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URINARY URIC ACID INDUCES PROSTATIC INFLAMMATION VIA AN OXIDATIVE STRESS PATHWAY

Hypothesis / aims of study

Urine reflux into the prostatic duct occurs during micturition in humans and might cause abacterial prostatitis. Uric acid in urine could cause prostatic inflammation. The current study examined whether uric acid induces inflammation in the rat prostate and cultured human prostate cells.

Study design, materials and methods

We prepared artificial urine containing ×0, ×0.5, and ×1 uric acid compared with the previously reported original composition. Male Sprague-Dawley rats were catheterized into the urethra and 500 μL of artificial urine was instilled. On day 7, the ventral lobes of the prostate were excised for histological examination and cytokine quantification after microcirculation and cystometrogram evaluation. Additionally, human prostatic epithelial, stromal, and smooth muscle cells were cultured in medium containing uric acid and oxidative stress was evaluated.

Results

Prostatic histopathology showed that the expansion of stromal areas with infiltration of inflammatory cells in the ×0.5 and ×1 uric acid groups (Fig. 1). Proinflammatory cytokines (IL-1α, IL-1β, IL-6, and TNFα) and oxidative stress markers (malondialdehyde and HIF-1α) were upregulated in the prostate with increasing amounts of uric acid in a dose-dependent manner (Fig. 2). The microcirculation on the surface of the prostate was altered in the ×1 group (Fig. 3). Cystometrogram revealed a shorter intercontraction interval in the ×1 group (Fig. 4). In cultured cells, uric acid activated the oxidative stress pathway (NADPH oxidase 4, reactive oxygen species, ERK1/2, JNK, p38 MAPK, NF-κB, and proinflammatory cytokines) in stromal cell; these changes were ameliorated by probenecid.

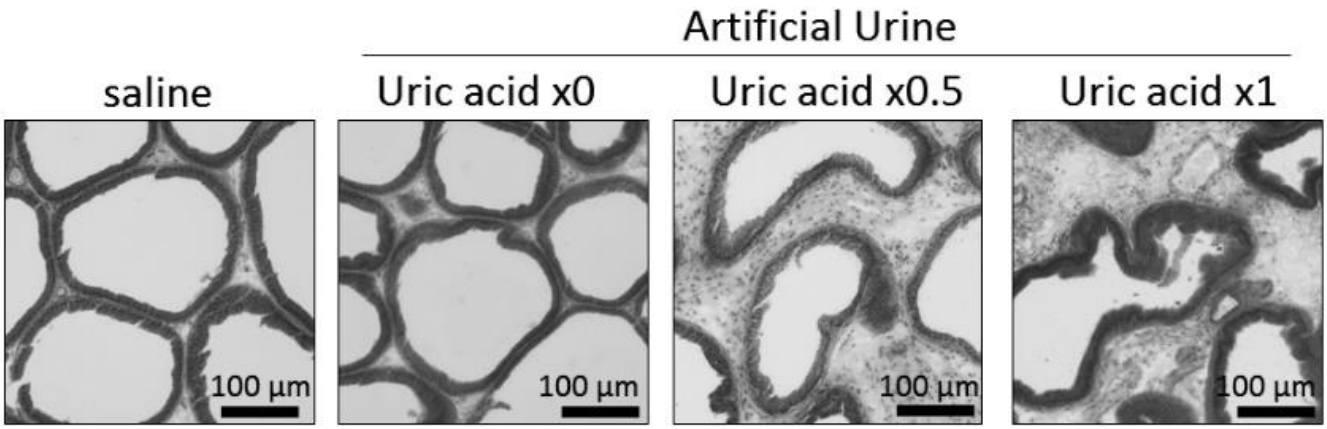
Interpretation of results

Previously, we reported that urine inflow into the prostatic duct induced stromal inflammation in rats, however, the ingredient causing this inflammation were unknown. Urine contains more than 100 uremic toxins. In this study, we identified that uric acid in urine causes stromal inflammation in the prostate due to oxidative stress injury, even at physiological concentration that does not form crystal deposits. Uric acid and the secondary oxidative stress pathway could be therapeutic targets for the treatment for abacterial prostatitis.

