Metoprolol succinate efficacy in patients with chronic heart failure on the background of obesity:
genetic aspects of individual sensitivity and tolerability

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Background. The cornerstone of modern cardiology is the problem of comorbidity, the combination of chronic heart failure (CHF) with obesity as well. Efficacy of treatment with beta-blockers in different patients varies significantly, partly depending on genotypically determined features of its metabolization with enzymes.

Purpose. To improve the CHF treatment with metoprolol succinate efficacy in patients with obesity by detection of genetic aspects of individual sensitivity and tolerability.

Methods. A prospective randomized dynamic (1 year) study was conducted involving 127 patients with CHF II–III stages at the age of 32–87 years; they were distributed into main group with combination of CHF and obesity (73 patients) and control group with only CHF (54 patients). The examination included an assessment of CYP2D6 gene 1846G/A polymorphism, clinical symptoms, quality of life (by Minnesota questionnaire), 6-minute walk test data, doppler echocardiography, heart rate variability, serum insulin, N-terminal prohormone of brain natriuretic peptide (NT-proBNP). Metoprolol succinate was administered according to a standard regimen with dose titration every 2 weeks from 12.5 to 100–200 mg. The critical p-level was 0.05.

Results. An association of "unfavorable" allele A with an increase in body weight was found (p=0.05). As a result of treatment, better indicators of the clinical status were found in control group (6 [5; 7] versus 7 [6; 8] points in obese patients, p=0.05) and quality of life in patients with genotype GG than the GA genotype (p<0.05).

The use of metoprolol succinate in patients with GG genotype is associated with more pronounced positive dynamics of treatment efficacy. In contrast to the carriers of the GA genotype, in patients with the GG genotype there were an increase in left ventricle ejection fraction (by 21.5% versus 9.3%, p <0.01) and the reduction of the left ventricle end-diastolic size (p=0.02). The GG genotype carriers significantly increased the amount of exercise tolerance (p<0.05), and showed a more pronounced improvement in quality of life (p<0.03) and the clinical state (p=0.05), as well as the normalization of the vegetative balance (LF/HF index). The level of serum NT-proBNP in the GG genotype was lower than in patients with GA genotype (p=0.05). At the same time, patients with a GA genotype showed a more pronounced decrease in heart rate compared to those with a GG genotype (p<0.05).

In carriers of the GA genotype, a tendency to a greater incidence of side effects compared with the GG genotype (bradycardia 42.0% vs. 28.0%, p<0.05; cold extremities 44.0% vs. 32.0%, p <0.05, fatigue 39.0% vs. 31.0%, p <0.05, headache 32.0% vs. 24.0%, p<0.10, drowsiness 38.0% vs. 27.0%, p<0.05).

Conclusions. It is useful to take into account the CYP2D6 gene 1846G/A polymorphism in order to improve the CHF treatment with metoprolol succinate in patients with obesity.