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Magari T[1], Shibata Y[2], Arai S[2], Kashiwagi B[2], Suzuki K[2]
1. *Department of Urology, Kurosawa Hospital,* ***2.*** *Department of Urology, Gunma University Graduate School of Medicine*

THE INFLUENCE OF CASTRATION ON BLADDER BLOOD FLOW AND FUNCTION DURING RAPID PHASE OF ANDROGEN DEPRIVATION

Hypothesis / aims of study

Androgen may participates in male lower urinary symptoms (LUTS) , mainly through its effects on prostate growth and function. Although effect of androgen on prostate is beyond dispute, there are symptoms that cannot be explained by prostate size and function. There are only occasional reports on relation between androgen and bladder function1)2). So we examined the relativity of androgen and bladder function from the aspect of bladder blood flow which is attracted a lot of attention related to overactive bladder（OAB）3). In this study, we examined the effect of androgen on bladder blood flow and also effect on the reaction to bladder irritability in acute phase shortly after androgen deprivation using castrate rat model.

Study design, materials and methods

The difference of blood flow by the affection of sex hormone

We used over 8 week-old mature male Wistar rat. We utilized following groups to our experiment (n=8 rats for each group); before castration group (Group P), 1 day after castration group (Group A), 12 -weeks after castration group (Group M), normal rat control group for Group M(Group C). Bood flow of the bladder was measured by either one of the following method.

Fluorescent microsphere method : Left carotid artery of the rats were cannulated under pentobarbital anesthesia and a constant quantity of fluorescent microspheres were injected intra-arterially, then bladder was excised and weighted. Left femoral artery was simultaneously cannulated to retrieve reference blood. The absorbance of microsphere in blood and bladder tissue were measured by fluorescence microplate reader and the local blood flow rate was calculated. Blood Flow rate is shown as absorbance rate of bladder weight per 1g×reference blood retrieval rate(ml/min)/absorbance rate of entire microsphere within the reference blood（ml/min/g).

Laser Doppler method : Bladder of the rats were exposed under urethan anesthesia by laparotomy. Thin NS Laser Probe (Advance Inc.) was irradiated to the surface of bladder utilizing balancer, and the bladder blood flow was measured with Laser Doppler rheometer（ALF21RD, Advance Inc.）. Blood flow measurements were performed at least 3 surface location of the bladder and averaged. Blood flow rate was shown as ml/min/100g.

２．Androgen and bladder function, examination of reaction to irritative symptoms

To clarify the relation between androgen deprivation and bladder hyperesthesia, we utilized Group A, Group M and Group C for the experiment. Bladder cystostomy was created under Urethan anesthesia using polyethylene tube（PE-50、Becton Dickinson Co.Ltd. USA）and cystometry was performed. Bladder was irrigated with Saline(NS) for 1hour with 5ml/h, then 0.25% acetic acid(AA) liquid solution was perfused for 1hour with the speed of 5ml/h.

Results

The difference of bladder blood flow by sex hormone

By fluorescent microsphere method, the bladder blood flow of each group were 1.34±0.19, 1.92±0.34, 1.25±0.52（mL/min/g）, respectively for Group P, Group A and Group M, showing significant increase in bladder blood flow at acute phase after castration ($p<0.001$, Fig.1).The increase in bladder blood flow at acute phase was also assured by Laser Doppler method. The actual bladder blood flow value were 46.2±4.7, 66.2±7.4,45.6±2.0(mL/min/100g), respectively for Group P, Group A and Group M, showing significant temporary bladder blood flow increase ($p<0.001$).

