THE EFFECT OF ROSUVASTATIN ADDED TO A STANDARD ANTIHYPERTENSIVE THERAPY ON ARTERIAL STIFFNESS IN PATIENTS WITH UNCONTROLLED HYPERTENSION

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INTRODUCTION

Uncontrolled hypertension (HTN) is a common clinical problem faced by both primary care clinicians and cardiologists worldwide. Blood pressure (BP) is under control only in 30.9%and 14.4% of Russian women and men respectively.

BP is a powerful cardiovascu lar (CV) risk factor that acts on the arterial wall and is responsible in part for various CV events, such as cerebrovascular accidents and ischemic heart disease.

Increased arterial stiffness is an independent predictor of CV risk in normotensive and hypertensive populations. Studies in subjects with high CV risk have shown that the reduction of CV morbidity and mortality is significantly improved when the blood pressure reduction is associated with arterial stiffness attenuation.

Lipid-lowering agents may have various consequences on arterial stiffness. First, statins are known to have a beneficial effect on endothelial function, thereby restoring nitric oxide (NO) bio-activity in atherosclerotic populations and thus producing an NO-induced large artery dilatation and reduction of stiffness. Secondly, statins cause, at an early phase,a rapid reduction of lipid vascular content, and thereby may be responsible for an absolute or relative increase in collagen, a process causing an increase of arterial stiffness. Finally, in subjects with hypercholesterolaemia, statin treatments are associated with either decreased or unchanged alterations of arterial stiffness. In subjects with hypertension, the situation may be even more complex to evaluate since increased stiffness may be the consequence of both high blood pressure and intrinsic modifications of the arterial wall. Combined effects of hypertension and hypercholesterolaemia are known to result in a further increase of arterial stiffness, at least at the site of the radial artery.

Reduction of the PWV is considered a potentially useful therapeutic strategy in the overall management of patients with cardiovascular disease. However, there is little or no information on the synergistic effects of the combination of rosuvastatin treatment and standard HTN therapy on arterial wall stiffness.

PURPOSE

The aim of our study was to assess the influence of rosuvastatin added to a standard therapy on central aortic blood pressure, augmentation index (AIx), pulse wave velocity (PWV) in patients with uncontrolled hypertension.

METHODS

We investigated 60 patients (31 men and 29 women aged 51.1±9.1) with uncontrolled hypertension (HTN) which were randomized into two groups. Group 1 included 30 patients who received a fixed combination of 10 mg/day lisinopril and 5 mg/day amlodipine (Ekvator, Richter Gedeon, Hungary). Group 2 consisted of 30 patients who followed the same regimen of therapy with addition of 20 mg/day of rosuvastatin.The office and central (aortic) BP, augmentation index (AIx), carotid-femoral and carotid-radial pulse wave velocity (PWV) were evaluated before and after a 48-week follow-up period (Fig.1). Arterial stiffness parameters were evaluated by non-invasive automatic device SphygmoCorCPV System(«AtCor», Australia).

