458

Chaliha C[1], Al-Buheissi S[2], Khasriya R[2], Khan S[2], Lunawat R[2], Bishara S[2], Malone-Lee J[2]

1. *Department of Obstetrics and Gynaecology, Royal London and St Bartholomews Hospitals, London,* ***2.*** *Research Department of Clinical Physiology, Div. of Medicine, University College London Medical School, Whittington Campus, London*

CHARACTERISING THE PHENOTYPE OF THE PAINFUL BLADDER SYNDROME IN PATIENTS PRESENTING WITH LOWER URINARY TRACT SYMPTOMS

Hypothesis / aims of study.

The Painful Bladder Syndrome (PBS), synonymous with Interstitial Cystitis (IC) is a chronic condition affecting women predominantly, with prevalence estimates ranging from 1.2/100,000 to 24,000/100,000. As yet there is no consensus on the definition of IC/PBS but it must be discriminated from the overactive bladder (OAB) to target therapy. At present the diagnosis seems to rest on history and physical examination focusing on exclusion of other conditions. Invasive procedures such as cystoscopy and potassium sensitivity are of limited value and are not universally employed.

The characteristic symptoms of PBS/IC are bladder/urogenital pain, urgency, frequency and nocturia which can be difficult to distinguish from OAB for which many of the symptoms overlap. To date, measures of PBS/IC have relied on symptoms tautologically validated against symptom-based diagnosis. This hampers progress in studies on the pathophysiology of PBS/IC. It also makes it difficult to exclude, with confidence, other disease entities such as the overactive bladder. As yet the aetiology of PBS/ IC is undefined but the pain experience, reported by patients, suggests underlying inflammation and afferent neuropathic activity. If this condition is different from the overactive bladder, there should be a clear difference in the qualitative nature of the symptoms and their relation to non-symptomatic, biological markers of disease and treatment.

The aim of this study was to define the phenotype of a patient with PBS/IC that contrasted from OAB. The study started with a symptom set volunteered exclusively by patients with PBS/IC. The key symptoms elucidated were then explored for points of discordance with OAB and their relationship with markers of lower urinary tract infection and inflammation.

Study design, materials and methods

In 1997 the then extant Interstitial Cystitis Association (ICA) in the UK conducted a survey of its members on their symptoms. This self-selecting group provided an exhaustive dataset on their disease experience. Scrutiny of the record identified eight recurring dysaesthesic/pain symptoms which are shown in Table 1.

The eight symptoms were used to construct eight questions which were written into a bespoke clinical symptom database. These were included as part of the assessment of all patients, with previously untreated lower urinary tract symptoms (LUTS), presenting to secondary care facilities located in Urology and Urogynaecology departments. In addition to the dysaesthetic manifestations, symptoms of urgency were assessed by means of a well validated, sensitive, urgency scale (1). Reported 24-hour urinary frequency and incontinence were also recorded.

A midstream urine specimen (MSU) was obtained and an aliquot was examined fresh, unspun by microscopy in order to quantify the pyuria. An aliquot was sent for routine laboratory culture with a diagnostic threshold of 10^5 colony forming units (cfu) ml^{-1}. The patients were reviewed during treatment and these same data elements collected. Patients with pyuria and/or bacteriuria were treated for an assumed urinary tract infection with antibiotics. After treatment, and on resolution of the pyuria and bacteriuria, the symptoms questionnaire was repeated.

The data on the eight dysaesthesic/pain symptoms were analysed as follows: (i) Internal consistency was examined using Cronbach's alpha. (ii) Construct validity was assessed using comparisons of symptom counts between groups: (a) pyuria/no pyuria & (b) bacteriuria/no bacteria. (iii) Responsiveness was assessed by comparing symptom count before and after clearance of pyuria; and clearance of bacteriuria. (iv) External responsiveness was assessed by correlating the summed pain symptoms against the urgency score; 24-hour frequency; and 24-hour incontinence. Test-retest and inter-observer reliability were not assessed in this study. Comparisons used the t-test for unpaired samples, X^2, and Spearman's R with alpha=0.05.

