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## COMBINED CONTROL OF THE HEART RHYTHM IN PATIENTS WITH ACUTE CORONARY SYNDROME

**Abstract.** *One of the main factors influencing on a short-term and remote prognosis of patients experienced acute myocardial infarction is heart rate. Administration of Ivabradine decreases HR at the expense of inhibition of electric activity of the sinoatrial node (Keith-Flack node) resulting in reduction of heart rhythm, increase of diastolic time during perfusion as a result of decreased oxygen supply to the myocardium without any harmful changes – arterial pressure values, coronary blood supply and contractile capacity of the myocardium. Monotherapy with Bisoprolol is indicative of an effective control of the heart rhythm in patients with ACS, but after a combined therapy with Ivabradine and Bisoprolol better results were found during the first 3-4 days of treatment. Insufficient decrease of HR in patients with ACS during the first 3-7 days of hospitalization is associated with an increased risk of post-infarction angina or relapse of myocardial infarction.*

**Key words:** *congenital developmental defects; heart rhythm; acute coronary syndrome.*

**Introduction.** A high mortality rate due to ischemic heart diseases in Ukraine outside inpatient departments is caused by low levels of detection and diagnostics of acute coronary syndromes (ACS). One of the main factors influencing on a short-term and remote prognosis of patients experienced acute myocardial infarction (MI) is heart rate (HR). Administration of *Ivabradine* decreases HR at the expense of inhibition of electric activity of the sinoatrial node (Keith-Flack node) resulting in reduction of heart rhythm, increase of diastolic time during perfusion as a result of decreased oxygen supply to the myocardium without any harmful changes – arterial pressure values, coronary blood supply and contractile capacity of the myocardium [1,3]. In patients with coronary failure and reduced ejection fraction *Ivabradine* demonstrated a positive effect in improvement of clinical results in addition to standard therapy [2]. However, a clear value concerning administration of *Ivabradine* in case of acute coronary syndrome has not been found.

**Objective:** to detect a potential value of *Ivabradine* in clinical context of treatment of

patients with ACS.

**Materials and methods.** 135 patients with ACS were included into the study. The possibility to improve treatment and clinical-prognostic role of ACS reduction was assessed with administration of *Ivabradine*. The patients were divided into the following groups: patients with the diagnosis of unstable angina – 62 individuals (45,9%), patients with MI without ST elevation – 52 individuals (38,5%), patients with MI and ST elevation – 21 individuals (15,5%), including 4 cases when thrombolysis had been performed (33%). Pharmacological therapy correlated with the national recommendations concerning management of patients with ACS. In addition to clinical and hemodynamic indices, the causes when  $\beta$ -adrenoreceptor blocking agents ( $\beta$ -AB) had not been indicated were analyzed, the frequency of achieving target HR values, dynamics of HR and BP against the ground of treatment by means of  $\beta$ -AB, causes limiting the titration of  $\beta$ -AB doses, frequency of side-effects after  $\beta$ -AB administration, the character of the disease at the hospital stage depending on the peculiarities of  $\beta$ -AB indication have been detected. The rates of

HR, BP, ECG indices were assessed after admission to the hospital: during an acute period (on the 2-4<sup>th</sup> day, the 3<sup>rd</sup> day on an average), during sub-acute period (on the 14<sup>th</sup> day) of staying in the hospital. The patients were divided into two groups: the one included patients receiving *Bisoprolol* with the aim to control HR (group I, 93 patients), and another one - patients receiving *Bisoprolol* in the combination with *Ivabradine* (group II, 42 patients). The groups were similar by their major clinical-demographic indices. Mathematic analysis of the results obtained estimating the mean value and standard deviation of the mean value. Probability of quantitative indices was detected by means of the method of "null hypothesis" control using Student t-criterion (for equal and unequal dispersions – checked according to Fisher criterion), reliable results were considered with the index  $p < 0,05$ .

**Results and discussion.** Analysis of the main parameters of the clinical-instrumental examination was not indicative of reliable differences between the patients of the examined groups at the beginning of treatment. On admission to the hospital the rates of HR and BP and on the 3<sup>rd</sup> day of treatment in both groups did not differ considerably. More than in half of the cases in both groups HR decreased – 49 patients (44,6%) of I group and 24 (57,1%) - II group ( $p=0,55$ ) respectively. In comparison with *Bisoprolol* as monotherapy, a combined administration of *Ivabradine* and *Bisoprolol* at the beginning of treatment was associated with more frequent achievement of a target value of HR and less probability of side-effects [2,3]. More considerable decrease of HR in 62% of patients was found in combination with *Ivabradine*. The target rate of systolic pressure (SP) was achieved in 54 (57,2%) and 31 (73,8%) patients ( $p=0,21$ ), diastolic pressure (DP) – in 65 (68,9%) and 34 (81,9%) patients ( $p=0,47$ ), and SP and DP – y 54 (54,1%) and 28 (68,6%) patients ( $p=0,39$ ) of I and II groups respectively. On the 14<sup>th</sup> day the target HR was achieved in 58 (62,4%) patients from I group and 34 (83%) patients of II group ( $p=0,05$ ). The target levels of SP and DP were achieved in all the patients of the examined groups. Inconsiderable decrease of HR during the first week of hospitalization was associated with an increased relapse risk of angina or myocardial

infarction without consideration of a reduced regimen of a medical agent. While analyzing the causes restricting the possibility to reach a target value of HR the following results were obtained: in I group in 14 (13%) cases symptomatic hypotension was found (in 1 patient was associated with the development of AB-block, 1<sup>st</sup> degree), in 5 (4,3%) – development of bronchial-obstructive syndrome, in 16 (17,7%) – only disorders of AB-conductivity to the 1-2<sup>nd</sup> degree. *Bisoprolol* was not cancelled in any of the cases. Hypotension, disorders of AB-conductivity and bronchial obstruction were eliminated by means of decreasing the dose of the drug, correction of doses of APP inhibitor and diuretics, a short-term administration of bronchodilators. In II group transient visual signs were the cause to cancel further increase of the dose of *Ivabradine* only among 4 (9,5%) patients after achieving an average value of HR 66 b/min.

Complicated course of ACS in the form of relapse of MI and/or post-infarction angina was registered in 33 (35,5%) patients of I group and 13 (18,5%) patients of II group ( $p=0,70$ ). At the same time, with reliably higher values of HR during the study the patients with complicated course of ACS (subgroup A) demonstrated reliably lower decrease of HR, than those without variant angina and/or relapse of MI (subgroup B) during all the stages of the hospital investigation. Similar dynamics of HR changes can be found in both groups of HR correction. Maximal decrease of HR was found since the first days of the study, which was similar for both groups of comparison. Considering selective decrease of HR without loss of the myocardial contractility, *Ivabradine* can be recommended as an effective agent to treat ACS without decrease of ejection fraction.

**Conclusion.** Monotherapy with *Bisoprolol* is indicative of an effective control of the heart rhythm in patients with ACS, but after a combined therapy with *Ivabradine* and *Bisoprolol* better results were found during the first 3-4 days of treatment. Insufficient decrease of HR in patients with ACS during the first 3-7 days of hospitalization is associated with an increased risk of post-infarction angina or relapse of myocardial infarction.

**Prospects of further studies.** Further improvement of therapeutic tactics,

determination of possible combination of Ivabradine and  $\beta$ -adrenoreceptor blocking agents will enable to reduce side effects and improve a remote prognosis in patients with acute coronary syndrome.

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