

IN SHR RAT GIVEN SOLUTION OF SALINE AND HIGH-FAT FEED, IT REVEALS A BLADDER BLOOD FLOW DECREASE AND A BLADDER AND ARTERIAL FIBROSIS, AND IT BECOMES MORE REMARKABLE BY CASTRATION.

Hypothesis / aims of study

Some reports have investigated the relationship between androgens and bladder function, and an evaluation of the effect of androgens on blood vessels has indicated that vascular endothelial cell growth is suppressed due to low testosterone along with enhanced calcification of the blood vessel wall 1). Similarly, a previous report has examined the association between bladder blood flow (BBF) and bladder outlet obstruction; however, there are few studies that examined the association between male hormone and BBF 2). SHR rat has hypertension that is one of the vascular risk factors 3). Therefore, in this study, we examined the effect of androgen on BBF, bladder irritability, and histological changes after androgen deprivation using SHR rat model.

Study design, materials and methods

We used nine-week-old adult male SHR and Wistar rat. We utilized following groups to our experiment (eight rats per group); SHR rat 12 -weeks post castration group (Group C), SHR rat no operation group (Group S), Wistar rat no operation group (Group W). Group C and S were given 1% solution of saline and high-fat feed for 12-weeks.

1. Differences in BBF caused by androgen changes: 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.

2. Relationship between androgen changes and bladder function: Examination of bladder irritability

Bladder cystostomy was created using a polyethylene tube. One week later, the rats were placed in metabolic cages, and cystometry was performed without anesthesia or restraint. The bladder was irrigated with normal saline (NS) at room temperature, and 0.25% acetic acid (AA) liquid solution was then injected for 1 h at a speed of 5 mL/h. The parameters examined included maximum voiding pressure (cmH₂O) and voiding interval (sec).

3. Examination of androgen-related histological changes in bladder and blood vessels

We used Mallory-stained specimen for the examination of histological change such as denaturation or fibrosis. Sections of stained tissues were observed under light microscope. The images were analyzed using Photograb-2500 and Macintosh PowerMac G4, and quantified using Image J 1.46 software. The components of smooth muscles and connective tissues were calculated from at least 10 fields from each tissue section.

Results

1. Differences in BBF caused by androgen changes: Fluorescent microsphere method

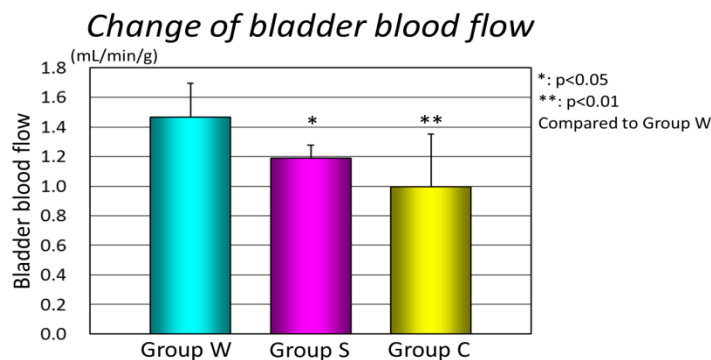


Fig. 1 : change of BBF

The mean BBF for the experimental rats were 1.47 ± 0.23 , 1.19 ± 0.09 , and 1.00 ± 0.36 (mL/min/g) for Group W, S, and C, respectively. Compared to Group W, the mean BBF were significantly decreased in Group S ($p < 0.05$), and in Group C ($p < 0.01$) (Fig. 1).

2. Relationship between androgen changes and bladder function

Maximum voiding pressure : No significant difference was noted in the maximum voiding pressure between NS irrigation and AA irrigation among Group W, S, and C (39.9 ± 8.1 to 37.5 ± 4.6 , 33.4 ± 5.4 to 34.6 ± 5.8 , and 33.9 ± 5.5 to 39.8 ± 3.5 (cmH₂O), respectively).

