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# URINARY ATP REFLECTS INFLAMMATORY DISEASE BUT DISAPPOINTS AS A CLINICAL DIAGNOSTIC TOOL IN PATIENTS WITH LOWER URINARY TRACT SYMPTOMS

Hypothesis / aims of study
There is growing interest in chronic cystitis in the aetiology of overactive bladder (OAB). However the routine midstream urine culture and urinary dipstick, used to screen for infection, have come under much criticism and are inadequate for excluding urinary tract infection (1). There is therefore much need to explore other surrogate urinary markers that can be used in clinical practice. A particularly popular candidate has been ATP. Adenosine-5'-triphosphate (ATP) is a neurotransmitter and inflammatory cytokine implicated in the pathophysiology of lower urinary tract disease. ATP additionally reflects microbial biomass thus may have potential as a surrogate marker of urinary tract infection (UTI) (2). The optimum clinical sampling method for ATP urinalysis has not been established. The aim of this study was to test the potential of urinary ATP in the assessment of lower urinary tract symptoms, infection and inflammation, and validate sampling methods for clinical practice. We examined the relationship of age, gender, symptom experience, pyuria and midstream urine culture on urinary ATP levels.

Study design, materials and methods
A prospective, blinded, comparative, cross-sectional observational study of adult patients presenting with lower urinary tract symptoms (LUTS) and asymptomatic controls was conducted in an incontinence clinic between October 2009 and October 2011. Urinary ATP was assayed by a luciferin-luciferase method, pyuria counted by microscopy of fresh, unspun urine and symptoms were assessed using validated scales.

Results
75 controls and 340 patients with LUTS were grouped as without pyuria (n = 100), pyuria 1-9 wbc µl-1 (n = 120) and pyuria ≥10 wbc µl-1 (n = 120). Urinary ATP was higher in association with female gender, voiding symptoms, pyuria and negative MSU culture. In contrast, age, average 24-hour frequency and incontinence, number of urgency, stress incontinence, and pain symptoms explained little of the variance in urinary ATP.

The urinary ATP signal decayed with storage at 23ºC but was prevented by immediate freezing at ≤ -20ºC, without boric acid preservative and without the need to centrifuge urine prior to freezing.

Interpretation of results
ATP can be easily measured in the urine either immediately or by storing unspun urine below 20°C. However these data discourage the idea that urinary ATP should be developed as a clinical surrogate test for UTI. This assay does not appear more effective than markers used in current clinical practice. However, abundant urinary ATP is certainly evident in the presence of significant disease amongst patients with LUTS and these data do encourage continued interest in the pharmacology and pathophysiology of purinergic functions in the bladder.

Table 1: Output from regression analysis

| **Model 1 Pyuria described by dichotomy** | | | | |
|---|---|---|---|---|
| | | | **95% Confidence Interval for B** | |
| | **B Coefficient** | **p** | **Lower Bound** | **Upper Bound** |
| (Constant) | -8.059 | .000 | -8.563 | -7.555 |
| Age | .003 | .375 | -.004 | .011 |
| **Gender 0 = female, 1 = male** | **-.531** | **.023** | **-.989** | **-.074** |
| **MSU 0=negative 1=positive** | **-.410** | **.010** | **-.721** | **-.099** |
| Average 24-hour frequency | .001 | .963 | -.030 | .031 |
| Average 24-hour incontinence | .024 | .697 | -.096 | .144 |
| Number of stress incontinence symptoms | -.070 | .235 | -.185 | .046 |
| **Number of voiding symptoms** | **.117** | **.014** | **.024** | **.209** |
| Number of pain symptoms | .065 | .610 | -.187 | .317 |
| Number of urgency symptoms | -.029 | .267 | -.079 | .022 |
| **Pyuria 0= none 1= any** | **.273** | **.029** | **.028** | **.518** |

| **Model 2 Pyuria described by ordinal scale** | | | | |
|---|---|---|---|---|
| | | | **95% Confidence Interval for B** | |
| | **B Coefficient** | **p** | **Lower Bound** | **Upper Bound** |
| (Constant) | -8.061 | .000 | -8.564 | -7.558 |
| Age | .003 | .394 | -.004 | .011 |
| **Gender 0 = female, 1 = male** | **-.567** | **.012** | **-1.011** | **-.124** |
| **MSU 0=negative 1=positive** | **-.426** | **.008** | **-.741** | **-.112** |
| Average 24-hour frequency | .003 | .858 | -.028 | .033 |
| Average 24-hour incontinence | .014 | .820 | -.106 | .134 |
| Number of stress incontinence symptoms | -.066 | .257 | -.181 | .049 |
| **Number of voiding symptoms** | **.116** | **.013** | **.024** | **.208** |
| Number of pain symptoms | .063 | .621 | -.188 | .314 |
| Number of urgency symptoms | -.028 | .266 | -.079 | .022 |
| Pyuria1 to 9 wbc $\mu l^{-1}$ | .213 | .135 | -.067 | .492 |
| **Pyuria ≥ 10 wbc $\mu l^{-1}$** | **.355** | **.022** | **.052** | **.659** |

Dependent variable is urinary $\log_{10}$ ATP concentration

Conclusions

Urinary ATP does not improve on the use of microscopy as a surrogate marker of urinary tract infection and is therefore not a promising clinical diagnostic marker. It can easily be assayed either immediately or in unspun, preservative-free urine stored at ≤ -20ºC.We need to continue to explore other potential markers that can be used to screen LUTS patients for UTI, particularly applicable to those that have lower levels of pyuria, where significant disease may currently be overlooked.

References

1. Khasriya, R., et al., J.Urol., 2010. 183(5): p. 1843-1847
2. Burnstock, G., BJU Int, 2011. 107(2): p. 192-204.

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