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THE EFFECT OF TAMSULOSIN ON BLADDER MICROCIRCULATION IN BLADDER ISCHEMIC/REPERFUSION MODEL RATS

Hypothesis / aims of study

Patients with benign prostatic hyperplasia (BPH) are known to show both voiding and storage symptoms. Alpha1-adrenoceptor antagonists, which are widely-used as a BPH therapy, reportedly improve not only voiding symptoms in patients with BPH, but storage symptoms as well. Bladder outlet obstruction (BOO) is widely though to contribute to voiding symptoms; therefore, relaxation of the urethra and prostate via blockade of alpha1-adrenoceptors may be the main mechanism by which voiding function can be improved. On the other hand, because etiologies of storage symptoms are multifactorial, neither the mechanism responsible for the storage symptoms induced by BOO, nor that behind the improvement in symptoms seen with alpha1-adrenoceptor antagonist is clearly understood. In this study, focus was placed on bladder microcirculation as one of the possible mechanisms causing the storage symptoms. The effect of tamsulosin, the most common alpha1-adrenoceptor antagonist, on bladder capillary blood flow was evaluated in bladder ischemic/reperfusion model rats.

Study design, materials and methods

A polyethylene catheter was inserted into bladder via the external urethral orifice of pentobarbital anesthetized female rats. Physiological saline (2 mL) was infused into the bladder at the rate of 0.05 mL/min to overdistend the bladder. Overdistension was maintained for 120 min, and then the bladder was emptied. Bladder capillary blood flow before overdistension, immediately and 120 min after overdistension, and after bladder emptying (immediately, 5 min, 15 min, 30 min, 60 min, 120 min after) were measured using pencil lens CCD microscopy (PLCMS). The system consists of a pencil lens with light guides, a charge-coupled device (CCD) image sensor, a control unit, a light source, a monitor and a videocassette recorder. The tapered pencil lens (tip diameter: 1 mm) contains a gradient-index (GRIN) lens surrounded by 18 annular optical-fiber light guides. It has a 0.5 inch monoclonal CCD image sensor (IK-C41MF, Toshiba, Tokyo, Japan). Bladder capillary and the surrounding tissues were illuminated by a xenon lump (150 W) through a green filter to accentuate the contrast between the vessels and other tissues. In the capillary vessel, the erythrocytes are shown as black colour, and the plasma pocket white colour. The spatial resolution of this system, determined by the use of a United States Air Force 1951 target, is 0.86 μm, and the temporal resolution is 33 ms (30 frames/s). Tamsulosin (1 μg/kg/h) was continuously administrated using a subcutaneously implanted osmotic pump from 1 week before the experiment.

Results

Following to bladder distension, it was noted that the red blood cell movement becomes slow. With over-distension of the bladder, the blood flow in the capillary vessel finally stoped at 2 mL of bladder capacity (Fig. 1).

During bladder capillary blood flow measurements, the numbers of animals in the control and tamsulosin-treated groups were 6 and 6, respectively. Bladder capillary blood flow decreased significantly (approximately 1.4% of pre value) as a result of overdistension and remained slow throughout the overdistension period (120 min). This decrease in the capillary blood flow recovered partially (approximately 70% of the pre-distension value) after bladder emptying, which indicated that bladder ischemia/reperfusion is achieved by bladder overdistention and emptying. However, the reperfusion was found to be incomplete. Tamsulosin (1 μg/kg/h, 1 week) increased bladder capillary blood flow after overdistension and rapidly increased it after emptying compared to the control group (Fig. 2).

Interpretation of results

This is the first report which directly verify that bladder ischemia/reperfusion induced by overdistension and emptying changes bladder capillary microcirculation. Reduced bladder blood flow [1] or a prolonged ischemic period [2] has been reported in animals with BOO. In addition, a decrease in bladder blood flow has also been reported for patients with BPH [3] as in the animal models. In BOO, the bladder ischemia following bladder overdistension has been reported to be associated with a variety of functional changes of detrusor, causing storage symptoms. In the present study, bladder overdistension induced bladder ischemia with incomplete reperfusion after bladder emptying. Tamsulosin increased bladder capillary blood flow during the period of ischemia and reperfusion. The present results indicate that tamsulosin has a potential to improve the bladder blood flow.

Concluding message

PLCMS could visualize that mucosal capillary blood flow in rats urinary and bladder during filling contributed to changes in capillary microcirculation.

The results of the present study suggest a possibility that tamsulosin improves storage symptoms by increasing bladder capillary blood flow in patients with BPH.

References

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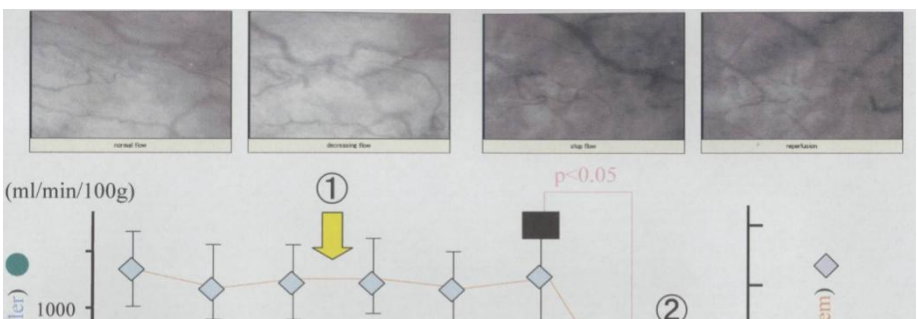

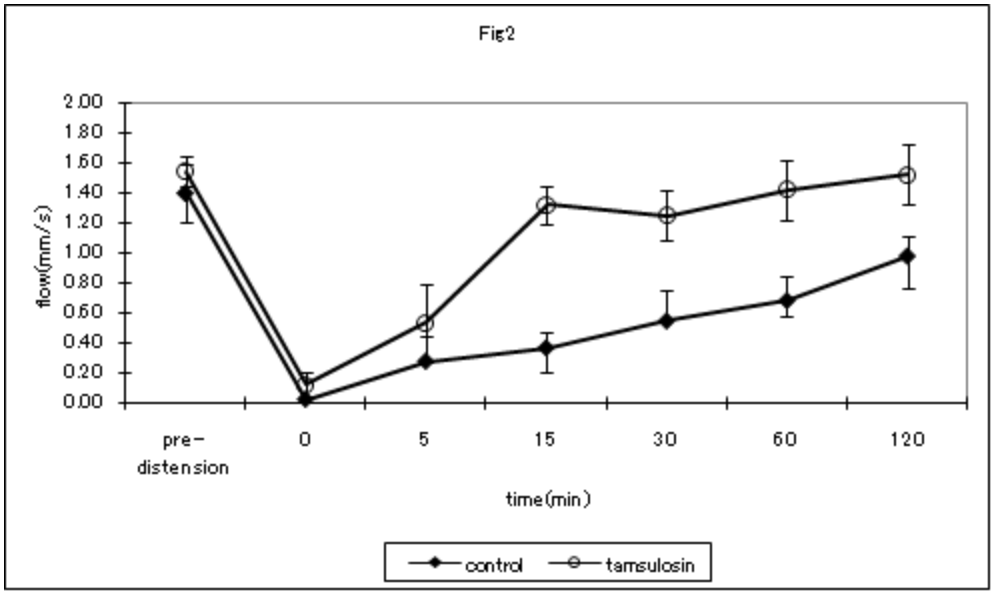

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Ethics committee of Nagoya University**