

## ATP RELEASE DURING CYSTOMETRY IN WOMEN WITH DETRUSOR OVERACTIVITY AND PAINFUL BLADDER SYNDROME: CONTRIBUTION TO “URGENCY”?

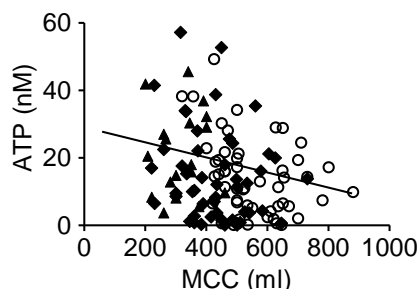
### Hypothesis / aims of study

ATP is an important signalling molecule whose release from the bladder urothelium in response to stretch is thought to stimulate afferent nerves and thus convey information about bladder fullness (and the sensation of urgency). Our aim was to measure the release of ATP during urodynamic filling of bladders of women with idiopathic detrusor overactivity (DO), painful bladder syndrome (PBS) and stress incontinence (controls), in order to test the hypothesis that ATP release might play a role in bladder function and/or dysfunction.

### Study design, materials and methods

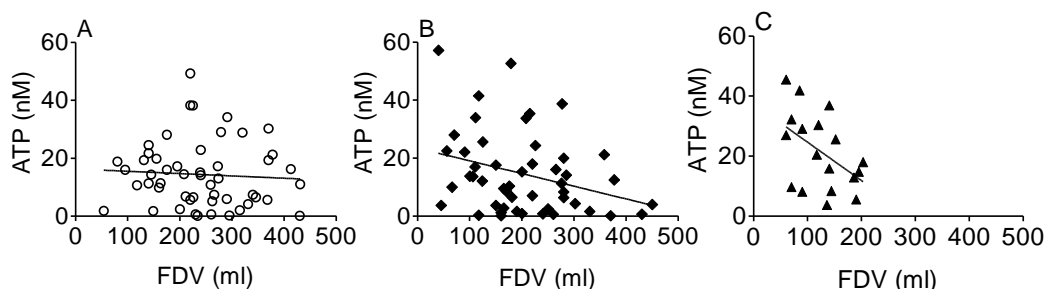
Routine cystometry was performed on 118 women aged 28-87 years. Informed consent was obtained and the study was approved by the local human ethics committee. Saline was infused into the bladder at a filling rate of 75ml / min. The volumes at first desire to void (FDV) and maximal cystometric capacity (MCC) were noted. The presence of any detrusor contractions during filling, erect provocation and tap water stimulus were recorded. After voiding, the saline bladder washings were collected, the volume voided noted and the bladder washings were snap frozen at -30°C. ATP was measured using a bioluminescence assay (Sigma) and a luminometer (GloMax 20/20). The concentration of ATP (nmoles/l) in each sample was calculated. Patients were characterised as (a) DO (involuntary detrusor contractions during the filling phase which may be spontaneous or provoked), (b) PBS (FDV ≤200 ml, MCC ≤400 ml, stable bladder) or (c) control (neither DO or PBS, i.e. pure urodynamic stress incontinence, involuntary leakage of urine during increased abdominal pressure in the absence of detrusor contractions). Subjects found to have bacterial cystitis on a catheter specimen of urine on the test day ( $10^7$  c.f.u./l with pyuria >10 wbc/l) were excluded from the study. Overall subject numbers comprised 49 DO, 18 PBS and 51 control women. Data were expressed as median (interquartile range, IQR). Correlations between two factors were tested by linear regression analysis.

### Results



**Figure 1.** Correlation of ATP concentration in bladder washing with maximal cystometric capacity (MCC) in all patients (control (○), DO (◆) and PBS (▲) patients).

There was a significant inverse correlation between maximal bladder capacity and ATP concentration in the bladder washings from all of the patients ( $r^2 = 0.07$ ,  $P = 0.003$ ): that is, the smaller the maximal capacity, the greater the ATP concentration (Fig 1). Analysis of the correlation between the ATP concentration in the individual patient sub-groups revealed a similar trend in control and DO patients, but this was significant only in control patients ( $P = 0.013$ ,  $r^2 = 0.12$ ).



**Figure 2.** Correlation of ATP concentration in bladder washings with first desire to void (FDV) in (A) control patients, (B) DO patients and (C) PBS patients. There was a significant correlation between FDV and ATP concentration in the bladder washings in DO (Fig 2B,  $r^2 = 0.096$ ,  $P = 0.03$ ) and PBS (Fig 2C,  $r^2 = 0.23$ ,  $P=0.04$ ) patients, but not in control patients (Fig 2A,  $r^2 = 0.004$ ,  $P = 0.65$ ).

### Interpretation of results

This appears to be the first study showing that ATP release can be analyzed in the fluid voided after cystometry testing, which opens new avenues of research. In the present study, there was a general correlation between ATP release and MCC. That is, the lower the MCC, the higher the ATP concentration in the bladder washing. This is in accordance with data from human mucosal strips where stretch increases ATP release [1]. Our findings suggest that the intravesical concentration of ATP might be an important factor in the sensation of maximum bladder capacity. As regards the first desire to void, there was no correlation between bladder washing ATP concentration and FDV in control patients. However, there was a significant correlation between ATP and

FDV in DO and PBS patients. That is, higher ATP release was related with a lower FDV, in these two groups. This is in accordance with recent studies in bladder mucosal strips showing enhanced ATP release in response to stretch in patients with PBS [2].

#### Concluding message

The measurement of ATP in cells from cystometry washings is a novel approach to understanding the signals that may contribute to the sensation of "urgency" (the sudden compelling desire to void). The inverse correlation between ATP release and maximum capacity suggests that ATP released during bladder filling plays a role in modulating afferent sensation. The relationship between ATP and FDV seen only in the DO / PBS patients suggests that ATP release may be more readily triggered in these women.

#### References

1. Kumar V, Chapple CC, Chess-Williams R J Urol (2004) Characteristics of adenosine triphosphate release from porcine and human normal bladder. J Urol 172: 744-747
2. Kumar V, Chapple CR, Surprenant AM, Chess-Williams R (2007). Enhanced adenosine triphosphate release from the urothelium of patients with painful bladder syndrome: a possible pathophysiological explanation. J Urol 2007 178: 1533-1536

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<b><i>Is this a clinical trial?</i></b>	<b>No</b>
<b><i>What were the subjects in the study?</i></b>	<b>HUMAN</b>
<b><i>Was this study approved by an ethics committee?</i></b>	<b>Yes</b>
<b><i>Specify Name of Ethics Committee</i></b>	<b>St George Hospital Human Ethics Committee, Sydney, Australia</b>
<b><i>Was the Declaration of Helsinki followed?</i></b>	<b>Yes</b>
<b><i>Was informed consent obtained from the patients?</i></b>	<b>Yes</b>