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The effectiveness of a fixed double combination (bisoprolol, perindopril) in patients with stable coronary artery disease and arterial hypertension in different degrees

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Abstract

The use of beta-blockers (bisoprolol) and ACE inhibitors (perindopril) is pathogenetically and clinically justified in patients with stable coronary artery disease (CAD) and concomitant arterial hypertension (AH). The study showed that prescribing a fixed combination of previously used drugs (perindopril, bisoprolol) for 4 weeks in patients with clinical symptoms or documented CAD can effectively reduce heart rate (HR) and blood pressure (BP) (heart rate levels ≤ 70 bpm were reached in 84.9%, blood pressure ≤ 140/90 mm Hg - 86.9% of patients), reduce the number of angina attacks from 4.4 to 2.6 per week and the need for nitroglycerin - from 4.8 to 2.7 tablets per week, and improve adherence to therapy (66.5% of patients).

Keywords: fixed double combination therapy; bisoprolol; perindopril; stable coronary artery disease; arterial hypertension

Introduction

Most patients with CAD and AH are treated in outpatient settings. [1, 2] Timely diagnostics, prevention, and appointment of optimal drug therapy reduce the risk of complications, improve the quality of life save working capacity, and reduce cardiovascular and general morbidity and mortality. Control of HR and (BP for a patient with stable CAD is the most important condition for effective antianginal therapy and is directly related to long-term prognosis. [3, 4] Adherence to therapy remains a pressing problem, especially in patients with coronary artery disease who are forced to take a large number of medications. As a result, patients often interrupt treatment, including life-threatening ones, on their own. This affects not only the symptoms of the disease but also the prognosis, which is associated with an increased risk of CV complications and mortality from all causes. [5] Modern recommendations to solve this problem suggest using fixed combinations of different groups of drugs in one tablet, which greatly simplifies the treatment regimen and is one of the most effective ways to increase adherence.

This study aimed to evaluate the profile of patients with coronary artery disease and concomitant arterial hypertension who took bisoprolol as part of previous therapy, but did not reach normal levels of heart rate and blood pressure; to estimate the percentage of achievement of recommended levels of heart rate, blood pressure and treatment adherence in patients after 4 weeks of using the fixed-dose combination of bisoprolol/perindopril with a correction of doses.

Methods

All of the experiments described here were conducted with permission from the Institutional Ethics Committee at National academy of medical sciences of Ukraine. The study involved 170 cardiologists from various regions of Ukraine. Each researcher selected 15 consecutive outpatients with CAD who came for a regular visit. Inclusion criteria: age over 18 years old, BP above 140/90 mm Hg, HR above 60 bpm, bisoprolol as part of antihypertensive therapy in the last ≥ 3 months. The study included two visits. At each visit, the patient's objective status was assessed; an

individual questionnaire with office systolic and diastolic BP, HR, ECG data, clinical manifestations of CAD, risk factors, lifestyle features, concomitant diseases, and current therapy was filled out. Medication adherence was also evaluated by the Girerd X. et al. questionnaire, the treatment was corrected if necessary and the presence of side effects and adverse events was registered. We analyzed the levels of BP and HR at the beginning and end of the study, the percentage of achievement of the recommended levels of these indicators, the antianginal efficacy of treatment and adherence to therapy in patients with CAD, and different degrees of hypertension after 4 weeks of treatment.
To evaluate the hypotensive and antianginal efficacy of a fixed combination (FC) (bisoprolol, perindopril) in patients with CAD and concomitant hypertension. ((table.1)

Table 1. Doses of FC of bisoprolol and perindopril in patients depending on the degree of AH

Doses	Doses	AH I (n=505)	AH II (n=1027)
5/5 mg	204 (40,4%)	293 (28,5 %)	28(13,0%)
5/10 mg	201 (39,8%)	464 (45,2 %)	93 (43,3%)
10/10 mg	78(15,4%)	258 (25,1 %)	93 (43,3%)