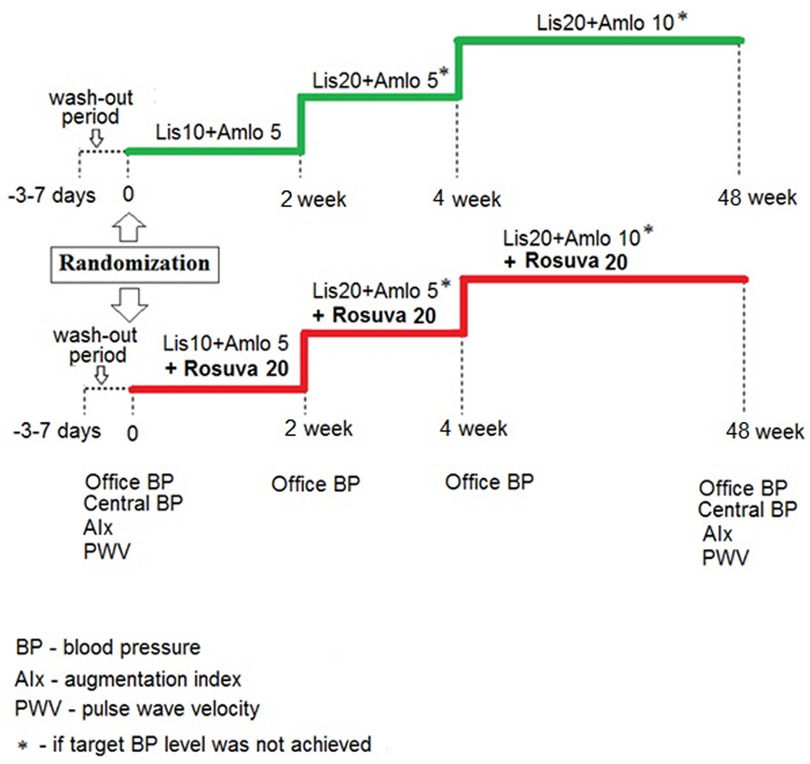

Fig. 1.Design of the study

Data analysis was done by Statistica 8.0 analysis software («Statsoft», USA). Average values are expressed as mean (M) ± standard deviation (SD). As distribution of variables was different from normal the Mann-Whitney and Wilcoxon tests were used to assess the differences.We applied Chi-square test for evaluating the relative values differences. P-value of less than 0.05 was used to assess the significance.

RESULTS

The baseline clinical characteristic of the groups is shown at the Table.

Table

Baseline characteristic of the groups

Parameter	Amlo+Lis	Amlo+Lis+Rosuva
Age, years, M±SD	48.9±10.4	53.5±8.0
Men/women	14/16	17/13
Body mass index, kg/m^2, M±SD	30.4±5.2	29.6±5.0
SBP, mmHg, M±SD	172.4±24.3	170.8±20.0
DBP, mmHg, M±SD	105.4±13.5	104.0±14.3
Central SBP, mmHg, M±SD	153.6±22.1	157.0±20.3
Central DBP, mmHg, M±SD	100.5±13.2	100.0±10.6
AIx, %, mmHg, M±SD	30.6±14.0	35.2±8.2
PWVcf, m/s, M±SD	9.2±2.0	9.5±1.7
PWVcr, m/s, M±SD	9.7±2.0	9.5±1.9

All p>0.05.

As it follows from Table the groups were comparable by gender, age, body mass index, office and aortic BP, AIx and PWV.

After 48 week follow-up period the office systolic/diastolic BP decreased in both groups from 172.4±24.3/105.4±13.5 to 136.7±12,8/88.1±9.4 mmHg (p<0.001) in the first group and from 170.8±20.0/104.0±14.3 to 131.0±9.1/83.3±7.7 mmHg (p<0.001) in the second one (Fig. 2).
The average dose of lisinopril/amlodipine at the end of follow-up period was 5.5/13.4 mg in the first group and 5.6/13.5 mg in the second one (p>0.05).

Central BP also decreased in both groups from 153.6±22.1/100.5±13.2 to 121.3±17,6/83.3±10.4 mmHg (p<0.001) in the first group and from 157.0±20.3/100.0±10.6 to 119.8±15.8/80.1±9.7 mmHg (p<0.001) in the other (Fig. 3). The extent of office and central BP decline did not differ.

