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Title: The pharmacogenetic effect of ADRB2 polymorphisms on therapeutic response in COPD

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Body: Background Most pharmacogenetics studies of COPD have focused on the role of variants in the b2-adrenergic receptor gene on bronchodilator response, but the findings have been inconclusive. Objective To investigate lung function responses following a 24-week treatment with a long-acting b2 agonist combined with a steroid inhaler in patients with COPD with various ADRB2 genotypes. Methods In 73 patients with stable COPD, polymorphisms in the amino acid position 16 (Arg16/Gly16) and 27 (Gln27/Glu27) of the ADRB2 gene were assessed by allele-specific polymerase chain reaction. Long-term response was evaluated using observed change in spirometric values before and after the treatment with formoterol (12 ug) combined with budesonide (400 ug) inhalation twice daily for 24-week. Results In terms of codon 16 variants, the FEV1 changes following the 24-week treatment were 5.64 ± 1.49% predicted in Gly/Gly patients, -3.40 ± 0.85% predicted in Arg/Gly patients, and -7.00 ± 1.38% predicted in Arg/Arg patients ($p < 0.1$). In terms of codon 27 variants the FEV1 changes after 24-week treatment was 3.32 ± 0,89% predicted in Glu/Glu patients, 2.01 ± 0.97% predicted in Gln/Glu patients, and -1.36 ± 0.42% predicted in Gln/Gln patients ($p < 0.1$). Conclusion Arg16-Gln27 haplotype was associated with decreased lung function after 24-week treatment with long-acting β2-agonists plus inhaled corticosteroids in a Russian population.