Voiding interval : Voiding intervals in each group was significantly shortened ($p < 0.001$) following AA irrigation (402.6 ± 98.1 to 202.9 ± 72.6 , 349.7 ± 95.9 to 168.2 ± 58.6 , and 373.0 ± 80.8 to 180.0 ± 37.0 (sec) for Group W, S, and C, respectively). Further, compared to Group W, the voiding intervals were significantly shorter in Group S following NS irrigation ($p < 0.05$), and in Group S and C following AA irrigation ($p < 0.05$) (Fig. 2).

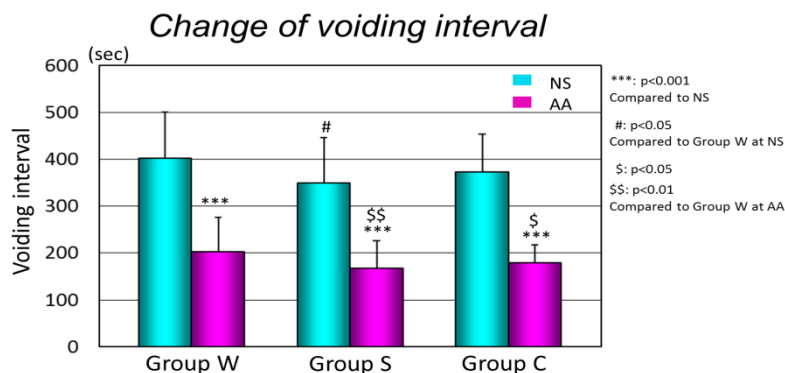


Fig. 2 : change of voiding interval

3. Examination of androgen-related histological changes in bladder and blood vessels

The mean bladder smooth muscle/collagen ratio (m/c ratio) were 3.28 ± 0.99 , 1.43 ± 0.38 , and 0.98 ± 0.24 for Group W, S, and C, respectively. Compared to Group W, m/c ratio was significantly lower in Group S and C ($p < 0.001$), and compared to Group S, m/c ratio was significantly lower in Group C ($p < 0.01$) (Fig. 3a). The m/c ratio at the iliac artery were 2.71 ± 0.89 , 0.71 ± 0.25 , and 0.56 ± 0.29 for Group W, S, and C, respectively. Compared to Group W, m/c ratio was significantly lower in Group S and C ($p < 0.001$), and compared to Group S, m/c ratio was significantly lower in Group C ($p < 0.05$) (Fig. 3b).

Smooth muscle/collagen ratio

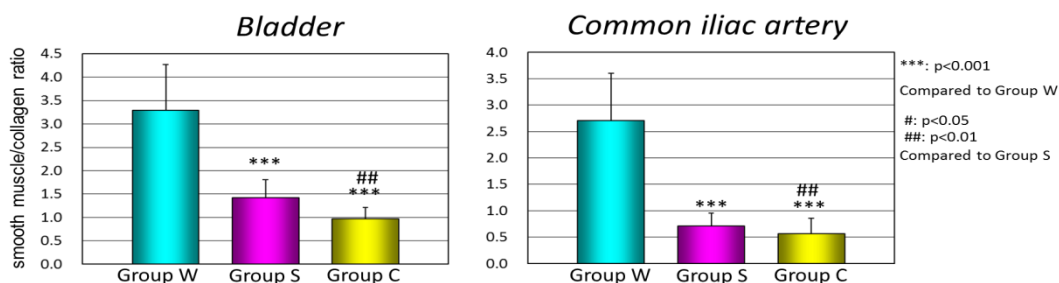


Fig. 3 : smooth muscle/collagen ratio bladder (a) and common iliac artery (b)

Interpretation of results

BBF decreases with SHR rat, and it becomes more remarkable by castration. Fibrosis is found in not only the bladder but also the artery histologically. So we considered it could be possible for both BBF and histological change to influence on bladder function. In addition, a part of relation between androgen and blood vessel could be confirmed as well.

Concluding message

This is the first report for considering androgen deprivation and BBF and bladder function by using SHR rat given solution of saline and high-fat feed. Furthermore, the report for confirming the histological change of common iliac artery with androgen deprivation was also provided for the first time. We consider the results at this time would be important results that clarify a relation between androgen and blood vessel, bladder function.

References

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Disclosures

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