Androgen and bladder function, examination of reaction to irritative symptoms

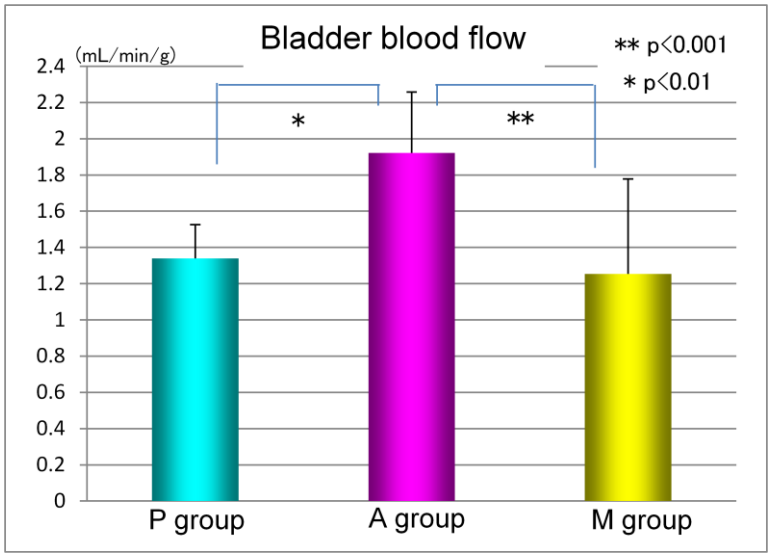
There was no significant difference in the maximum voiding pressure between the NS irrigation and AA irrigation among Group A, Group M and Group C (37.06±4.14 to 37.52±3.82, 40.46±4.36 to 42.58±5.63, 38.65±7.37 to 39.19±1.9（cmH2O）, respectively for 3 groups). Voiding interval is shown as AA/NS and actual value for three groups were 0.866±0.12, 0.448±0.015 and 0.438±0.12 for Group A, Group M and Group C, respectively, showing shortened voiding interval by acetic acid perfusion was significantly small in Group A ($p<0.001$, Fig.2).

Interpretation of results

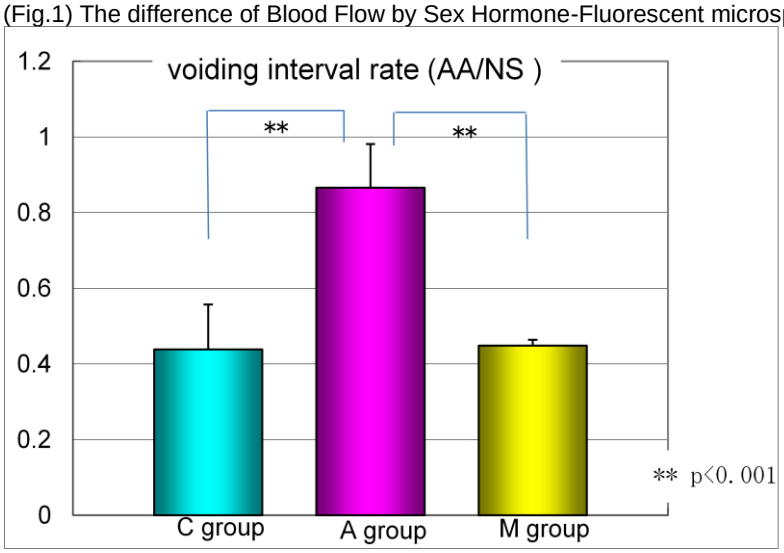
In acute phase after androgen deprivation by castration, bladder blood flow was significantly increased and bladder becomes durable to stimulation. The results show the suppressive effect of androgen on bladder blood flow that imply the possible androgenic effect on bladder function partly through the regulation of bladder blood flow.

Concluding message

This is the first report on the participation of androgen in the bladder blood flow regulation and effect on bladder function. The result may be important evidence to reveal mechanisms of LUTS especially in male.



(Fig.1) The difference of Blood Flow by Sex Hormone-Fluorescent microsphere method



(Fig.2) Androgen and Bladder Function, Examination of reaction to irritative symptoms

References

1. Effects of castration on contraction and alpha(1)-adrenoceptor expression in rat prostate.
2. Testosterone has potent, selective effects on the morphology of pelvic autonomic neurons which control the bladder, lower bowel and internal reproductive organs of the male rat.
3. Bilateral iliac artery endothelial injury and hypercholesterolemia lead to bladder overactivity in the rat.

Specify source of funding or grant	**We carried out this experiment with a part of the subsidy for Scientific Research subsidy in 2007-2008 year.**
Is this a clinical trial?	**No**
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	**We carried out all animal experiment under approval of Gunma University animal experiment committee.**