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URINARY URIC ACID INDUCES PROSTATIC INFLAMMATION IN A RAT

Hypothesis / aims of study

Intraprostatic urine reflux occurs especially in patients with benign prostatic hyperplasia and is a possible cause of abacterial prostatitis, however, the ingredient that causes inflammation is still unknown. Uric acid is rich in urine and causes inflammation in various tissue, therefore, uric acid in urine can be a possible candidate for abacterial prostatitis. This study investigated whether inflow of uric acid into the prostatic duct induces prostatic inflammation in a rat.

Study design, materials and methods

Artificial urine was shown to have all parameters within their physiological ranges in normal human urine and the same physiological effects on cell culture as ultrafiltrated urine (1). We prepared 3 types of artificial urine; ×0, ×1, and ×2 of uric acid compared to the original composition (Table 1). After the preparation of the medium, it was sterilized by passing through a 0.22 μm nylon membrane filter. Twelve-week old male Sprague-Dawley rats were catheterized into the urethra with PE-10 tubing under isoflurane anesthesia. The rats were injected with 500 μL of artificial urine in 5 sec. We evaluated histopathology, the expression of proinflammatory cytokines in the prostate and bladder on day 7, after assessing cystometrogram.

Results

Prostatic histopathology showed no inflammation in the x0 group, whereas, the expansion of stromal areas with infiltration of inflammatory cells in the x1 and x2 groups. There were no apparent histological changes in the bladder among groups. Inflammation-associated proteins (IL-1α, IL-1β, IL-6, and TNFα) were increased in the prostate in uric acid-dose dependent manner, while there were no significant changes in the bladder among groups. Intercontraction intervals measured by cystometrogram were shortened in the x1 and x2 groups compared to the x0 group.

Interpretation of results

Urine refluxes into the prostatic ducts during micturition in humans and can cause chemical irritation and inflammation. Our results demonstrated that uric acid in urine induced abacterial prostatic inflammation associated with a disturbed prostatic microcirculation and frequent micturition. As a mechanism that uric acid induces inflammation in the tissue, uric acid crystals is reported to result in the activation of the NALP3 inflammasome. Future study is warranted whether normalization of uric acid level improves prostatitis symptom.

Concluding message

We evaluated the influence of uric acid on the prostatic inflammation using a rat model. Uric acid induces abacterial prostatitis and bladder overactivity in a dose dependent manner. Urinary uric acid can be a possible target for the treatment of abacterial prostatitis.

Table 1. The composition of artificial urine

	x0	x1	x2
Uric acid	0	1.0	2.0
Urea	200	200	200
Creatinine	4.0	4.0	4.0
$Na_3C_6H_5O_7$	5.0	5.0	5.0
NaCl	54	54	54
KCl	30	30	30
NH_4Cl	15	15	15
$CaCl_2$	3.0	3.0	3.0
$MgSO_4$	2.0	2.0	2.0
$NaHCO_3$	2.0	2.0	2.0
$Na_2C_2O_4$	0.1	0.1	0.1
Na_2SO_4	9.0	9.0	9.0
NaH_2PO_4	3.6	3.6	3.6
Na_2HPO_4	0.4	0.4	0.4

All medium were adjusted to pH 6.2. All composition was expressed as mM

References

1. Chutipongtanate, S., Thongboonkerd, V.: Systematic comparisons of artificial urine formulas for in vitro cellular study. Anal Biochem, 402: 110, 2010.

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