Pharmacogenetics of asthma

Andrzej M. Fal, Marta Rosiek-Biegus, Marita Marszalska

Clinic of Internal Diseases and Allergology, Medical University of Wroclaw, Traugutta 57/59, PL 50-417 Wroclaw, Poland

Correspondence: Andrzej M. Fal, e-mail: amfal@pro.onet.pl

Abstract:
The paper reviews current knowledge on genetic background of action of drugs used in asthma treatment. In this aspect, glucocorticosteroids, leukotriene modifiers, β2 adrenoceptor agonists as well as methylxantines are discussed. The authors analyze different outcomes of treatment in subjects with non-wild-type genotype as compared to wild-type ones. For glucocorticosteroids, we focus on the polymorphism of corticotropin-releasing hormone receptor1 and the intracellularly located glucocorticoid receptor that exists in two variants (glucocorticoid receptor α – GRα and GRβ) created during alternative splicing of exon 9α to exon 9β. It is hypothesized that this polymorphism may be responsible for the reduced responsiveness to glucocorticosteroids in GRβ-predominant-subjects. For leukotriene, modifiers of two enzymes are reviewed: arachidonate 5-lipoxygenase (ALOX5) and leukotriene C4 (LTC4) synthase. Especially LTC4Ss promoter has several described single nucleotide polymorphisms (SNPs), where the –444C is supposed to be associated with enhanced LTC4 production and, therefore, poorer response to leukotriene receptor antagonist treatment. β2 Adrenoceptor polymorphism has been widely studied recently. At least 55 SNPs have been identified, with Arg-Gly16 polymorphism and Ghn-Glu27 polymorphism being the most frequent ones. It has been demonstrated that patient’s homozygous for Arg 16 produce significantly diminished response to β2 agonist treatment. Further, we discuss a possible role of CpG DNA motifs as adjuvants in immunotherapy of allergic diseases as well as modulators of children’s immune system preventing development of allergic diseases. We conclude that, however there are medical disciplines where pharmacogenetics is in clinical use, in allergy and asthma we need further studies to evaluate potential risks and benefits.

Key words:
pharmacogenetics, asthma, β2-adrenoceptor, glucocorticosteroids, 5-lipoxygenase