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## THE IMPLICATIONS OF OCCULT URINARY TRACT INFECTION IN MS

### Hypothesis / aims of study

Over 75% of MS patients describe lower urinary tract symptoms (LUTS) [1]. We have reported frequent urinary tract infection (UTI) which was missed by routine methods of urinalysis in these patients [2]. Whilst the diagnostic thresholds employed in routine microbiological practice render standard laboratory urine culture insensitive, even those samples reported as positive are frequently dismissed as asymptomatic bacteriuria (ABU) in the absence of acute frequency-dysuria; the notion that UTI is ubiquitously associated with acute symptoms is not grounded in evidence. Consequently, the generation of LUTS in patients with MS is attributed almost universally to neuropathology, confounded by the performance of current diagnostics, assumptions about the nature of infective symptoms, and the expectation of bacteriuria associated with catheter use.

The key question is whether these patients would benefit from antimicrobial treatment, or whether the occurrence of bacteriuria, irrespective of quantitative microbiological constructs, is simply an epiphenomenon associated with the MS bladder. We present preliminary data from a prospective study examining the effects of antibiotic treatment in these patients.

### Study design, materials and methods

This study was prospective, blinded, observational cohort study including patients with MS and OAB symptoms, and asymptomatic control subjects. These preliminary data compare outcomes at baseline and twelve months. MS patients provided CSU samples whilst control subjects submitted a clean-catch MSU. All samples were subject to immediate cytological analysis for pyuria, culture of the spun urinary sediment, and routine laboratory culture.

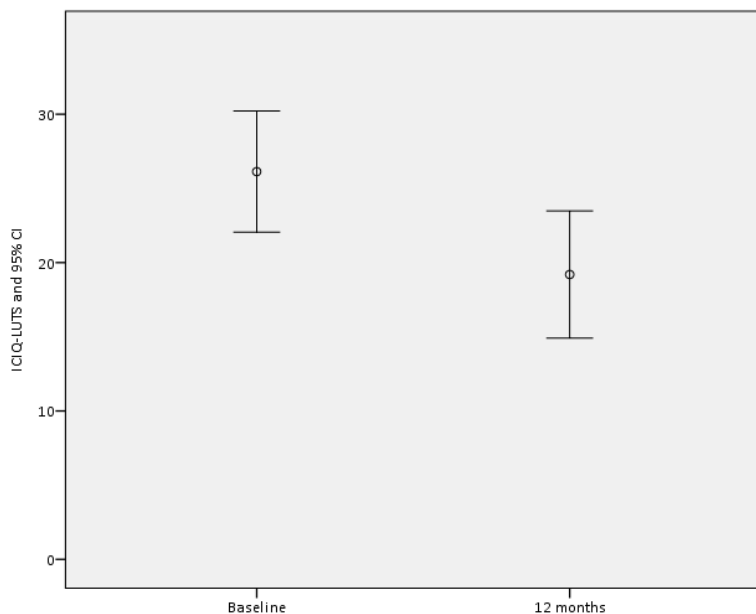
A single blinded clinician treated patients with empirical antimicrobial therapy based on clinical assessment and urine microscopy findings, without access to study culture data. Treatment was continued until microscopy demonstrated clearance of pyuria, and patients reported maximal symptom control defined by a sustained symptom nadir. Symptom and QoL data were assessed using ICIQ measures and a patient-reported improvement scale. IBM SPSS 21 (IBM, New York) was used to conduct the analysis and the data presented using standard descriptive statistics. SPSS Sample Power was used to determine sample sizes.

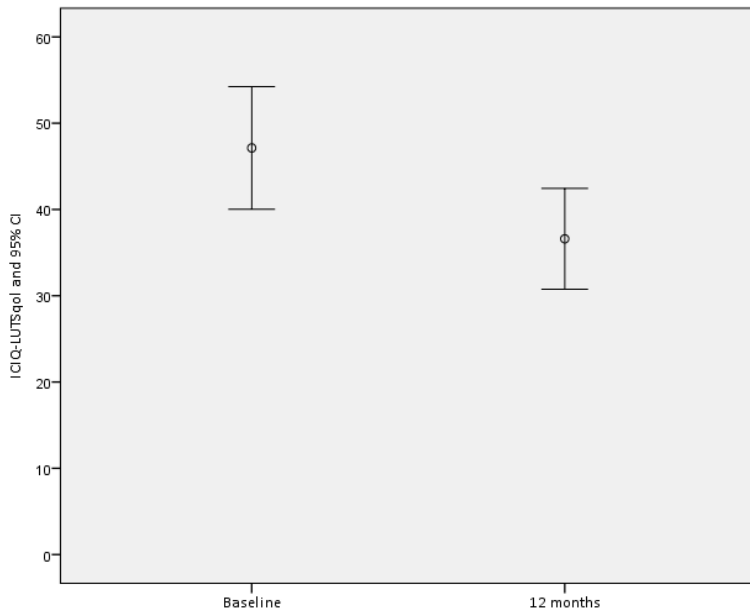
### Results

Fifteen patients with MS and OAB (F=13; M=2; mean age=53.5; SD=10.6y) and 15 asymptomatic control subjects (matched for age, sex, BMI, and menopausal status) were included in the analysis. All patients had chronic symptoms (minimum duration six years) and did not demonstrate acute frequency-dysuria. Seventy percent of patients demonstrated a negative routine culture at baseline. Between baseline and twelve months, antimicrobial treatment was associated with a reduction in bacterial growth (Wilcoxon  $Z=-3.464$ ;  $p<0.001$ ) and microscopic pyuria (Wilcoxon  $Z=-3.43$ ;  $p<0.001$ ). Median duration of antimicrobial treatment was 4.6 months

Patients demonstrated significant improvements in symptoms and QoL (see figures). Ninety-three percent of patients reported a marked ( $n=10$ ) or moderate ( $n=4$ ) improvement in bladder function. There were no significant changes in any of the measured outcomes for control subjects during the follow-up period.

Figures: Patient scores for ICIQ-LUTS and ICIQ-LUTSqol assessments at baseline and 12 months.





#### Interpretation of results

These preliminary data suggest that bacterial infection, largely undisclosed by routine culture methods, may contribute to the generation of OAB symptoms in patients with MS. Improvements in symptoms and bladder-related quality of life were associated with a reduced bacterial load and a reduction in pyuria, an independent marker of urothelial inflammation.

#### Concluding message

The relationship between bacterial infection and chronic LUTS associated with MS may need to be re-examined. This treatment effect is currently being tested in an RCT.

#### References

1. J Neurol (1999) 246: 1027–1032
2. Int Urogynecol J (in press)

#### Disclosures

**Funding:** Project grant from MS Society (UK) **Clinical Trial:** No **Subjects:** HUMAN **Ethics Committee:** Central London REC 3 (Ref: 10/H0716/84) **Helsinki:** Yes **Informed Consent:** Yes