

## VISCERAL AND CUTANEOUS SENSORY TESTING IN SUBJECTS WITH PAINFUL BLADDER SYNDROME

### Hypothesis / aims of study

Our objectives were (1) to determine whether visceral hyperalgesia is present in patients with painful bladder syndrome (PBS), (2) to determine whether PBS subjects have altered localization of bladder sensation, (3) to determine whether repeated bladder filling alters the magnitude and location of perceptions of bladder filling, (4) to determine whether PBS subjects have lower thresholds to cutaneous stimulation than controls, (5) to determine whether PBS subjects demonstrate altered sensation to repetitive cutaneous stimuli in dermatomes to which the bladder refers.

### Study design, materials and methods

Patients were included in the **PBS** arm of these studies if they complained of bladder pain and urinary frequency, had O'Leary-Sant scores of at least 12 (ICSI) and 12 (ICPI) and bladder pain had been present for at least 3 months. Patients were included in the **stress urinary incontinent (SUI) control** arm of these studies if they had symptoms of stress incontinence, had symptoms of urge incontinence no more often than 'rarely' and had no bladder pain. Patients were included in the **asymptomatic control** arm of these studies if they had no symptoms of incontinence or bladder pain. To test for the presence of visceral hyperalgesia, subjects underwent bladder filling at 50ml/minute. Subjects rated intensity of bladder distension sensation at incremental 50 ml bladder volumes up to a maximum volume of 300 ml, and indicated the area over which they felt a sensation of bladder fullness/discomfort/pain using a body map. Subjects voided and bladder filling and sensory ratings were repeated twice more. We then used the Neurometer (Neurotron Inc., Baltimore, MD) to establish cutaneous thresholds to electrical stimulation at frequencies of 2000 Hz, 250 Hz and 5 Hz in C5, T6, T10, T12 and S3 dermatomes. Testing for response to repetitive stimulation was conducted at each stimulating frequency at T12 and S3 sites only. Suprathreshold, non-noxious skin stimulation was applied during six series of 15 stimuli at an interstimulus interval of 2 seconds. Subjects rated sensation intensity after the first and last stimulus in each series. All testing took place during days 1-5 of any premenopausal patient's menstrual cycle. We analyzed ratings of bladder pain during distension and cutaneous CPTs using repeated measures Kruskal-Wallis tests and used Chi-Squared tests of proportions to evaluate subjects' ability to sense repetitive stimulation. All tests were considered significant at a 5% level.

### Results

We recruited 8 PBS subjects, 10 SUI controls and 8 asymptomatic controls. PBS subjects demonstrated hyperalgesia to bladder filling. Maximum bladder capacity (MBC) was <150ml in 4(50%) of the PBS patients, while 17 of 18 subjects in the control groups permitted filling to 300ml. PBS patients had a median pain rating of 7 at MBC. Second and third bladder fills did not cause more pain than the first bladder fill (Figure 1). At MBC, 6 (80%) of PBS subjects indicated they sensed bladder fullness/discomfort at both suprapubic and vulvar sites (Figure 2). This pattern of sensation was present in just one SUI control and in no asymptomatic controls. Body maps of bladder sensation did not alter with repetitive bladder filling in any group. Current perception thresholds were lowered in subjects with PBS (median 9mA, range 2-27mA) and SUI (median 9mA, range 3-33) in S3 dermatome at 5Hz, compared to asymptomatic controls (median 17mA, range 11-55mA), but all groups were similar at all other sites and frequencies. When trains of repetitive, non-noxious, cutaneous stimuli were applied to T12 and S3 dermatomes, it was common that asymptomatic controls were unable to perceive the cutaneous stimulus after one or more series. Significantly more PBS and SUI

subjects were able to sense the last of 6 trains of 15 stimuli than asymptomatic controls.

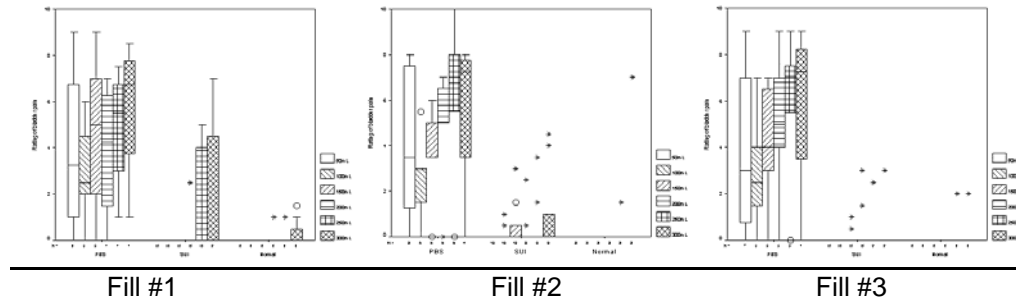


Figure 1: Perceptions of urgency/discomfort during three bladder fills in subjects with PBS and controls

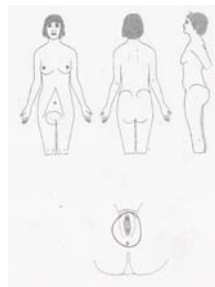


Figure 2: The majority of subjects with PBS reported bladder sensation was experienced at both suprapubic and vulvar/urethral sites.

#### Interpretation of results

Our results are consistent with the theory that PBS is a visceral pain syndrome. Differences in localization of bladder sensation and decreased sensory threshold in the S3 dermatome at 5Hz may also prove to be clinically useful. Our finding of decreased habituation to non-noxious cutaneous stimuli in PBS subjects is novel. If confirmed, this offers further insight into the pathophysiology of this and other visceral pain syndromes and may prompt consideration of novel therapies aimed at altering central responses to visceral stimulation.

#### Concluding message

Our documentation of visceral and cutaneous hypersensitivity supports the idea that PBS is a visceral pain syndrome. Our tools for rating and mapping of bladder pain during cystometry distinguished between PBS subjects and controls and may prove to be useful when there are clinical questions about the presence of visceral hypersensitivity.

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