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Predicting of clinical efficiency of bisoprolol in patients with acute coronary syndrome by polymorphism RS776746 in the gene of CYP3A5 assessment

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Introduction: Bisoprolol is a beta-blockers, which has a high selectivity to beta-1-adrenergic receptors of the heart. For the best therapeutic effect of any drug, it is important to reach the effective therapeutic dose as soon as possible. Bisoprolol is a lipo-hydrophilic beta-adrenoblocker and its metabolism occurs in the liver under the action of isoenzymes CYP3A4 and CYP3A5. According to the literature, it is known that CYP3A5 has a similar substrate specificity with CYP3A4, and is characterized by genetic polymorphism. The most common are allelic variants *1 and *3. Studies devoted to the study of their role in predicting the efficacy of bisoprolol have not been carried out to date.

Purpose: Holter monitor, as a criterion of the clinical efficacy of bisoprolol in patients with acute coronary syndrome (ACS).

Materials and methods: The study included patients with ACS who was assigned bisoprolol according to clinical indications. All patients included in the study were Holter monitor on the 10th day of ACS - the minimum, mean, maximum heart rate during the day and the maximum heart rate were assessed at the time of exercise was evaluated against the background of the current therapy. All patients included in the study also underwent molecular genetic testing. The detection of polymorphic variants of T (CYP3A5 *1) and C (CYP3A5 *3) at the locus rs776746 of the CYP3A5 gene was carried out by real-time PCR.

Results: A total of 102 patients, 62 males and 40 females were included in the study. The average age of patients is 63.52±2.4 years. The allele frequency was: 0.073 for CYP3A5 *1 and 0.926 for CYP3A5 *3, which corresponds to its prevalence in the European population. The distribution of genotypes corresponded to the Hardy-Weinberg law. From the analysis excluded 5 patients with atrial fibrillation. By the time of the Holter monitor, both the carriers of the allele *1 and patients with the genotype *3 *3 achieved the same mean heart rate (68 beats/min) and the maximum heart rate at the load (116 and 114 beats/min), which says about the equal effectiveness of beta-blockers at this time.

However, to achieve this effect, patients of the two groups required different doses of bisoprolol. Thus, in carriers of at least one allele CYP3A5 *1 (n = 13), associated with an increased metabolic rate, the dose of bisoprolol on the 10th day of ACS was significantly higher, and amounted to 5.62 mg, and in carriers of the variant CYP3A5 *3 *3 - 4.51 mg (p <0.05); when analyzing the dose in mg/kg, the differences were even more pronounced - 0.15 and 0.07, respectively (p <0.01).

Conclusion: The results indicate that the carriers of the minor allele *1 in the CYP3A5 gene need significantly higher doses of bisoprolol to achieve a clinical effect, which makes this genetic polymorphism a useful factor for choosing the optimal initial bisoprolol dosing regimen in patients with ACS.