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RELATIONSHIP BETWEEN URINE PH AND IN VIVO ATP RELEASE DURING URODYNAMIC TESTS IN FEMALE URINARY INCONTINENCE.

Hypothesis / aims of study

In vitro animal studies have shown that increasing acidity, within the physiological range, will enhance release of ATP from the bladder [1]. Here, we explored the hypothesis that *in vivo* urinary pH would affect ATP release during bladder filling. The aim of this study was to test whether ATP release in bladder during stretch is related to the patient's urine pH.

Study design, materials and methods

Informed consent was obtained and the study was approved by local human ethics committee. A midstream urine sample was collected for pH measurement immediately before the routine urodynamic test was performed. These samples were also tested for bacteriuria, and subjects found to have bacterial cystitis on the test day (10^7 c.f.u / L with pyuria >10 wbc / L) were excluded from the study. Urine pH measurements were promptly carried out on fresh urine samples (mean +/- SEM).

During the urodymamic test, sterile saline was infused into the bladder at a filling rate of 75mL/min. The volumes at first desire to void (FDV) and maximum cystometry capacity (MCC) were noted. The voided urodynamic fluid was collected for ATP determinations. Patients were characterised as DO (involuntary detrusor contractions during the filling phase which may be spontaneous or provoked), bladder oversensitivity (BO, with FDV ≤ 200mL and MCC ≤ 400mL but with stable bladder) or control (neither DO or BO, i.e. pure urodynamic stress incontinence, involuntary leakage of urine during increased abdominal pressure in the absence of detrusor contractions).

Overall subject numbers (age range 28-87 years) comprised 90 DO, 24 BO and 74 controls (22 patients with bacteriuria on the test day were excluded). The urine and voided urodynamic fluid were frozen at -20^{o}C. ATP determinations were carried out on thawed urine and voided urodynamic fluid. ATP was measured using a bioluminescence assay (Sigma) and a luminometer (GloMax 20/20). In uninfected patients there is no difference in ATP measurement in fresh or frozen samples. The concentration of ATP (nmoles/L) in the bladder washing in each sample was calculated, and data were expressed as median (interquartile range, IQR). Correlations between two factors were tested by linear regression analysis. The three subject groups were compared using the Kruskal-Wallis test.

Results

There was no difference in urine pH between the control (6.27 ± 0.09), DO (6.18 ± 0.08) and PBS (6.14 ± 0.15) groups (P=0.8, ANOVA, Figure 1A). A significant correlation was found between urine pH and the ATP concentration in the voided urodynamic fluid when all patients were analysed together (Figure 1B, P=0.0013, n=216). This correlation was not significant in each individual groups, i.e., control (P=0.07), DO subjects (P=0.22), BO (P=0.08). There was no correlation between the concentration of ATP in urine and urine pH. Urine pH was significantly correlated with MCC in the control subjects (P=0.037, Figure 1C), but not in DO (P=0.7) or PBS (P=0.9).

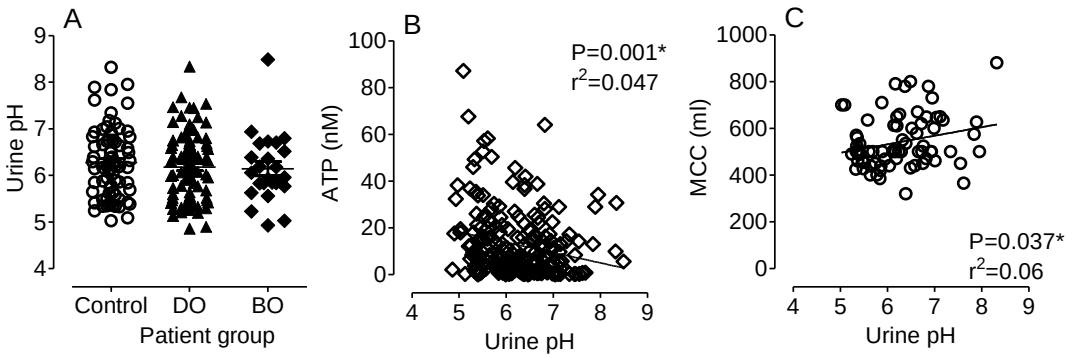

Figure 1. A, Urine pH measured in a series of women prior to undergoing urodynamics. B, ATP concentration in voided urodynamic fluid (at MCC) relative to urine pH; data represent all women (n=216). A significant negative correlation was observed. C, Positive correlation of MCC with urine pH in control subjects.

Interpretation of results

The lack of correlation of urine ATP concentration and urine pH may result from the presence of different chemicals in urine that could interfere with ATP release or measurement. In addition, subjects had different bladder volumes at the time of urine collection, and thus ATP measured in urine would result from different degrees of bladder stretch. However, our data from bladder washings where the bladder was stretched to maximum during cystometric testing is a good representation of the ATP

released by maximal stretch. This also suggests that pH has more effect on ATP release and sensation of bladder fullness or urge only when bladder was stretched.

Our data suggest that urine pH plays an important role on ATP release, which triggers the perception of bladder fullness through purinergic receptors P2X and P2Y. Urine pH can also be affected by the food intake or metabolism of individual subjects, indicating that these factors could also play a role in bladder symptoms.

Concluding message

A highly significant inverse correlation was found between urine pH and ATP release at maximum cystometric capacity in a group of 216 women undergoing urodynamics, that is the more acidic the urine the greater the ATP release, thus supporting our hypothesis.

References

1. Br J Pharmacol. (2009) 158:1655-62

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Was this study approved by an ethics committee?	**Yes**
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Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**