

PERSISTENT SIGNALS OF INFECTION AND INFLAMMATION IN PATIENTS WITH RECALCITRANT OAB

Hypothesis / aims of study

There is growing interest in chronic cystitis in the aetiology of overactive bladder (OAB). The tests used routinely to exclude urinary tract infection (UTI) have been discredited, catalysing a critical analysis of our assumptions. The methods used to test for infection are flawed and a negative result on culture and dipstick do not exclude infection or inflammation. The detection of microscopic pyuria remains the best surrogate marker of infection (1,2). There are other measures of immune activation in the urinary tract that are suitable as independent arbiters of the true pathology (3). Lactoferrin, which chelates iron thereby starving microbes, is elevated in urine in patients with acute UTI. Urothelial cells constitutively express IL-6 and studies show rapid increases in IL-6 after the onset of infection. Urothelial cells when infected with microbes visualised by fluorescent microscopy also signal their distress by expressing ATP and can be seen microscopically to be associated with microbes.

The aim of this study was to use a consilience approach in a longitudinal cohort of patients with OAB, compared to controls, to assess for the persistence of urinary infection and inflammation.

Study design, materials and methods

A prospective longitudinal study was conducted from April 2011 to October 2014. Patients presenting with OAB were recruited from incontinence clinics and clean-catch midstream urine samples obtained and compared to age and menopausal matched controls. Both cohorts were assessed at 4 weekly intervals for 1 year. Symptoms were measure using the ICIQ FLUTs questionnaire, Whittington Urgency and Pain score. Light microscopy was performed on fresh clean catch urine samples for leucocytes and urothelial cell counts by blinded investigators and cultured using the enhanced sediment culture. Urothelial cells were stained and assessed with fluorescent microscopy. Aliquots of spun urine were frozen at -80°C which were analysed for Lactoferrin and IL6 by high sensitivity ELISA and ATP using a luciferin-luciferase assay.

Results

24 female patients with OAB (mean age=63; sd=11) and 22 asymptomatic controls (mean age 59; sd = 9) were recruited. These results are from 144 OAB patient visits and 136 control visits. The linear mixed-effects models procedure was used to analysis the longitudinal data and explore the relationship between urinary IL6, Lactoferrin and urgency score, pain score, LUTS score, pyuria and microbial growth on enhanced sediment culture. Mean urinary IL6 was found to be significantly higher in patients when compared with controls across each visit (figure 1). Similarly mean urinary Lactoferrin was found to be significantly higher in the patient group when compared with controls across each visit (figure 2).

