

ATP: A NOVEL URINARY BIOMARKER OF DETRUSOR OVERACTIVITYHypothesis / aims of study

There is today a considerable bulk of evidence showing that ATP has a prominent role in the regulation of human urinary bladder function, and in the pathophysiology of detrusor overactivity. It has been shown that the nonadrenergic-noncholinergic detrusor contractions seen in overactive bladders are mediated by ATP. This might, in part, be due to increased bioavailability of ATP due to reduced extracellular breakdown of the nucleotide by ectonucleotidases. Furthermore, distension of the urothelium induces ATP release that act on suburothelium afferent nerves via P2X receptors, conveying sensations of bladder fullness and pain. *In vitro* studies demonstrated that uroepithelial cells and cholinergic nerves from overactive human bladder samples (OAB) release more ATP than controls. We, therefore, hypothesized that patients with detrusor overactivity would have higher urinary concentrations of ATP than controls.

Study design, materials and methods

A total of 39 women submitted to urodynamic examinations were enrolled in this study. These, include 19 patients with overactive bladder symptoms and detrusor overactivity and 20 controls without overactive bladder symptoms and/or detrusor overactivity. Patients with neurologic diseases, urinary tract infections or renal impairment (creatinine clearance < 70 ml/min) were excluded. All patients completed a 3-day voiding diary, a 24h urine collection and blood sample to evaluate creatinine clearance. Urine samples were collected from two separate voids and immediately freeze-preserved for ATP determination by bioluminescence (ATP kit from Roche). Mann-Whitney U Test was used to evaluate statistical differences, and ROC curves were performed using SPSS software.

Results

Urinary ATP was significantly higher in OAB samples than in controls (see table); this was consistent in the two urine samples collected for each individual. The ATP concentration was independent of the volume voided.

Area the curve for was (95% to		OAB (mean ± SE)	Controls (mean ± SE)	p	under ROC for detrusor OAB detection 0,805 CI 0,663 0,947)
	Age	55,0 ± 3,3	53,6 ± 2,1	0,415	
	Mean voided volume (ml) from 3-day chart	170,4 ± 19,7	191,2 ± 13,4	0,423	
	Creatinine clearance (ml/min)	114,8 ± 5,7	120,1 ± 8,9	0,966	
	Urine pH	6,0 ± 0,2	6,5 ± 0,2	0,155	
	Urine creatinine (mg/dl)	75,3 ± 6,3	72,9 ± 7,0	0,593	
	Urine LDH (IU/L)	35,1 ± 4,8	46,2 ± 8,0	0,536	
	Urine ATP (nM)	12,1 ± 1,7	6,5 ± 1,3	0,001	

Interpretation of results

As previously shown *in vitro*, overactive bladders release more ATP which is insufficiently hydrolysed by ectonucleotidases. We hypothesized that released ATP could then diffuse into the bladder lumen increasing its content in urine samples. Our results clearly demonstrate that the urine of women with idiopathic detrusor overactivity exhibit increased amounts of ATP compared to age-matched controls; ATP levels showed no correlation with voided urine volume and urinary creatinine. Determination of a high AUC is consistent with urinary ATP being a highly sensitive biomarker of detrusor overactivity, providing that urinary tract infection is ruled out.

Concluding message

Women with OAB have higher ATP concentrations in the urine. Making urinary ATP a potential marker of the disease.

References

1. Harvey RA et al, 2002; J Urol:168,1235-1239
2. Ford A et al, 2006; Br J Pharmacol:147, S132-S143
3. Kumar V et al, 2009, Eur Urology, doi:10.106/j.eururo.2009.11.042

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Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes

<i>Specify Name of Ethics Committee</i>	Ethics Commitee of Hospital Geral de Santo António - Centro Hospitalar do Porto
<i>Was the Declaration of Helsinki followed?</i>	Yes
<i>Was informed consent obtained from the patients?</i>	Yes