Concluding message

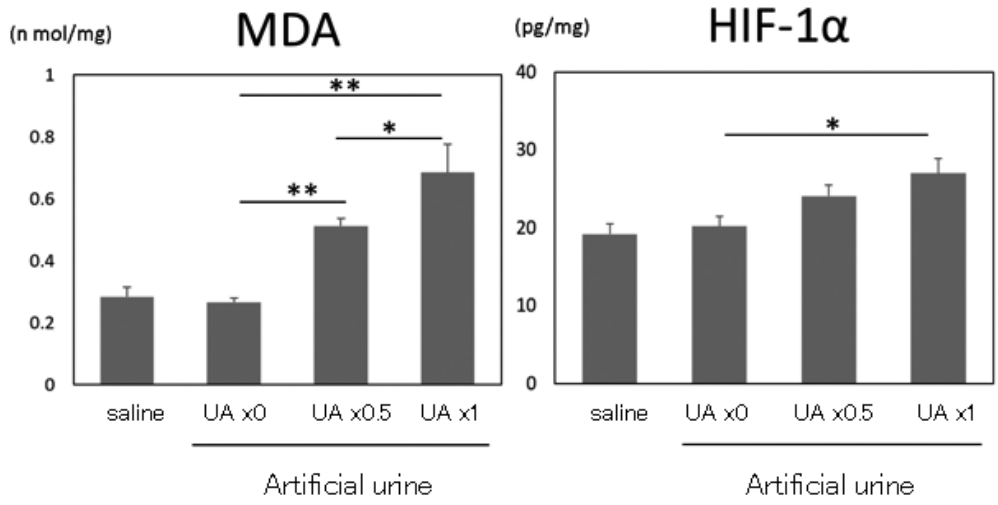
This study demonstrated that urinary uric acid induces abacterial prostatitis and bladder overactivity when refluxed into the prostatic duct. The activation of oxidative stress is involved in this inflammation.

Figure 1. H&E staining of the prostate



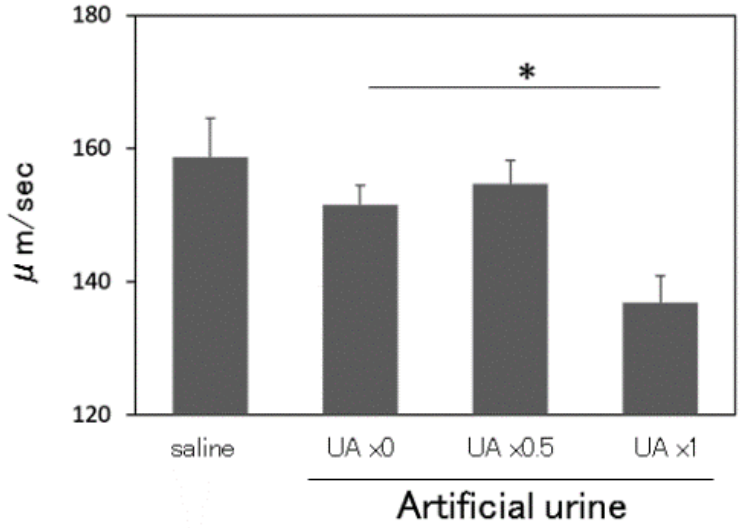
Stromal inflammation was observed in the rat prostates that were infused artificial urine containing uric acid.

Figure 2. Hypoxia markers of the prostate



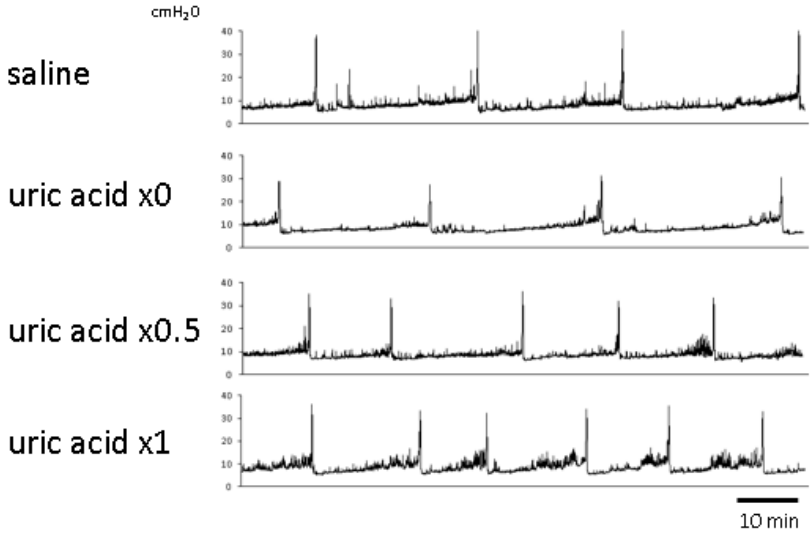
Hypoxia markers were increased in the prostate with increasing amounts of uric acid in a dose-dependent manner.

Figure 3. Microcirculation of the prostatic surface



Erythrocyte speed in the capillary vessels on the prostatic surface was decreased in the ×1 group.

Figure 4. Cystometrogram



Intercontraction intervals were shorter with increasing amounts of uric acid in a dose-dependent manner.

Disclosures
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