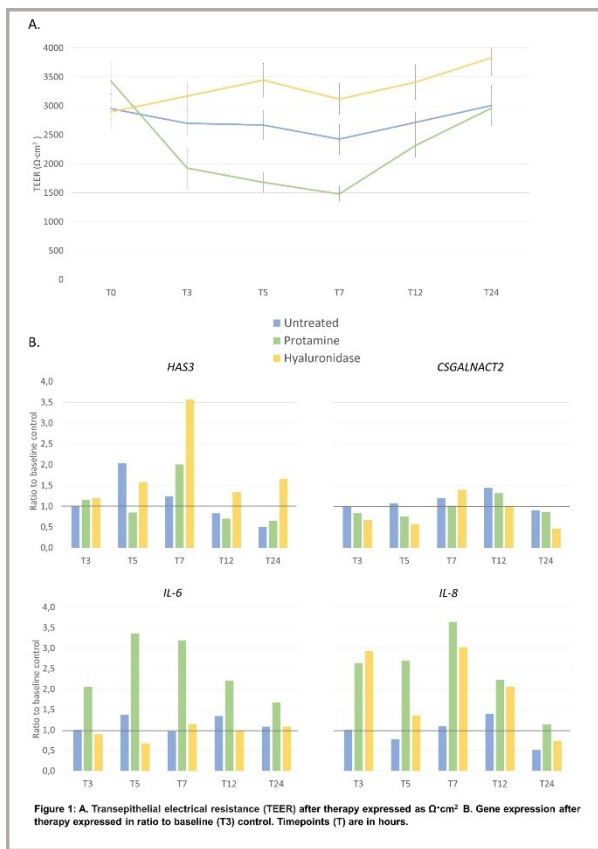
#### CONCLUSIONS

Overall, removal of only HA has no negative effect on the barrier function and induces limited inflammatory response.

#### REFERENCES

1. Janssen, D.A., et al., The distribution and function of chondroitin sulfate and other sulfated glycosaminoglycans in the human bladder and their contribution to the protective bladder barrier. *J Urol*, 2013. 189(1): p. 336-42.





Syndrome/Interstitial Cystitis) than in women with chronic non-neoplastic pain with or without fibromyalgia, to examine possible correlations between urological and psychiatric symptoms.

**METHODS**

The patients included in the study were divided into two groups:

- Group 0: patients with an existing diagnosis of BPS/IC. BPS/IC was confirmed by reviewing medical record.
- Group 1+2: patients with chronic non-neoplastic pain, suffering from fibromyalgia or other types of chronic pain (chronic arthralgia or lower back pain).

Three questionnaires were administered: PHQ-9 to investigate psychological symptoms, O’Leary Saint (ICSI-ICPI) to investigate urological symptoms in women with BPS/IC and BPI to investigate specifically pain .

**RESULTS**

The survey included 69 patients, 42 patients had a diagnosis of BPS/IC while 27 of them had chronic non-neoplastic pain. The average PHQ-9 score was 10.3 in BPS/IC group, considered as major depression (score between 10 and 14); the average score of PHQ-9 was 6.9 in group 1+2, as in sub-threshold depression (between 5-9).

**CONCLUSIONS**

The chronic pain of BPS/IC can affect mood more than in other painful conditions, as more than half of this population has a score that identifies depression with the PHQ-9 questionnaire, confirming the hypothesis that the syndrome is associated with a higher prevalence of an anxious-depressive condition.

**14. QUALITY OF LIFE ANALYSIS IN BLADDER PAIN SYNDROME/ INTERSTITIAL CYSTITIS: IMPLICATIONS FOR A MULTIMODAL INTEGRATED TREATMENT**

**Presenter: Daniele Porru**

Daniele Porru (1) - Daniela Anselmo (1) - Magliano Amanda (2) - Scalmati Serena (2) - De Silvestri Annalisa (3) - Richard Naspro (1)

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**OBJECTIVES**

To evaluate whether there is a higher prevalence of anxiety-depressive disorders in women with BPS/IC (Bladder Pain

# 15

## 15. COMORBID CONDITIONS IN BPS/IC: PREVALENCE AND CLINICAL SIGNIFICANCE.

**Presenter: Jorgen Quaghebeur**  
Jörgen Quaghebeur (1)

*University of Antwerp, University Hospital of Antwerp, Department of Urology, Antwerp, Belgium. Faculty of Medicine and Health Sciences, University of Antwerp (Campus Drie Eiken) Wilrijk*

### INTRODUCTION AND AIM OF THE STUDY

In BPS/IC, comorbid conditions are common complications. This study describes BPS/IC comorbidity and explains the neuropathological association and clinical significance in the literature.