Results
2785 patients' questionnaires were provided by doctors, and 1747 patients were included in the substudy. Av. age 60.9 ±10.2 y.o, men – 57.1 %, women – 42.9 %. The diagnosis of CAD was based on:
•chest pain – 554 (31.7 %),
•a history of documented MI – 935 (53.5 %),
•coronary angiography results – 536 (30.7 %),
•revascularization (CABG/PCI) – 344 (19.8 %) patients. Risk factors and concomitant disease (% patients) HF: 38,4%; T2DM: 18,7%; Arrhythmia: 46,4%; Obesity: 34,9%; Current smokers: 10%; Av. glucose level: 5,91 mmol/l; GI > 7mmol/l: 11,3%; Av. total cholesterol: 5,6 mmol/l; Physical activity: low - 31%,medium-intensity - 55%, energetic - 13% The use of FC of previously taken drugs (perindopril, bisoprolol) for 4 weeks allows to
•reduce with statistical significance (p<0,001 vs.baseline) HR and BP effectively (HR ≤ 70 bpm reached 84.9 % of patients, HR ≤ 60 bpm – 31.6%, BP ≤ 140/90 mm Hg – 86.9 %, BP ≤ 130/80 mm Hg – 51,8 % of patients). The most significant absolute decrease in BP and HR was in patients with a more severe degree of hypertension (decreased systolic BP was – 40.8 mm Hg, diastolic BP was – 21.4 mm Hg, HR – 21.8 bpm).
•reduce the number of angina attacks (from 4.48, 4.5, and 4.7 per week at the beginning of the study to 2.4; 2.9 and 2.3 per week in patients with 1, 2 and 3 degrees of hypertension, respectively) and the nitroglycerin consumption from 4.5; 4.9 and 5.9 tabs per week up to 2.4; 2.9 and 2.3 tabs per week (p<0,001 vs.baseline).
•Improved patients' adherence to the prescribed therapy in all study groups: it increased by 66.5%, remained unchanged in 27.6%, and decreased in 2.9 % of the subjects (p<0.001) as shown in Figure 1 and 2.

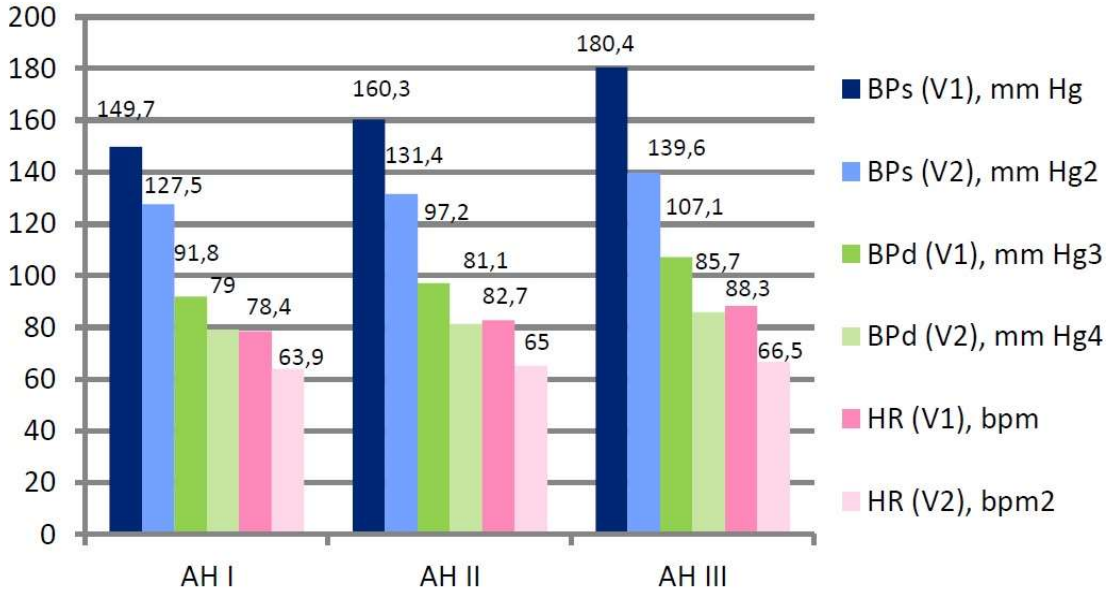

Figure 1. BP and HR levels after 4 weeks of taking a fixed combination of bisoprolol and perindopril in patients with varying degrees of AH

