

TRANSPLANTATION OF MATURE ADIPOCYTE-DERIVED DEDIFFERENTIATED FAT (DFAT) CELLS IMPROVED VESICoureTERAL REFLUX (VUR) IN A RAT VUR MODEL.

Hypothesis / aims of study

The Overactive Bladder Syndrome (OAB) and the Bladder Pain Syndrome (BPS) are considered to be distinct entities, defined by their primary presenting symptom. Although storage symptoms are common to both conditions, urgency is the key feature of OAB, whilst pain is the defining symptom of BPS.

There are many symptom scores available to measure the majority of lower urinary tract symptoms (LUTS); nociception, the appreciation of pain, is less well served. In 1997, the Interstitial Cystitis Association UK conducted a survey of members (N=736), providing an exhaustive dataset on their disease experience. Analysis of this dataset identified eight recurrent nociceptive responses; these were used to formulate a series of questions to assess pain referred from the lower urinary tract. These eight questions were entered into a clinical symptom database to record the responses of all patients presenting to an incontinence clinic with previously untreated LUTS.

In 2009, a cross-sectional analysis of these data was reported (1). The eight questions, when applied generally outside the boundaries of BPS, functioned impressively as a measure of nociceptive symptoms. Internal consistency, construct validity, internal and external responsiveness were all corroborated. It was noted that OAB was associated with measurable pain. An important component missing from that analysis was data on the longitudinal changes in these symptoms, related to disease resolution under treatment. This study was a further analysis of this pain measure, and scrutinised its performance when evaluating changes in symptoms associated with treatment.

Study design, materials and methods

Between 2002 and 2010, data were collected relating to pain symptoms (Table 1). These were recorded using a fixed protocol, prospectively, from patients at presentation, and whilst under treatment. Symptoms of urgency were measured using a validated score (2).

Table 1 Pain and nociceptive symptoms described by patients in the incontinence clinic between 2002 and 2010.

Symptom	Frequency (%)
1. Pain/discomfort with bladder filling	51
2. Dysuria	45
3. Loin pain	44.5
4. General abdominal pain	22.8
5. Suprapubic pain/discomfort	15.6
6. Pain/discomfort radiating to the legs	13.1
7. Iliac fossa pain/discomfort	8.8
8. Genital pain/discomfort	7.5

These questions discriminated between those with and without pyuria, and those with or without bacteriuria, distinguishing patients with urinary tract infection (UTI) contributing to OAB or LUTS.

At each assessment, a mid-stream sample of urine (MSU) was obtained. The urine was examined fresh by microscopy to quantify pyuria, and sent for routine culture with a diagnostic threshold of 10^5 colony forming units ml^{-1} . Patients with pyuria and/or bacteriuria were treated for a presumed UTI with antibiotics. LUTS were treated according to standard guidelines. During questioning the patient and clinician were blinded to urinalysis results. This study had a greater than 80% power to detect a clinically significant between group difference ($\alpha=0.05$).

Results

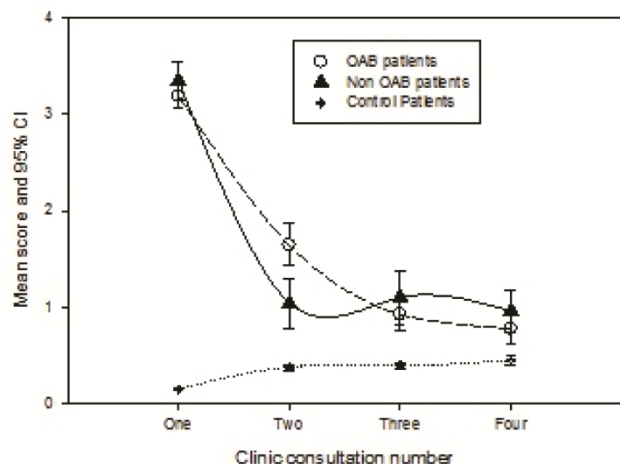
Assessments were undertaken on 958 women presenting with at least one pain symptom, contributing to 8822 patient episodes (mean age=51, sd=19). At presentation 42% had OAB; 31% mixed incontinence; 8% Stress Urinary Incontinence; 19% had pain symptoms without LUTS. Pyuria was evident in 30% of this sample, with only 8% manifesting a positive culture. Patients with voiding disorders were excluded from the analysis. Control data was provided by 1057 similar women, presenting without pain, over 2854 patient episodes.

Higher pain scores were associated with OAB, pyuria, and antibiotic use; lower scores were associated with antimuscarinic use ($t=14$, $p<.001$). OAB and pyuria had a synergistic effect on the pain score. Dysuria was absent in 55%.

The urgency score and pain score did not correlate ($R = 0.08$, $p<.0001$).

There was a clear treatment response (Figure 1. $F=16$, $p<.0001$). OAB patients demonstrated a slightly slower recovery than those without OAB; the contrast with controls was striking. Amongst controls, there was no difference between those with, or without OAB.

Figure 1. Mean pain score at presentation and at three follow-up visits (OAB and no OAB).



Interpretation of results

OAB is commonly associated with pain symptoms, which are distinct from urgency. These symptoms are expressed particularly in the presence of pyuria, and often in the absence of dysuria. These nociceptive features respond to treatment, which can be measured using this simple scale. Whilst it remains widely perceived that pain symptoms are rare in OAB, these data presented herein serve to challenge that perception decisively.

Concluding message

Pain symptoms, typically associated with PBS, may occur independently in association with OAB. These symptoms are important because they appear to be present in a subset of OAB patients, perhaps indicating an inflammatory process associated with symptom generation.

Pain scores which explore symptoms related to the lower urinary tract have been developed mainly for the study of Interstitial Cystitis. These questionnaires commonly measure storage symptoms in addition to pain, often excluding many relevant nociceptive symptoms reported by patients. This measure targets specifically these key symptoms, and is responsive to changes in the patient condition related to treatment.

References

1. J. Cell. Physiol. (2008) 215: 210-222
2. J. Urology. (2009) 182: 355-365

Specify source of funding or grant	none
Is this a clinical trial?	No
What were the subjects in the study?	ANIMAL
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
Name of ethics committee	Animal Research and Care Committee at the Nihon University School of Medicine