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A pilot study to assess the effects of tiotropium bromide on the airflow obstruction of asthmatics with decreased pulmonary functions

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Introduction: Tiotropium bromide, a new long-acting anticholinergic agent, is approved for the maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease. However, its role for the treatment of asthma has not been evaluated. **Objective :** To assess the effects of tiotropium bromide on the airflow obstruction of asthmatics with decreased lung functions. **Methods :** Fifty seven asthmatics were enrolled in this study whose % predictive values of forced expiratory volume in 1 second (FEV1%) were less than 80%. They were treated with conventional medications based on guideline and the variability of their pulmonary functions measured by FEV1 was less than 5% at least for the previous 8 weeks. Once a day, one puff of tiotropium bromide (22.5mcg) was added to their current medications and responders were defined as those whose FEV1 increased over 15% after the start of tiotropium bromide and was maintained at least for the successive 8 weeks. **Results :** Twenty six asthmatics (45.6%) were categorized as responders after 38.3 weeks (mean duration of follow up). Mean increase of FEV1 was 26.6% (15.3-119.6%) and mean duration (from the start of tiotropium bromide to the appearance of response) was 12.1 weeks (4-28 weeks). Mean age, gender, the prevalence of smoker, and the duration of conventional medications before the stat of tiotropium bromide were not significantly different between responders and non-responders. **Conclusion :** These results indicate a prominent role of tiotropium bromide in the management of asthmatics, especially those with decreased pulmonary functions in spite of conventional medications, although factors to predict response need to be characterized.

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Association analysis of ACE polymorphisms with inhibitory efficacy of LTRA against aspirin-induced bronchospasm

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Background : Angiotensin I converting enzyme1(peptidyl-dipeptidase A1, ACE) gene on chromosome 17q23 is membrane-bound peptidase having 44770bp. and distributed on epithelial cells, endothelial cells and macrophaes in the lung. We studied association of ACE polymorphisms with the variance of long-term effects of LTRAs against aspirin-induced bronchospasm. **Methods :** Forty-six adult patients with AIA, as diagnosed by the aspirin challenge test, were recruited to this study. The subjects underwent the aspirin challenge test after administration of montelukast (MLK; 10 mg daily for 12 weeks). We assessed the protective effect as the inhibitory efficacy (percentage fall in FEV1; %fall FEV1) following aspirin challenge before and after 12 weeks of treatment. The inhibitory efficacy rate (IER) was calculated according to the formula: [(%fall FEV1 before treatment-%fall FEV1 after treatment) / %fall FEV1 following aspirin challenge before treatment]×100. We scrutinized genetic polymorphisms of ACE gene and evaluated this locus comparing with the inhibitory efficacy rate(IER). **Results :** The %fall FEV1 following aspirin challenge was significantly reduced from 28.6±1.9% to 10.2±1.7% (p=0.0001) by 12 weeks of MLK treatment. The IER values varied from -50%~139%, with a median value of 62%. The subjects were grouped as good or poor responders according to the median value. The SNP polymorphisms of ACE gene associated with IER were 29301C>T, 30265A>T, 34810T>C, 42093C>A, and 43663T>C. The frequencies of rare alleles on 29301C>T, 30265A>T, 34810T>C, 42093C>A, and 43663T>C were higher in good reseponders than in poor responders (p=0.008-0.019). Aspirin induced asthmatics who had rare alleles for 29301C>T, 30265A>T, 34810T>C, 42093C>A, and 43663T>C exhibited a more pronounced IER than did those who carried the common allele (p= 0.005-0.028). **Conclusions :** ACE polymorphisms are associated with inhibitory efficacy rate of LTRA against aspirin-induced bronchospasm in AIA. This work was supported by a grant from the Korea Health 21 R&D Project, Ministry of Health and Welfare, Republic of Korea (01-PJ3-PG6-01GN04-03).