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CHANGES IN URINARY PROSTAGLANDIN E2 EXCRETION IN WATANABE HERITABLE HYPERLIPIDEMIC RABBITS, A BLADDER ISCHEMIA MODEL

Hypothesis / aims of study

Many studies have detailed ischemia-related changes in function of the bladder that may contribute to the overactive bladder. A Watanabe heritable hyperlipidemic (WHHL) rabbit has been developed as an animal model for hypercholesterolemia and atherosclerosis, and now it has been widely used as a model of various organ ischemia and related diseases. It has been also reported that prostaglandins act as neuromodulators and contribute to the increased excitability to the bladder afferent nerves. Prostaglandins are synthesized locally in both bladder smooth muscle and urothelium and the synthesis is initiated by various pathologic conditions. In the present study, we evaluated the effect of ischemia on bladder function and urinary prostaglandin E_2 (PGE_2) level in WHHL rabbits.

Study design, materials and methods

WHHL rabbits and the age and sex-matched Japanese white rabbits (control group) were prepared. All rabbits were housed in metabolic cages, and the volume and the frequency of micturition was recorded for three days, and 24-h urine samples of all rabbits were collected. Cystometrograms were performed under anesthesia using constant infusion (1 ml/min) of saline into the bladder to elicit voiding, and voided volume, residual urine, micturition pressure, and micturition interval were evaluated. 24-h urinary PGE_2 levels were assayed by enzyme immunoassay (EIA) by using PGE_2 EIA kit-Monoclonal (Cayman Chemical).

Results

The number of micturition per day was higher in WHHL rabbits (4.24 ± 1.07 times/day) than in control rabbits (1.8 ± 0.3 times/day), and the voided volume was lower in WHHL rabbits (14.81± 4.6 ml) than in control rabbits (43.8 ± 5.1 ml). In cystometrograms, WHHL rabbits showed premicturition contractions, higher frequency of micturition (7.55 ± 1.25 times/20 min) and lower voided volume (6.92 ± 1.5 ml) than in control rabbits (1.44 ± 2.51 times/20 min and 20.8 ± 3.2 ml, respectively). The urinary excretion of PGE_2 was significantly higher in WHHL rabbits (6.44 ± 1.87 ng/ml) than in control rabbits (0.91 ± 0.14 ng/ml; p = 0.03). Analysis of relationship between parameters of bladder function and urinary PGE_2 level in WHHL rabbits indicated a significantly negative correlation (r = 0.81) (figure 1) between urinary PGE_2 level and voided volume.and a significant positive correlation between urinary PGE_2 level and the number of micturition (r = 0.86) (figure 2) and

Figure 1

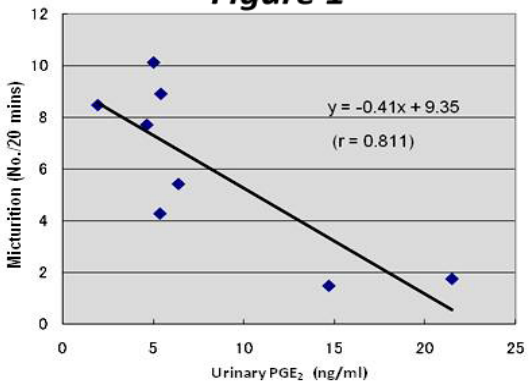
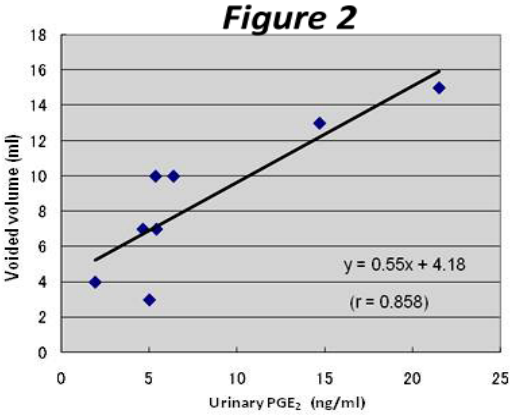


Figure 2



Interpretation of results

In the present study, the cystometric findings of WHHL rabbits showed bladder overactivity. Our previous study showed the atherosclerosis of internal iliac arteries, suggesting the poor blood supply to the bladder. These data suggested the relationship between detrusor overactivity and bladder ischemia in WHHL rabbits. In addition, the present study demonstrated that the urinary excretion of PGE_2 in WHHL rabbits was significantly higher than that in control rabbits. We assumed that the possible sources of the increased PGE_2 might be bladder smooth muscles and urothelium, because there was no significant finding of renal dysfunction or infection in both rabbits. The correlation between urinary PGE_2 level and the number of micturition and voided volume suggested the relationship between detrusor overactivity and urinary PGE_2.

Concluding message

The present study demonstrates that an increase in PGE_2 release from bladder may contribute to the detrusor overactivity of bladder dysfunction induce by bladder ischemia.

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Kumamoto University**