Hypothesis / aims of study
For decades the urothelium has been viewed as a primary barrier, recently it has increasingly been recognized as a responsive structure releasing signalling molecules including nitric oxide (NO) in response to physiological and chemical stimuli. The localization of neuronal nitric oxide synthase (NOS) within the urothelium suggests that NO has a role in the micturition reflex [1]. NO released from the urothelium or other cells is believed to play a role in modulation of the activity of bladder afferent nerves, nitric oxide mediated suppression of detrusor overactivity in spinal cord injury patients [2] and deficiency of NO causes detrusor overactivity in rat. In some pathologic conditions, NO release can be altered due to the disruption of the urothelial barrier associated ultra-structural changes, e.g., NO was induced in cats with interstitial cystitis, but NO was reduced in DO with spinal cord injury in rat.

In this study, we aimed to investigate whether intravesical NO release during bladder filling and micturition in bladder was altered in detrusor overactive (DO) patients by comparing with controls.

Study design, materials and methods
A midstream urine sample was taken for immediate microbiology test. Patients with UTI symptoms and/or positive with dipstick were excluded. The patient was catheterised with a dual lumen catheter and saline was infused into the bladder at a filling rate of 75ml/min. The volumes at first desire to void (FDV) and maximal cystometric capacity (MCC) were noted, as was the presence of any detrusor contractions during filling or provocation. After removal of 10ml (deadspace), aliquots of intravesical fluid (5ml) were collected at bladder volumes of 200ml, 400ml, and at MCC, a sample was also collected after voiding as voided fluid. Total nitrogen oxides (NO\textsubscript{x}) were measured after enzymatic reduction of nitrate using a fluorimetric modification of the Greiss reaction [3] NO was measured in duplicates of each sample, and average of duplicates was used to calculate NO concentration against standard curve, the errors of duplicates were about +/- 10%. Data were expressed as median (interquartile range, IQR) for each group of patients. Patients were characterised as (a) DO (n=30) (involuntary detrusor contractions during the filling phase which may be spontaneous or provoked) or (b) control (n=19) (pure urodynamic stress incontinence, involuntary leakage of urine during increased abdominal pressure in the absence of detrusor contractions).

Results
It seems that ATP was lower in DO than controls, but the difference did not reach significant between DO and controls at each bladder filling volumes, 200ml (Fig 1A), 400ml (Fig 1B), MCC (Fig 1C) or voided fluid (Fig 1D).

In DO group, NO was significantly increased after voiding, i.e., NO was significantly higher in voided fluid (after voiding) than in MCC (before voiding) (Fig 2B), but this was not seen in controls (Fig 2A).

Interpretation of results
There is a variation of NO release among individuals in both DO and controls, therefore NO release was not significantly different between DO and controls. Bladder stretch did not alter intravesical NO in either DO or control groups. However, voiding has resulted an increase of intravesical NO release in DO patients, but not in controls.

Concluding message
Intravesical NO release itself may not be a suitable prognostic indicator for DO symptoms, but the comparison of NO release between MCC (before micturition) and voided fluid (after micturition) might provide a better indication of DO. Micturition may facilitate intravesical NO release in DO patients but not in controls.

Figure 1. Comparison of NO release between Controls and DO at 200ml (A), 400ml (B), MCC (C) and Voided Fluid (D).
Figure 2. Comparison of NO release between MCC (before voiding) and voided fluid (after voiding) in controls (A) and DO (B).

References

Disclosures
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