Figure 1 – Mean urinary IL6 in patients and controls at visits over 1 year

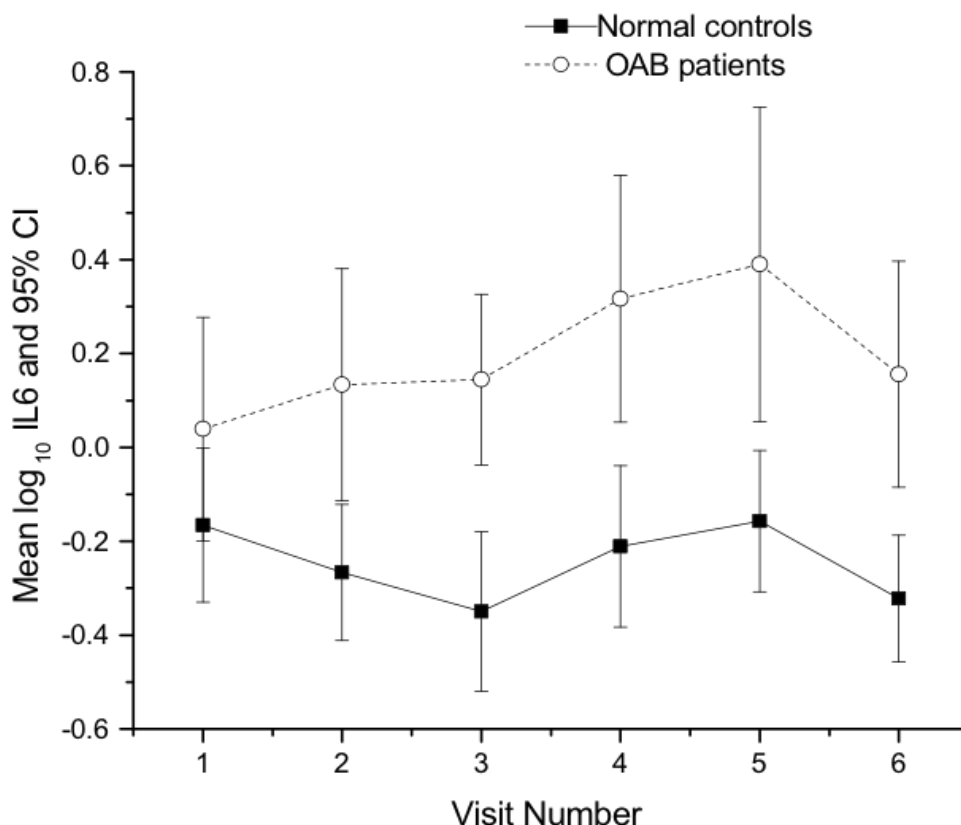
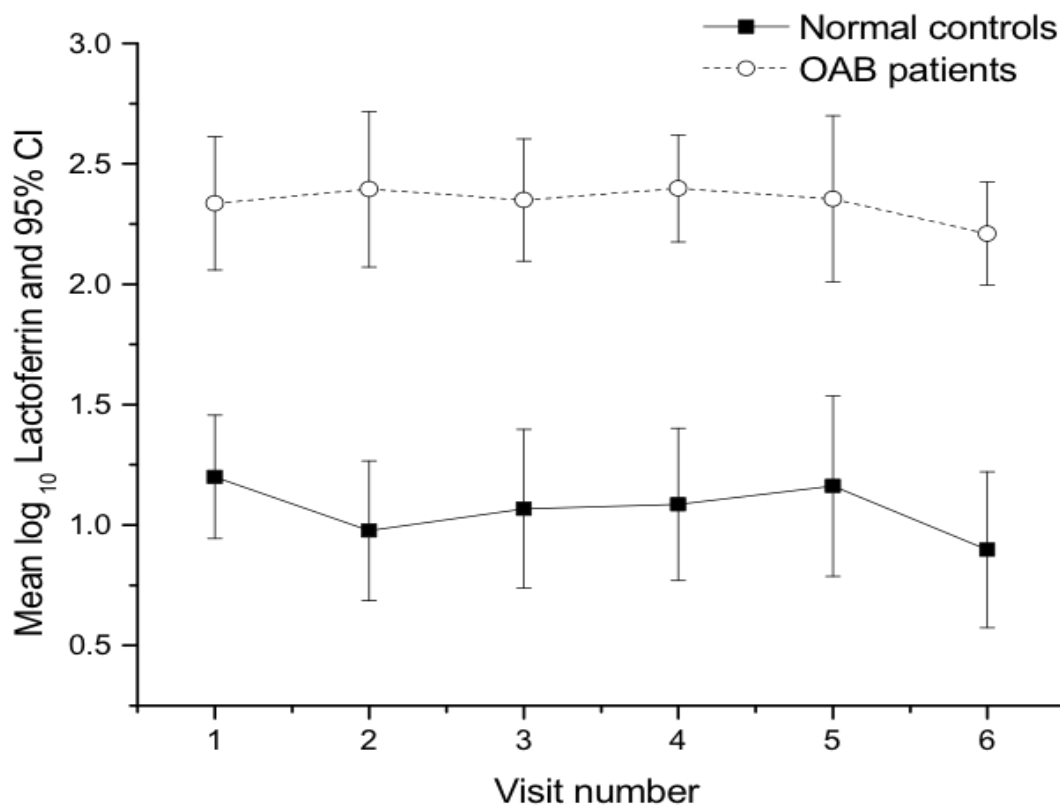


Figure 2 – Mean urinary Lactoferrin in patients and controls at visits over 1 year



Interpretation of results

There is strong evidence to suggest that patient with OAB have persistent signs of infection and inflammation, which is distinct from matched controls. This provides an alternative hypothesis to the pathophysiology of overactive bladder.

Concluding message

In patients with recalcitrant OAB, infection and inflammation may play a role in the pathophysiology and hence provide a new therapeutic pathway.

References

1. JUrol. 2010;183(5):1843-7.
2. PLoS medicine. 2007 Dec;4(12):e329. PubMed PMID: 18092884
3. J Clin Micro 2013: PubMed PMID: 23596238

Disclosures

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