

THE HYPOXIC ENVIRONMENT DECREASES BOTH AQUAPORIN3 AND UROPLAKIN III EXPRESSIONS AND BLADDER STORAGE FUNCTIONS IN SPONTANEOUS HYPERTENSIVE RATS.

Hypothesis / aims of study

Lifestyle related diseases, such as hypertension, diabetes mellitus and dyslipidemia are associated with lower urinary tract symptoms. Lower urinary tract symptoms patients with hypertension are often complain about storage functions.

There are reports that hypoxic environment induced from hypertension effects on bladder sensory nerves and/or secretions from the bladder urothelium. In addition, there are also reports that the hypoxic environment changes structures within the bladder walls. In this study, we determined if the histological changes induced from hypoxic environment could effect on bladder functions in spontaneously hypertention rats (SHRs).

Study design, materials and methods

1) Effects of acetic acid treatments

Ten weeks-old female SHRs and age-matched female Wistar Kyoto Rats (WKYs) were kept for 4 weeks giving 8% salt pellet (n=16 in each). They were divided into 4 group. One day prior to the cystometric investigation, the urinary bladders of SHRs and WKYs were treated with 0.08% acetic acid (n= 8 in each) or physiological salt solution (PSS, n=8 in each) for 30 minutes. Next day, cystometric investigations were performed.

2) Effects of adenosine triphosphate infusions

Ten weeks-old female SHRs and age-matched female WKYs were kept for 4 weeks giving 8% salt pellet (n=8 in each). In cystometric investigations, baselines were recorded, and then adenosine triphosphate (ATP) /PSS (pH 7.0) was instilled.

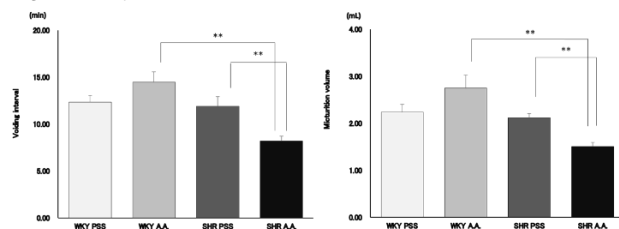
3) Histological analysis

After the cystometric investigations, the urinary bladders were analysed with hematoxylin and eosin (HE) stain, Masson Trichrome stain, and immunohistochemistry by using uroplakin III (UP_{III}), aquaporin₃ (AQP₃) and hypoxia inducible factor 1 α (HIF 1 α) antibody.

Results

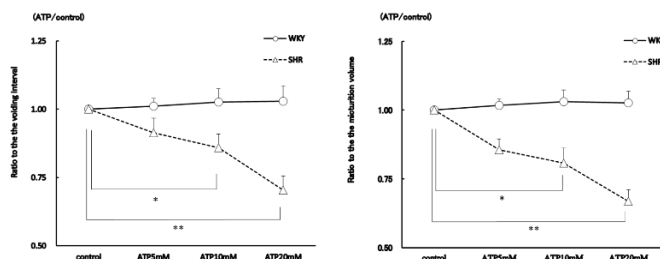
1) Effects of acetic acid treatments

In WKYs treated with 0.08% acetic acid, basal and micturition pressure, voiding interval, and micturition volume were similar to the PSS-treated WKYs. Both basal and micturition pressure of SHRs treated with 0.08% acetic acid were not any differences compared to the PSS-treated SHRs. However, voiding interval, and micturition volume of the 0.08% acetic acid-treated SHRs were significantly lower than these of the PSS-treated SHRs. (Bonferroni test. **: p< 0.01)



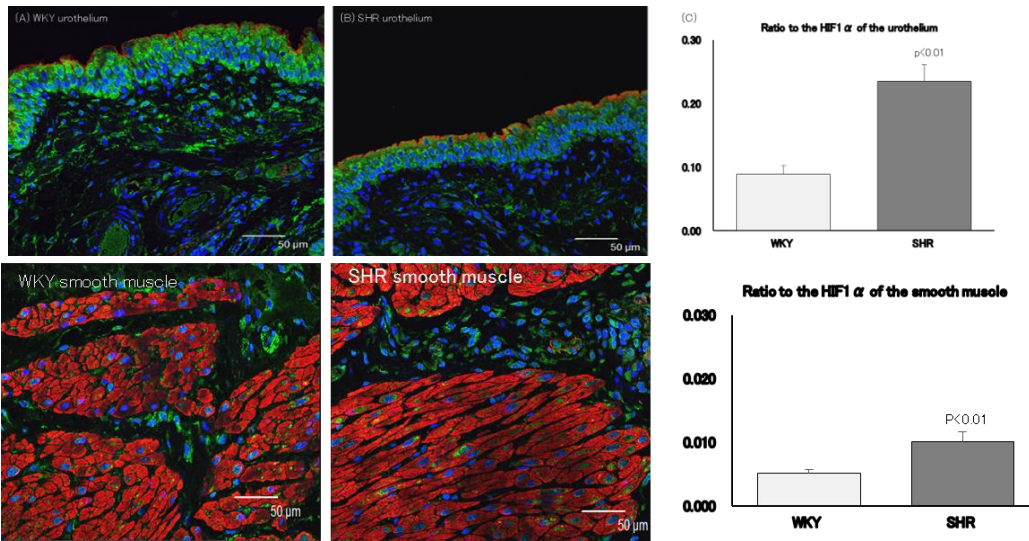
2) Effects of ATP infusions

In WKYs, cystometric parameters, basal and micturition pressure, voiding interval, and micturition volume were not altered by accumulation of ATP concentration. In SHRs, both basal and micturition pressure were also not altered. However, voiding interval and micturition volume of SHRs were decreased as dose dependent manners. (Bonferroni test. *: p< 0.05, **: p< 0.01)



3) Histological analysis

Expression level of HIF1 α within the urothelium and smooth muscle layers in SHRs was significantly higher than that in WKYs. Within suburothelium that was bottom of muscular layer, WKYs did not show edematous pathological findings. In contrast, SHRs exhibited edematous pathological findings within the suburothelium. Both expression levels of UP_{III} and AQP₃ within the urothelium in SHRs significantly decreased compared to the WKYs.



Interpretation of results

In SHRs, the storage functions, such as voiding interval and micturition volume were decreased by acetic acid and ATP solutions compared to WKYs. The urinary bladders in SHRs showed hypoxic environment compared to WKYs and edematous pathological findings within suburothelium. In addition, the expression levels of UP_{III} and AQP₃ in SHRs were lower than these in WKYs.

Concluding message

This study suggested that the hypoxic environment within the urinary bladders might effect on the histological change and bladder storage functions in SHRs.

Disclosures

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