

Relationship between ADRB3, ARHGEF10 and ROCK2 gene polymorphisms and clinical findings in over active bladder patients
Elif Firat¹, Zafer Aybek², Sakir Akgun³, Kursat Kucuker², Hakan Akca³, Hulya Aybek¹

¹ Department of Medical Biochemistry, Medical School of Pamukkale University– Denizli, Turkey

² Department of Urology, Medical School of Pamukkale University–Denizli, Turkey

³ Department of Medical Biology, Medical School of Pamukkale University– Denizli, Turkey,

Hypothesis / aims of study

In human urinary bladder, beta3-ARs play an important role in promoting detrusor relaxation during the storage phase of the micturition cycle and stimulation of M3 receptor in detrusor muscle results in activation of RhoA pathway leading to contraction (1, 2, 3). Thus, the polymorphism in the ADRB3, ARGHEF10 and ROCK2 genes may result in an insufficient relaxation or increased contraction of detrusor (4, 5, 6). We aimed to determine the impact of gene polymorphisms on detrusor contraction-relaxation harmony in women with over active bladder (OAB) syndrome.

Materials and methods

In this study 60 women with idiopathic OAB and age-matched control women without OAB were enrolled. Genomic DNA was isolated from all patients and subjected to PCR for amplification. The Trp64Arg polymorphism in ADRB3 gene, Arg338Thr polymorphism in ARGHEF10 gene and Thr431Asn polymorphism in ROCK2 gene were detected by quantitative Real Time Polymerase Chain Reaction.

Results

The mean weight, height and body mass index in the OAB group were not significantly different from those in the non-OAB group and also we found no statistically significant difference in the genotype and allele frequencies between the patients and controls for all three SNP. In addition within OAB patients, OAB symptom scores in the 64Arg and 338Thr variant carriers were not significantly different from normal gene carriers. On the other hand, within patients, OAB symptom score which was higher in the heterozygous 431Asn variant carriers were significantly different from the homozygous 431Asn variant carriers ($p=0,039$).

Concluding message

Genotypic distribution of ADRB3, ARHGEF10 and ROCK2 genes in OAB patients is not different from the control group. Although the polymorphism of gene in the adrenergic pathway did not significantly differ the severity of clinical findings, OAB patients also have a heterozygous polymorphic structure of the ROCK2 gene which increases OAB symptom score in muscarinic pathway. As a result of our study, we found that the polymorphisms of the ADRB3, ARGHEF10 and ROCK2 genes were present in both OAB group and healthy subjects, but the polymorphisms were not associated with OAB syndrome.

References

1. Yoshimura N, Chancellor MB. Neurophysiology of Lower Urinary Tract Function and Dysfunction. *Rev Urol.* 2003;5(Suppl 8):S3-S10.
2. Chess-Williams R. Muscarinic receptors of the urinary bladder: Detrusor, urothelial and prejunctional. *Auton Autacoid Pharmacol.* 2002;22(3):133-145.
3. Hashim H, Abrams P. Overactive bladder : an update. *Curr Opin Urol.* 2007;17:231-236.
4. Fatima T, Altaf S, Phipps-Green A, et al. Association analysis of the beta-3 adrenergic receptor Trp64Arg (rs4994) polymorphism with urate and gout. *Rheumatol Int.* 2016;36(2):255-261.
5. Teitsma C, Rosette J, Michel M. Are Polymorphisms of the B3-Adrenoceptor Gene Associated With an Altered Bladder Function? *Neurourol Urodyn.* 2013;32:276-280.
6. Fukata Y, Kaibuchi K, Amano M, Kaibuchi K. Rho-Rho-kinase pathway in smooth muscle contraction and cytoskeletal reorganization of non-muscle cells. *Trends Pharmacol Sci.* 2001;22(1):32-39.