— 183 —

Polymorphisms in FCER1B gene may predict the requirement of H1 antihistamines in patients with chronic urticaria

JH Choi※, SH Kim, YM Ye, CH Suh, DH Nahm, HS Park, Department of Pulmonology and Allergy, Bundang JeSaeng General Hospital, Department of Allergy and Rheumatology, Ajou University Hospital, Korea

Backgrouds and objectives:The pathogenic mechanism of chronic urticaria (CU) and its prognosis is still unclear. Histamine, a key mediator is released via high-affinity IgE receptor (FCER1) and antihistamine is the mainstay for drug treatment. To investigate the role of genetic polymorphisms in pathogenic mechanism and drug response, we screened 11 SNPs in FCER1B, H1 histamine receptor (HRH1), HRH2, histamine N-methyltransferase (HNMT) gene in patients with CU from Korean population and analyzed an association with drug response to H1 antihistamine. ***Materials and methods***: 63 CU patients followed for 1 year and 99 normal controls were enrolled. CU was defined as the occurrence of daily widespread itchy wheals for > 6 weeks. We calculated cumulative dose of H1 antihistamines for 1 year and anti-histamine requirement was expressed as loratadine equivalent dose per week. 11 SNPs in FCER1B (-109T>C, RsaI_in2G>A, I181A, E237G, RsaI_ex7T>C), HRH1 (-17C>T, D349A), HRH2(543G>A, 826C>T) and HNMT (T105I, 939A>G) were screened using single base extension method. ***Results***: There were no significant differences in allele frequencies and genotype frequencies of all 11 SNPs between CU and healthy controls. However, the CU patients with FCER1B109C/C variant homozygote showed significantly lower cumulative dose of H1 antihistamines than those with T/C, T/T genotypes ($p<0.01$), and the CU patients with *Rsa*I_in2A/A variant homozygote also showed significantly lower cumulative dose of H1 antihistamines than those with G/A, G/G genotypes ($p<0.01$). ***Conclusion:*** These results suggest that two variant homozygote of FCER1B (-109T>C and *Rsa*I_in2G>A) may be used for predicting drug requirement of H1 antihistamines in long term management of CU patients. This study was supported by a grant of KoreanHealth 21 R&D project, Ministry of Health&Welfare, Republic of Korea (01-PJ10-PG6-01GN14-0007).

— 184 —

Distinct association between nonsynonymous SNPs of candidate genes and bronchodilatory response to short-acting inhaled β2 agonist according to atopic status

Yong-Eun Kwon[1], Hye-Kyung Park[1], Tae-Bum Kim[1], Eun-Sun Shin[2], Jong-Eun Lee[2], Heung-Bum Oh[3], Yoon-Seok Chang[1], Yoon-Keun Kim[1], Sang-Heon Cho[1], Kyung-Up Min[1],You-Young Kim[1]

[1]Department of Internal Medicine, Seoul National University College of medicine. [2]DNA Link. [3]Department of Laboratory Medicine, Ulsan University College of Medicine.

Background: Inhaled short-acting β2-agonist is the most effective reliever for exacerbated asthma symptoms, but drug response to this drug is known to have genetic components. The cellular mechanism that β2-agonist induce smooth muscle relaxation may interact with lots of signal pathway induced by other molecules. Our previous study revealed that atopic subjects may have less bronchodilatory response to this drug when compared with nonatopic subjects

Objective: Under the hypothesis that bronchodilatory response (BDR) to inhaled short-acting β2 agonist is associated with genetic polymorphisms of candidate genes that may influence signaling pathway of β2 adrenoceptor, association study was done in general population.

Method: Bronchodilatory responses (BDR) at 5 minutes after inhalation of 2 puffs of albuterol inhaler were done in 471 subjects with a reduction of FEV1 more than 20% after methacholine inhalation when compared with baseline FEV1. After screening of informative nonsynonymous coding single nucleotide polymorphism (SNP) with restriction fragment mass polymorphism for candidate genes, SNP scoring was determined by high throughput technique. The statistical significance was evaluated by multiple logistic regression analysis.

Results: BDR was associated with nonsynonymous SNPs of GM-CSF2 (I179T, p=0.04), IL12 receptor β1 (M365T, p=0.04) in atopic subjects. In contrast, BDR was associated with nonsynonymous SNPs of Fcε receptor 1 β chain (E237G, p=0.03), FGF receptor 4 (I10V, p=0.03 R388G, p=0.04), IL3 (P27S, p=0.04), IL4 receptor (Q576R, p=0.02), and IL12 (S226N, p=0.04) in non-atopic subjects.

Conclusion: BDR to short-acting inhaled b2 agonist was significantly associated with nonsynonymous SNPs of candidate genes that influence signaling pathway of b2 adrenoceptor, and the association significance was different according to atopic status.

Keyword : bronchodilator, SNP, Asthma, atopy