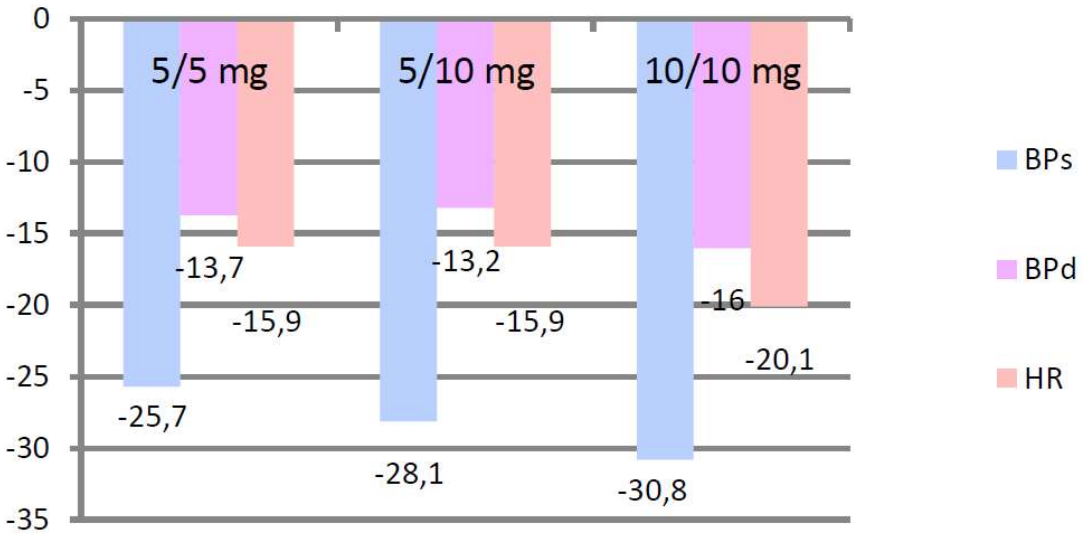

Figure 2. Av. decrease of BP and HR depending on the dose of an FC of bisoprolol and perindopril

Discussion

Prescribing the beta-blocker bisoprolol and the ACE inhibitor perindopril is pathogenetically and clinically justified for patients with stable coronary artery disease and concomitant hypertension. According to the results of a large-scale meta-analysis (11,418 patients from the EUROPA, ADVANCE, PROGRESS studies, 2017) Ilona Golikova, the combination of BB and perindopril compared with BB therapy with placebo demonstrated a reduction in cardiovascular mortality, non-fatal MI, stroke - by 20%, non-fatal MI - by 23% and, most importantly, overall mortality - by 22% in patients with CV pathology regardless of the presence of hypertension. Adherence to therapy also remains an urgent problem, especially in patients with coronary artery disease, who are forced to take a large number of drugs. As a result, patients often independently interrupt treatment, including life-threatening ones. This affects not only the symptoms of the disease but also the prognosis, which is associated with an increased risk of CV complications and all-cause mortality. Current recommendations to solve this problem suggest using fixed combinations of different drug groups in a single tablet, which greatly simplifies the treatment regimen and is one of the most effective ways to increase adherence.

Conclusion

The study demonstrated that the use of the fixed combination of bisoprolol and perindopril in patients with CAD and concomitant hypertension (different degrees) helps to improve treatment efficacy and achieve recommended levels of BP and HR. It also has a significant antianginal effect (reliable decrease in the number of angina attacks and nitroglycerin consumption) and increases adherence to therapy.

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