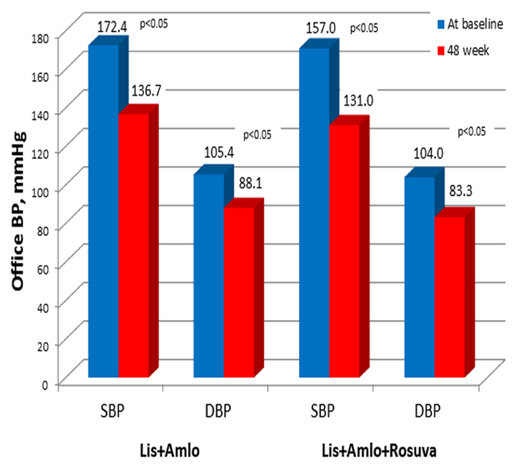

Fig. 2. Office BP dynamics under the influence of two treatment regimens

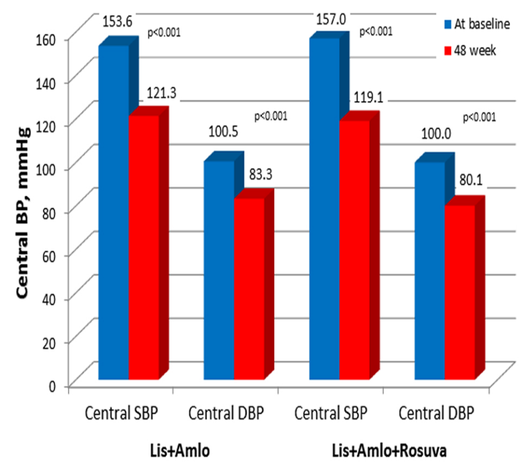

Fig. 3. Central BP dynamics under the influence of two treatment regimens

AIx decreased from 30.6±14.0 to 23.5±15.2% (p=0.01) in the first group and from 35.2±8.2% to 24.1±13.0% in the second group (p<0.001) with more prominent AIx decrease in the latter (-6.2% and -9.8% respectively, p=0.15) (Fig. 4). Mean carotid-femoral PWV decreased statistically only in the 2nd group from 9.5±1.7 to 8.7±1.6 m/s (p=0.04). The carotid-radial PWV did not change in both groups (Fig. 5).

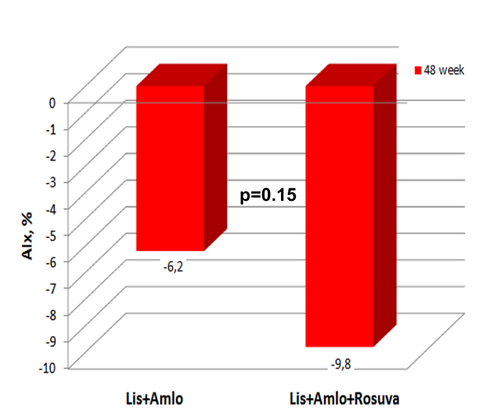

Fig. 4. AIx dynamics under the influence of two treatment regimens

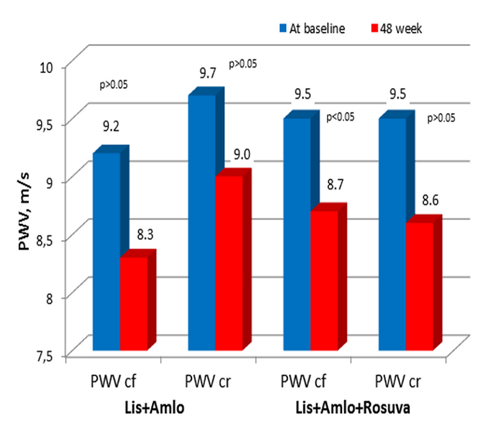

Fig. 5. PWV dynamics under the influence of two treatment regimens

CONCLUSION

Addition of rosuvastatin to a fixed lisinopril/amlodipine combination in treatment of patients with uncontrolled hypertension resulted in the carotid-femoral pulse wave velocity decline, but was beneficial neither for the decrease of aortic systolic and BP nor augmentation index.

REFERENCES

1. Boytsov S.A., Balanova Yu. A., Shalnova S.A. et al. Arterial hypertension among individuals of 25-64 years old: prevalence, awareness, treatment and control. By the data from ECCD // Cardiovascular Therapy and Prevention. 2014; 13(4): 4-14.
2. Safar M.E. Systolic blood pressure, pulse pressure and arterial stiffness as cardiovascular risk factors. CurrOpinNephrolHypertens. 2001; 10: 257-261.
3. Guerin A.P. et al. Impact of aortic stiffness attenuation on survival of patients in end-stage renal failure. Circulation. 2001; 103: 987-992.
4. Steinberg H.O. et al. Endothelial dysfunction is associated with cholesterol levels in the high normal range in humans. Circulation. 1997; 96: 3287-3293.
5. Fukumoto Y. et al. Statins alter smooth muscle cell accumulation and collagen content in established atheroma of Watanabe heritable hyperlipidemic rabbits. Circulation. 2001; 103: 993-999.
6. Kool M. et al. Does lowering of cholesterol levels influence functional properties of large arteries? Eur J ClinPharmacol. 1995; 48: 217-223.
7. Giannattasio C et al. Combined effects of hypertension and hypercholesterolemia on radial artery function. Hypertension 1997; 29: 583-586.

ABBREVIATIONS

AIx - augmentation index
Amlo – amlodipine
BP – blood pressure
CV - cardiovascular
DBP – diastolic BP
HTN – essential hypertensiom
Lis – Lisinopril
NO- nitric oxide
PWVcf - carotid-femoral pulse wave velocity
PWVcr - carotid-radial pulse wave velocity
Rosuva - rosuvastatin
SBP – systolic BP