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THE INFLUENCE OF ANDROGEN ON BLADDER FUNCTION AND BLOOD VESSEL ～IF THERE IS A CHANGE OF BLADDER BLOOD FLOW～

Hypothesis / aims of study

The reports about androgen and LUTS have been seen occasionally1)2). The reports about bladder blood flow are also occasionally shown related to bladder outlet obstruction (BOO) model3), but the relativity of androgen and bladder blood flow is not yet confirmed. So we examine the relativity of androgen and bladder blood flow from the aspect of bladder blood flow which is attracted a lot of attention related to overactive bladder（OAB）. At the time of androgen is depressed, how bladder blood flow could be different, and the difference of reactions to irritable bladder are examined. The difference between mature and immature is going to be revealed as well.

Study design, materials and methods

1. The difference of Bladder Blood Flow by Sex Hormone

Male Wistar Rat 12 weeks after castration was utilized. 3 groups(n=8) as follows are used, 4 weeks-old castrated immature group (Group Y), 8 week-old castrated mature group (Group M) and Control group (Group C). We utilized fluorescent microsphere method for the measurement of blood flow.

Fluorescent microsphere method : Under Pentobarbital（30-40mg/ kg, i.p.）anesthesia, cannulate left carotid artery, after intra-arterially administration of constant quantity of fluoro-microsphere, enucleate Bladder and weight. Cannulate left femoral artery retrieve blood in constant rate, measure absorbance of microsphere in blood and bladder tissue and determine local blood flow rate.Absorbance is measured by fluorescence microplate reader(equipment of genome resource center in our property). 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）.

2. Androgen and Bladder Function, Examination of Reaction to irritative symptoms

Examine if depression of androgen cause hyperesthesia. We utilized Group A, Group M and Group C for our experiment. 1 week after creating bladder fistula, take it into metabolic gauge and exercise cystometry without anesthesia or shackled. Saline(NS) is 5ml/h, and afterward perfused 1 hour with acetic acid(AA) 0.25% liquid solution for 5ml/h. As well as prior examination, 3 groups as follows, Group Y, Group M and Group C was utilized. As to void parameter, we defined as follows, maximum voiding pressure, voiding interval and single voided volume.

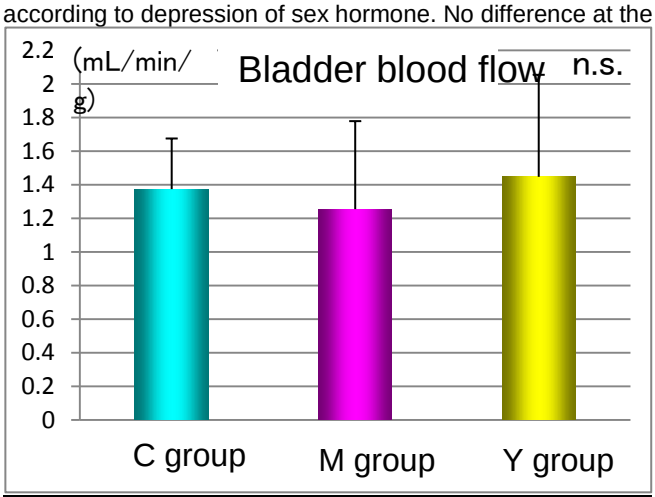
3. Examination of histological change of Bladder and Blood Vessel by Sex hormone

After measurement of bladder blood flow, enucleate bladder. Examine the difference of mucosa, smooth muscle, quantity of collagen fiber and vascular caliber. As well as bladder, enucleate upper vessels (abdominal aorta and common iliac artery) and examine existence or nonexistence of the difference, and if the difference exists, examine which part of vessel is it. Due to the difference of the timing of measurement, compare among Control, 12 weeks after castration and 12 weeks after castration (4 week-old and 8 week old) .

Results

1. The difference of Bladder Blood Flow by Sex Hormone

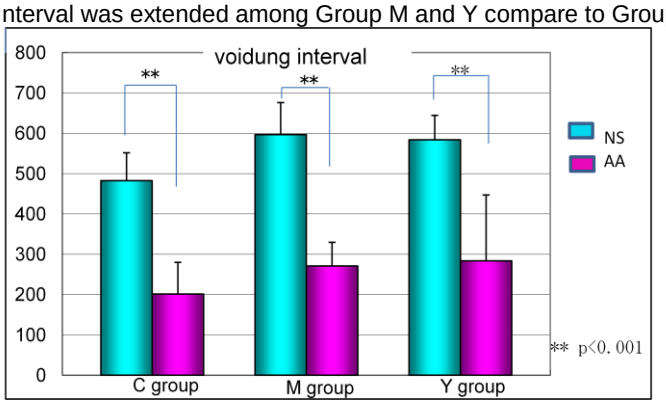
Group C 1.37±0.30, Group M 1.25±0.52, Group Y 1.45±0.61（mL/min/g）, No difference of bladder blood flow was shown according to depression of sex hormone. No difference at the time of castration was shown either.



2. Androgen and Bladder Function, Examination of Reaction to irritative symptoms

Maximum voiding pressure, in the order of Group NS, Group AA, in Group C(38.65±7.37、39.19±1.99), Group M(40.46±4.36、42.58±5.63) and Group Y(36.02±7.15, 42.03±3.42)(cmH2O), significant difference was not found among Group NS and Group AA. Among 3 Groups, significant difference was not found either.

Voiding Interval is, in Group C(482.67±69.17、201.35±78.43), Group M(596.55±79.70, 270.90±58.65), Group Y(584.00±60.18、283.63±163.22)（sec）, among all groups AA group was shown significant shrink. ($p<0.001$) . Voiding Interval was extended among Group M and Y compare to Group C but significant difference was not shown.



Single Voided Volume, in Group C, (0.467±0.15、0.441±0.21), Group M(0.633±0.18、0.427±0.15) and Group Y(0.783±0.19, 0.574±0.35)(mL), Among All groups in Group AA downward trend was shown but significant difference was not shown. At the examination of Group NS, among Group C in Group M and Y voided volume was increased but significant difference was not shown.

3．Examination of histological difference of bladder and blood vessel by sex hormone

At the examination of artery, at aorta, among Group Y in media muscular cell vacuolation was shown. At common iliac artery and bladder, significant difference was not shown.

Interpretation of results

After passage of extended period of time with depression of androgen, voiding interval decreased and single voided volume tends to increased and that shows the influence of androgen to bladder function. Histologically, castration since immature time period makes no difference to bladder and common iliac artery but the difference at aorta was observed to confirm the part of relativity of androgen and blood vessel.

Concluding message

Bladder blood flow showed no difference, so that low relativity of blood flow among androgen and bladder function.

References

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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. Effects of tamsulosin on bladder blood flow and bladder function in rats with bladder outlet obstruction.

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.**