### MATERIALS AND METHODS

An advanced literature search in PubMed searched for “bladder pain syndrome,” “interstitial cystitis,” and “comorbid\*” or “associated.” Only clinical trials, meta-analyses, randomized clinical trials, and systematic reviews were analyzed, including other studies about comorbidity not found in this search.

### RESULTS

PRISMA analysis showed only six publications meeting the criteria. BPS/IC showed higher odds of comorbid neurological and rheumatological diseases, mental illnesses, and an increased prevalence of multiple comorbidities. In BPS/IC, 61% experienced one or more significant non-urological associated somatic syndromes (NUAS) (e.g., chronic fatigue syndrome, fibromyalgia, IBS, and migraine) 1. Other comorbidities were allergies, endometriosis, and vulvodynia. Nearly 90% of BPS/IC patients report sensitivities for dietary comestibles. Psychosocial comorbidity analysis (n=34 studies) explained the prevalence of depression, anxiety, panic disorders, stress, catastrophizing, abuse, traumatic events during

childhood, and worsened quality of life 2. Forty-two percent of BPS/IC patients (n=64) had PTSD.

### INTERPRETATION OF RESULTS

Any physical or psychological stimulus disrupting homeostasis results in a stress response. Organ cross-sensitization and peripheral and central upregulation influence the symptom severity as a stress response due to visceral and emotional factors. Impaired PS function in BPS/IC has been described and might be explained as a primitive stress response in polyvagal theory 3. The parasympathetic stress response may be responsible for increased bladder tone and pain. Comorbidity makes it challenging to understand, make the diagnosis, and manage BPS/IC.

### CONCLUSIONS

BPS/IC has a significant prevalence of somatic, visceral, and psychosocial comorbid conditions. Stress response due to threat caused by the pain and symptoms results in a vicious cycle maintaining the chronic aspect and severity of the symptoms.

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3. Quaghebeur J, Petros P, Wyndaele JJ, De Wachter S. The innervation of the bladder, the pelvic floor, and emotion: A review. *Auton Neurosci* 2021; 235: 102868.

## ESSIC 2023 ABSTRACT PRESENTERS' BIO SKETCH

New York, 6-8 July. Lenox Health Greenwich Village

- 1. ABREU-MENDES, Pedro** Urologist at Centro Hospitalar de São João | CHSJ - Urology. His areas of interest are Urolithiasis, Urologic Oncology. Endourology and Urinary Incontinence.
- 9./10./13. BAARS, Cleo** Urologist at Radboudumc, Urology, Nijmegen, Netherlands
- 4. CERVIGNI, Mauro** Co-founder and current President of the International Society for the Study of Interstitial Cystitis (ESSIC). Mauro Cervigni is an expert in pelvic reconstructive surgery with trans-vaginal and robotic techniques, which are currently among the most advanced surgical techniques.
- 5. EVANS, Robert J.** Professor in the Departments of Urology and Gynecology at Wake Forest School of Medicine. Evans is currently also evaluating the use of bladder biopsy and genomic evaluation to subtype patients with IC/BPS.
- 6./7. KARASEV, Alexander** Urologist at Yevdokimov A.I. Moscow State University of Medicine and Dentistry, Department of urology FSBEI of Higher Education" Yevdokimov A.I. Moscow State University of Medicine and Dentistry», Mosciw, Russian Federation.
- 8.11 KUO, Hann Chorng** Professor of Buddhist Tzu Chi University School of Medicine  
special expertise: Neurogenic voiding dysfunction, Stress urinary incontinence, Bladder outlet obstruction in males and females, Neurourology & urodynamics.
- 8.11. JHANG J. Fong,** Practices in Hualien City, Taiwan. Her top areas of expertise are Interstitial Cystitis, Stress Urinary Incontinence, Urinary Tract Infection (UTI), Eosinophilic Cystitis, and Endoscopy.
- 2. MISHRA, Nagendra** Doctor of Medicine, Pramukhswami Medical College · Department of Surgery Division of Urology. His current research interest is diagnosis and treatment of interstitial cystitis /bladder pain syndrome.
- 14. PORRU, Daniele** MD Urology Dept Fondazione IRCCS Policlinico San Matteo Pavia, Italy
- 15. QUAGHEBEUR, Jorgen** Visiting Professor at the University of Antwerp, and Associated Researcher Medical University of Mazovia, Warsaw, Poland
- 12. SANDBERG Maxwell , MD** at Departments of Urology and Gynecology , Wake Forest School Of Medicine Medical Center.
- 3. SANTURRI, Laura** Associate Professor in the College of Health Sciences at the University of Indianapolis in Indiana She is the current Board Chair of the Interstitial Cystitis Association.
- 9./10./13. VAN GINKEL, Charlotte** Urologist at Radboudumc Radboudumc, Urology, Nijmegen, Netherlands

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