Results

There were 736 respondents to the 1997 ICA survey (698 women and 38 men: mean age 57 years, sd=15). The eight index questions are listed in the Table One.

Between 2003 and 2009, 892 patients were assessed in our unit using the symptom assessment database as described above. This group comprised of 768 women and 124 men (mean age=52 years, sd=18). 254 patients (28.5%, 95%CI=26% to 31%) described a least one dysaesthetic symptom. The frequencies of patients reporting each symptom are shown in Table One.

Table One – Symptom frequencies from ICA Survey of 1997 and STUDY patients

Symptom	ICA Survey (n=736)	Study sample (N=254)
Discomfort with filling	709 (96%)	198 (78%)
Bladder pain	528 (72%)	91 (36%)
Loin pain	121 (16%)	87 (33%)
Dysuria	12 (2%)	74 (29%)
Genital pain	402 (55%)	63 (25%)
Iliac fossa pain	460 (63%)	54 (21%)
Abdominal pain	402 (55%)	53 (21%)
Leg pain	13 (2%)	36 (14%)

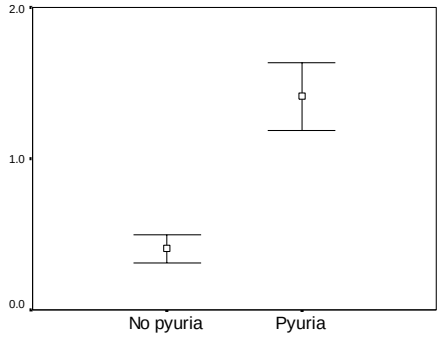
There was no correlation between the urge score and the number of pain symptoms reported (Spearman R= 0.07, p=0.042). Patients with incontinence were less likely to report a pain symptom X^2=50, df=1, p<0.001) whereas frequency scores did not differ in those with and without pain (OAB group) (Mean =11.96, 95% CI = 11.6 to 12.3).

The dysaesthesia score was related to the presence of pyuria and positive urine culture with pain symptoms more numerous in those with pyuria (t=4.7 p<0.001 95% CI diff 1.0 to 0.5) and bacteriuria (t=4.7 p<0.001 95% CI diff 1.0 to 0.5) (Figures One and Two).

In comparison there was no relation of pyuria and bacteriuria to the symptom of urgency.

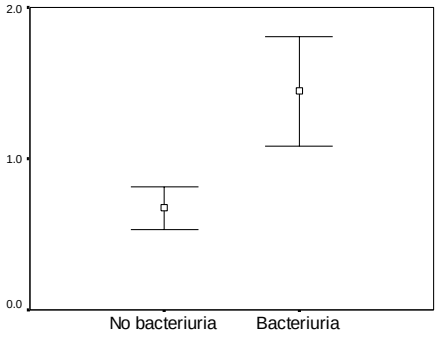
Patients treated with antibiotics showed significant differences in the number of reported pain symptoms following clearance of pyuria (t=2.9, p=0.004, 95% CI change= 0.98 to 0.53) and bacteriuria (t=2.41, p=0.016, 95% CI change= 0.083 to 0.805) but there was no differences in urge score, frequency or incontinence.

Figure One: Dysaesthesia and pyuria



Microscope WBC

Figure Two: Dysaesthesia and bacteriuria



MSU culture group

Interpretation of results

This study describes a symptom phenotype for PBS/IC which has been validated against independent biomarkers of lower urinary tract inflammation. The method identifies patients with PBS/IC so as to separate them clearly from those with OAB. The symptom set change coherently in response to plausible treatments which result in normalisation of biomarkers. Symptoms of urgency and incontinence are clearly dissociated from this phenotype.

Conclusion

This method opens a path for the scientific elucidation of PBS/IC and hopefully the development of treatments based on a better understanding of the pathophysiology.

References

1. Al Buheissi S, Khasriya R, Maraj BH, Malone-Lee J. A simple validated scale to measure urgency. J Urol 2008 March;179(3):1000-5

Specify source of funding or grant	**This study did not require funding and was not supported by a grant. None of the authors have any disclosures and there are no conflicts of interest.**
Is this a clinical trial?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Whittington NHS Trust Research Ethical Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**