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EFFECT OF ALPHA-1 ADRENOCEPTOR ANTAGONIST ON C-FOS AND NERVE GROWTH FACTOR EXPRESSION IN THE CENTRAL MICTURITION AREAS: HYPERTENSION ASSOCIATED RAT MODEL

Hypothesis / aims of study

The origin of overactive bladder (OAB), which is a leading cause of lower urinary tract symptoms (LUTS), remains unknown. Nerve growth factor (NGF) is one of the neurotrophic factors which are needed for the maintenance of neurons. It is known that too much expression of NGF may induce bladder hyperactivity. Although it is reported that alpha-1 adrenoceptor (AR) antagonist, including tamsulosin, improves not only voiding symptoms but also storage symptoms, the mechanism of alpha-1 AR antagonists to improve OAB remains controversial. The present study is to investigate the effects of tamsulosin on central micturition reflex by the degree of neuronal activation and NGF expression in the central micturition areas (medial preoptic area; MPA, ventrolateral periaqueductal gray; vlPAG, pontine micturition center; PMC) using spontaneously, hypertensive rat (SHR) model.

Study design, materials and methods

For this study, SHR and Wister-Kyoto rat (WKY) was used for experimental animals. Rats were randomly divided eight groups (n = 8, in each group): the WKY-control group (Group I), the SHR-control group (Group II), the SHR and 0.01mg/kg tamsulosin-treated group (Group III), the SHR and 0.1mg/kg tamsulosin-treated group (Group IV), the SHR and 1mg/kg tamsulosin-treated group (Group V). Tamsulosin-treated groups received orally once a day for a 30 consecutive days. Immunohistochemistry for c-Fos and NGF were performed for the dectection of neuronal activity in the MPA, vlPAG and PMC. Parameters of awake urodynamics were investigated before and after tamsulosin treatment in WKY and SHR. The mean blood pressures of the SHR and WKY were compared using polyethylene catheter inserted in the femoral artery and connected to a pressure transducer (Harvard Apparatus). The data was analyzed by one-way ANOVA followed by Duncan's post-hoc test.

Results

The mean blood pressure in the SHR increased compared with WKY. Hypertension associated rats enhanced non-voiding contraction (NVC) pressure and duration in Group II compared to Group I. In treatment groups (Group III-V) it was significantly suppressed. This suppression was reversely proportional to the dose of tamsulosin. The expression of c-Fos and NGF in all the central nerve system (CNS) regions was significantly enhanced in Group II compared to Group I. In treatment groups (Group III-V) it was significantly suppressed in all the CNS regions. This suppression was also reversely proportional to the dose of tamsulosin as the pattern of NVC.

Interpretation of results

Alpha-1 AR antagonist, tamsulosin, improved hypertension associated bladder hyperactivity. This might be caused by the suppression of central afferent and/or efferent neuronal activation on the lower urinary tract and NGF expression in the midbrain –brainstem control.

Concluding message

The present results demonstrated that irritative LUTS and symptoms of OAB could be alleviated by alpha-1 AR antagonist through the suppression of the central neuronal activation and NGF expression in the midbrain and brainstem. This might be considered as a one of the possible central mechanisms of alpha-1 AR antagonist, tamsulosin to improve OAB and irritative LUTS.

Specify source of funding or grant	**None**
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	**Gachon University Institutional Animal Care and Use Committee**