878

Kojima Y[1], Sasaki S[1], Shibata Y[1], Imura M[1], Hayase M[1], Kubota Y[1], Hayashi Y[1], Kohri K[1]
1. *Department of Nephro-urology, Nagoya City University Graduate School of Medical Sciences*

CORRELATION BETWEEN EXPRESSION OF ALPHA1-ADRENOCEPTOR SUBTYPE MRNA AND SEVERITY OF LOWER URINARY TRACT SYMPTOMS OR BLADDER OUTLET OBSTRUCTION IN BENIGN PROSTATIC HYPERPLASIA PATIENTS

Hypothesis / aims of study
Three alpha1-adrenoceptor (alpha1-AR) subtypes (alpha1a-, alpha1b- and alpha1d-AR) have been characterized pharmacologically and in molecular terms, and the expression of these subtypes has been reported to be observed in the prostate. Although the alpha1a-AR-subtype was reported to be the major subtype in the prostate of some benign prostatic hyperplasia (BPH) patients, we have demonstrated that BPH patients are divided two types, showing the predominance of alpha1a-AR mRNA expression levels and the predominance of alpha1d-AR mRNA expression levels using a more reliable method, real-time RT-PCR [1]. The expression level of alpha1-AR subtype mRNA in the prostate could be a predictor of the efficacy of subtype-selective alpha1-AR antagonists in BPH patients [2]. Our next question is whether this expression level could be responsible factor of LUTS and BOO in the patients with BPH. Although there are several reports about distribution and localization of alpha1-AR in the prostate, there has been no report to demonstrate the correlation with the clinical findings. In this study, therefore, we examined the correlation between the expression of alpha 1-AR subtype mRNA in the prostate and severity of LUTS or BOO in BPH patients to discuss the pathophysiology of lower urinary tract symptoms (LUTS) and bladder outlet obstruction (BOO) associated with BPH.

Study design, materials and methods
Sixty-eight men, 50 years old or older, with LUTS and BOO secondary to untreated clinical BPH diagnosed in our institute were enrolled in this study. Four prostate needle biopsy specimens were obtained from the transition zone to examine the expression level of alpha1-AR subtypes by Taqman RT-PCR. The correlation and regression between each expression level of alpha1-AR subtype and clinical findings such as patient age, prostate volume, IPSS, QOL idex, Qmax and PVR were assessed by Stepwise multiple regression analysis. Additionally, the correlation and regression between this expression level and individual symptoms of IPSS were assessed by Pearson's correlation coefficient and multiple regression analyses.

Results
The median expression level (interquartile range) of each subtype was 1.3 (0.7-4.4), 0.2 (0.1-0.4) and 1.3 (0.8-2.6) x 1,000 copies /beta-actin for alpha1a-, alpha1b- and alpha1d-AR mRNA respectively. The ratio of the mean expression level (interquartile range) of each subtype in the total alpha1-AR was 0.47 (0.35-0.57) %, 0.07 (0.04-0.11) % and 0.44 (0.35-0.56) % for alpha1a-, alpha1b- and alpha1d-AR mRNA, respectively. Stepwise multiple regression analysis showed that the expression levels of alpha1a-AR, alpha1b-AR, alpha1d-AR and total alpha1-AR mRNA showed a significant regression with patient age, but not with prostate volume, IPSS, QOL index, Qmax and PVR. Pearson's correlation coefficient and multiple regression analyses demonstrated no correlation and regression between each alpha1-AR subtype mRNA expression level and individual symptoms of IPSS.

Interpretation of results
We demonstrated no significant relationship between the expression level of alpha1-AR subtype mRNA and severity of LUTS and BOO, although the significant regression of this expression with patient age existed.

Concluding message
It is not likely that the expression level of alpha1-AR subtype in the prostate could be a major responsible factor of severity of LUTS and BOO, although the possibility remains to be a link between alpha1-AR stimulation and LUTS or BOO. The causes of LUTS and BOO could be multifactorial and complicated, and several other conditions may contribute to LUTS and BOO. Further study will be needed to clarify the pathogenesis of LUTS and BOO associated with BPH.

References
1. Kojima Y, Sasaki S, Shinoura H, Hayashi Y, Tsujimoto G, Kohri K. Quantification of alpha1-adrenoceptor subtypes by real-time RT-PCR and correlation with age and prostate volume in benign prostatic hyperplasia patients. Prostate. 2006;66:761-767.
2. Kojima Y, Sasaki S, Kubota Y, Hayase M, Hayashi Y, Shinoura H, Tsujimoto G, Kohri K. Expression of alpha1-adrenoceptor subtype mRNA as a predictor of the efficacy of subtype selective alpha1-adrenoceptor antagonists in the management of benign prostatic hyperplasia. J Urol. 2008;179:1040-1046.

Specify source of funding or grant	**none**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**

Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Nagoya CIty University Ethical Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**