THE EFFECT OF BISOPROLOL ON DISEASE COURSE FOR PATIENTS WITH HIGH SST2 LEVELS AND ACUTE MYOCARDIAL INFARCTION

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Data received in recent years confirm the sST2 value as a cardiac biomarker. Research of patients with heart failure demonstrated the sST2 role as independent mortality predictor for patients with severe congestive heart failure or acute heart failure. [3, 4, 5]. Taking into consideration sympathoadrenal system activation in patients with acute myocardial infarction (AMI), it is interesting to investigate beta-blockers (BB) therapy and its probable influence on disease course according to initial sST2 levels. The BB use for patients with AMI reduces left ventricular (LV) remodeling processes intensity and improves LV hemodynamic function, that decreases the area of myocardial infarction (MI) and duration of treatment [2]. Objective of the study is assessing of different bisoprolol doses effect on the incidence of adverse events for patients with AMI depending on the initial sST2 level.

Materials and Methods. 103 patients with ST-elevation myocardial infarction (STEMI) were included, 75 (72.8%) of them were men and 28 (27.2%) were women. Average age was (61,85±12,23) years old. All the patients underwent standard clinical and biochemical analysis in the first 24 hours. sST2 level was detected by enzyme linked immunoassay with the use of reagent kit «Presage ST2 Assay», Critical Diagnostics (the USA). Echocardiography was performed after patients admission to the hospital and after 6 months. Also all patients were going on six minute walk test (6MWT) for assessment of exercise tolerance. The cohorts of patients were divided according to initial sST2 level on admission to the hospital, sST2 distribution threshold was 35 ng/ml. This is the biomarker level, that has been proven in fundamental research [1]. First group with sST2 level < 35 ng/ml) was consist of 47 patients, and second group with sST2 level ≥ 35ng/ml) was consist of 56 patients. The combined endpoint was fatal event and hospitalization for decompensation of chronic heart failure or acute heart failure. Observation period for patients was 6 month. Subsequently 83 patients, who have no contraindications, were added to treatment BB, bisoprolol. Initial dose of the drug was 2.5 mg per day, with further increasing in the hospital and ambulatory. In one patients group the daily dose remained unchanged (2.5 mg) in connection with non-compliance of patients, in the second group it was possible to reach the target dose 5-10 mg. 40 patients with daily bisoprolol dose 2.5 mg were included to the first subgroup, 43 patients were included to the second subgroup with daily bisoprolol dose 5-10 mg.

Results. Outgoing sST2 blood serum level was 26.38 [20.96; 29.56] ng/ml in the first clinical group and 56.14 [44.83; 115.25] ng/ml in the second group (p< 0.001). The analysis revealed reliable sST2 level dependence on end systolic volume (p=0.025), left ventricular ejection fraction (LVEF) (p=0.007) and systolic blood pressure (p=0.006). In 6 months in the first group was significant increasing of sST2 blood serum level from 26.38 [20.96; 29.56] ng/ml to 63.36 [26.30-102.46] ng/ml (p<0.002), and heart rate deceleration (p=0.004), decreasing of systolic blood pressure (p=0.0001), and diastolic blood pressure (p=0.005). In the second group with initial high sST2 level (≥ 35 ng/ml) was less significant increasing of the biomarker from 56.14 [44.83-115.25] ng/ml to 100.09 [41.89-137.07] ng/ml (p=0.656) and reliable heart rate deceleration (p=0.001). Despite of the treatment, significant changes of LFEF and exercise tolerance were not determined in 6 months. The using low and target bisoprolol doses for patients with myocardial infarction with initial sST2 level (< 35 ng/ml) during 6 months was not associated with improvement of contractile myocardium function and functional state by going on 6MWT and also prevention of significant biomarker increasing. sST2 level increased from 25.99 [19.25-31.16] ng/ml to 40.28 [20.63-232.04] ng/ml (p=0.032) on the background of low bisoprolol dose and from 25.16 [21.75-28.54] ng/ml to 60.41 [29.26-123.20] ng/ml (p=0.051) on the background of high bisoprolol.
Both hypertension and obesity are key cardiovascular risk factors. Known mechanisms of combined impact of obesity and other major cardiovascular risk factors are still not clear, but the data of epidemiological and clinical studies indicate the leading role of adipokines (a group of cytokines produced by adipose tissue) in the onset and progression of cardiovascular complications in obese patients \[11\]. In this aspect, the recently discovered adipokines, chemerin and nesfatin-1, are of interest. Chemerin is mainly synthesized in adipocytes and preadipocytes of adipose tissue, and nesfatin-1 is produced primarily by the brain in hypothalamic neurons. The role of these adipokines in terms of obesity and cardiovascular diseases is of significant interest.

Results of our studies in this context expand the conception about relationship between sST2 activity and bisoprolol therapy efficiency, that may be valuable for detection of individual tactics of management of patients with AMI. In the present study we reported that there were not significant differences in adverse events number between patients with initial sST2 level < 35 ng/ml that were treating with different bisoprolol doses (\(\chi^2 = 0.70, p = 0.79\)). However, when we compared patients with initial sST2 level ≥35 ng/ml, that were treating with bisoprolol dose 2.5 mg per day during 6 months, we observed a significantly lower adverse events frequency (4.8% vs 10.3%) in the group with initial sST2 level < 35 ng/ml (\(\chi^2 = 6.62, p = 0.01\)).

Thus, high sST2 level confirms high risk of complications and requires using of optimal BB doses for patients with AMI.

Conclusions. Based on the obtained data we can do the following conclusions:

1. Comparing of patients with initial sST2 level ≤35 ng/ml, that were treating with different bisoprolol doses, demonstrated, that there were not significant differences in adverse events number (\(\chi^2 = 0.70, p = 0.79\)).
2. Patients with initial high sST2 level (≥35 ng/ml), that were treating with bisoprolol doses 2.5 mg per day during 6 months, had significantly lower adverse events frequency, 4 (10,8%) during observation period, (\(\chi^2 = 6.62, p = 0.01\)). In our investigation BB therapy was not accompanied during 6 months by decreasing of sST2 level, by improvement left ventricular function, but it significantly decreased adverse events frequency in the high risk group (sST2 ≥35 ng/ml) when there were using target bisoprolol dose.

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References:


Key words: sST2, acute myocardial infarction, beta-blockers, bisoprolol.