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DOES INTRAVESICAL ATP OR RECURRENT BACTERIAL CYSTITIS PREDICT RESPONSE TO ANTIMUSCARINICS IN DETRUSOR OVERACTIVITY?

Hypothesis / aims of study

It has been suggested that approximately 30% of patients with Detrusor Overactivity (DO) may be refractory to antimuscarinic therapy [i.e. failure to respond to detailed bladder training with more than 2 antimuscarinic agents for more than 12 months as per frequency volume chart] [1]. ATP is believed to be responsible for signalling bladder fullness and a correlation between ATP in voided urodynamic fluid and FDV in patients with DO has previously been reported [2]. However whether the magnitude of ATP release during bladder filling can predict treatment response has never been studied. In addition recent cross-sectional research suggests a link between bacterial cystitis [3] and the "refractory state" but prospective follow up of this concept is scanty.

The aims of the current study were to evaluate patient response to antimuscarinic therapy in relation to 1) ATP release at baseline urodynamics 2 to 5 years previously; and 2) patient history of bacterial cystitis at the first visit.

Study design, materials and methods

Patients who presented for urodynamic testing at our regional Department of Urogynaecology between January 2008 - April 2011 and who had been recruited into a study of ATP levels in voided urodynamic fluid (N=118) were routinely treated and followed up as per Clinic protocol with antimuscarinic agents and detailed bladder training.

At the first visit, the idiopathic nature of their DO was defined; patients with neurological disorders (N=1), any voiding dysfunction (N=2), or previous deep pelvic radiotherapy (N=3) were excluded. Patients with stress predominant mixed incontinence were excluded (N=48) as treatment response would not equate to antimuscarinic efficacy. Women who were unable to receive antimuscarinics (i.e. Dementia/Glaucoma N=3) were also excluded.

Patient history of bacterial cystitis was defined as: "recurrent UTI" = more than 3 proven episodes of infections in 5 years; "any UTI" = any proven UTI during the patient's adult life, or no history of UTI. Patient response to antimuscarinic therapy was determined by frequency volume chart (urge leaks, voids per day, nocturia). "Response" was denoted as >50% benefit on urge leaks. Results were analysed using a Mann-Whitney test. Because a correlation between ATP in voided fluid and the first desire to void (FDV) has previously been reported, we also examined this relationship in the responders and non-responders.

Results

Of the 118 patients diagnosed with detrusor overactivity who had ATP determinations at the time of their diagnosis, 61 met the inclusion criteria. Nine patients were lost to follow up (despite contacting the GP) and three were completely non-compliant with therapy, thus 49 patients underwent treatment and could be traced. Follow-up revealed that 37 of these (75%) had responded to antimuscarinic therapy and 12 (25%) were non-responders. Not surprisingly the non-responders had been treated with a significantly greater number of antimuscarinic agents than the responders (P=0.03, Table 1)

There was no significant difference between responders and non-responders in relation to age, parity, menopausal status, FDV, MCC, maximum detrusor pressure, duration of symptoms or duration of clinic treatment (data not shown). However, baseline severity of leakage gave some significant prognostic information (p=0.01, Mann-Whitney, Table 1).

Table 1: Demographics of patients included in the study

	Responders	Non-Responders
N	37	12
Number of antimuscarinics	1(1-2)	2.5 (2-3.75)
Baseline Leaks/Week	7 (2.5-17.5)	21 (11.88-28.75)
ATP concentration in voided urodynamic fluid (nM)	2.4 (0.6-14.9)	2.95 (1.465-5.875)
UTI History		
Recurrent UTI	24%	67%
Any UTI	54%	92%
No history of UTI	46%	8%

ATP concentration in voided urodynamic fluid did not differ between responders and non-responders (Table 1, Fig 1A). A correlation between ATP in voided urodynamic fluid and FDV was seen in the responders (p=0.039, r^2=0.12, Fig 1B) but not in the non-responders (p=0.25, r^2=0.14, Fig 1B) although this could be related to the small number of patients in this group.

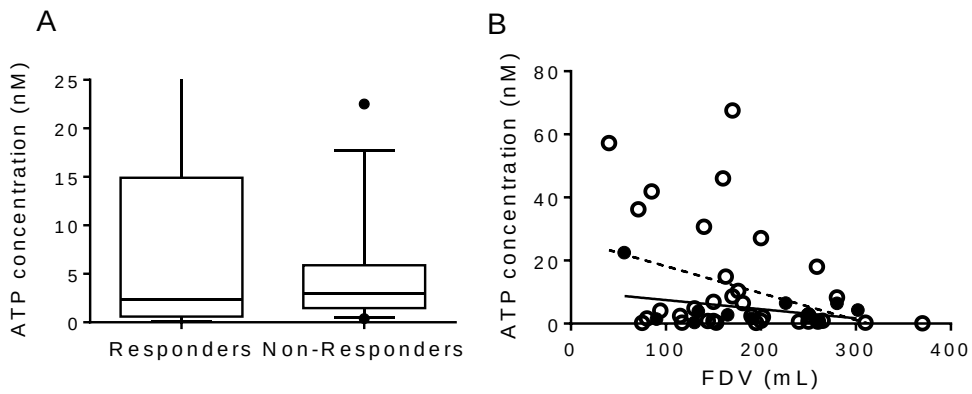

Figure 1. A) Comparison of ATP concentration in voided urodynamic fluid in responders versus Non-Responders (p=0.51); B) correlations between ATP concentration in voided urodynamic fluid and FDV in Responders (open circles, p=0.039) and non-responders (p=0.25, closed circles).

A significantly higher percentage of the non-responders had a history of both recurrent UTI (p=0.01) and any UTI episode (p=0.02, Chi square analysis, Table 1).

Interpretation of results

Based on the current results, ATP concentration in voided urodynamic fluid does not prognosticate response to antimuscarinic therapy. ATP is therefore not likely to be a useful biomarker for patients with DO. Baseline severity of leakage appears to give some prognostic information. The previously observed correlation between FDV and ATP in voided urodynamic fluid [2] was preserved in the responders, but was lost in the patients who were not responsive to antimuscarinic therapy.

In keeping with previous work, the likelihood of recurrent UTI in this study was three-fold greater in non-responders compared to responders. Thus our results contribute to a growing body of evidence suggesting that recurrent UTI may have importance in the acquisition of a “Refractory” state.

Concluding message

Although ATP remains important in the signalling of afferent impulses, it is not a useful prognostic indicator. Recurrent UTI increasingly appears to have a poor prognostic significance in patients with DO.

References

1. Br J Urol 1992;70:17-21
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Disclosures

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