Pleiotropic and Lipid-lowering Effects of Statins in Hypertension

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SUMMARY

Background. Data on the lowering effects of statins in hypertensive patients have been mixed and highly controversial. Some studies show reductions effects of statins in blood pressure, whereas others do not. The evidence in the literature on the effects of statins on blood pressure raises the possibility that statins may directly lower blood pressure in addition to reduce cholesterol levels—pleiotropic effects of statins.

Aim of the study. The role of statins as additional treatment in patients with severe hypertension and advanced aortic atherosclerotic plaques.

Methods. We enrolled 62 patients. Study has been approved by Committee of Ethics and patients signed a Term of Free Informed Consent. All patients were studied with transoesophageal echocardiography at baseline and 12 months after enrolment. Inclusion criteria were severe hypertension and presence of aortic atherosclerotic plaques. Patients have been divided into two groups; group A (treated with antihypertensives and statins) and group B (treated, just with antihypertensives).

Results. Twenty patients, of totally 38, from group A (20/38 or 52.6%) had significantly plaque reduction. One patient of totally 24 (1/24 or 4.1%) from group B had significantly atherosclerotic plaque reduction. Difference of plaques reduction between two groups was highly significant. Regarding blood pressure levels, statins users had significantly reduction on systolic and diastolic blood pressure compared to statins nonusers.

Conclusion. Hypertensive patients with presence of AA plaques treated with antihypertensives and statins have more BP reduction compared with hypertensive patients treated with antihypertensives alone.

Key words: statins, hypertension, atherosclerotic aortic plaque, pleiotropic effects of statin.
vascular production of reactive oxygen species (13, 14, 15, 16). Statins, finally, improve arterial compliance (2, 17). Of 96 patients with severe longstanding hypertension (investigated by transoesophageal echocardiography (TEE)), atherosclerotic plaques in thoracic aorta (AA plaques), grade 2 and/or grade 3 have been reported in 82.3% of cases (18). Previous studies have reported the role of lipid-lowering agents in the treatment of AA in patients with hyperlipidaemia and their effect on plaque regression (19). One study suggests that statins reduce the risk of AA progression and increase plaque thickness reduction (20).

2. METHODS

All of the 62 patients, enrolled in the study, approved by Committee of Ethics, signed a Term of Free Informed Consent. Inclusion criteria were severe hypertension (stage 2 by JNC 7) (21) not treated (different reasons) for at least 1 year and presence of aortic (thoracic part) atherosclerotic (AA) plaques. Patients have been divided into two groups; group A and group B. Group A, 38 patients, has been treated with the same antihypertensive medication including ACE-inhibitors (lisinopril 20 mg), diuretics (HCTZ 25 mg), beta-blockers (bisoprolol 5 mg) and statins (atorvastatin 20 mg); whereas, 24 patients of group B, has been treated with the same antihypertensive drugs but without statins. All of the patients selected to be with normal value of glicemia and lipid profile. A complete medical history, physical examination, clinical evaluation (heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, pulse pressure and electrocardiography (ECG) were recorded), transthoracic echocardiography (TTE) and TEE were used by expert cardiologists for clinical evaluation. The procedure that we used for performing TEE in our laboratory has been reported (18). Patients were studied with TEE at baseline and 12 months after enrolment in the study. Data from multiplanar views of the thoracic aorta were obtained in detail. Exactly same images of the position and extension of the plaques were used at follow-up for every patient measuring their distance (in millimeters) from the incisors, and dividing the short-axis plane of the aorta into four perpendicular clockwise sectors. Aorta has been divided as ascending aorta, and descending aorta using orientation landmark, right pulmonary artery and the left subclavian artery respectively. Aortic plaque progression was defined as an increase in maximal plaque thickness by ≥1 mm or regression was defined as a decrease in maximal thickness of atheromatous plaque by ≤1mm. Atherosclerotic plaques were defined as moderate (those with a thickness between 1 and 3.9 mm) and severe aortic plaques (those with a thickness ≥4 mm) (22). All examinations were recorded, reviewed and measured by two independent senior cardiologists blinded to each other. BP was measured and recorded three to four times at home following the recommendations of the American Heart Association (23). The results were analyzed by a standard method of descriptive statistics using Pivot Table of Excel Office 2007 and Simple Interactive Statistical Analysis (SISA).

3. RESULTS

Table 1. Detailes about values and statistical findings. * reduction; ** nonreduction; $ progression; & systolic blood pressure; ¥ diastolic blood pressure; E ambulatory blood pressure measurement.
One patient of totally 24 (1/24 or 4.1%) from group B had significantly atherosclerotic plaque reduction—subset group rB; one patient had atherosclerotic plaque progression—pr.

Difference of plaques reduction between two groups was highly significant (diagram 1). Regarding BP levels, statins users had significantly reduction on systolic BP compared to statins nonusers.

Systolic BP (SBP) was lowest in subgroup rA, followed by SBP of nrA and than nrB. Diastolic BP (DBP) was lowest in subgroup rA, followed by DBP of nrA and than nrB.

4. DISCUSSION

The role of statins in reduction of AA plaques have been reported (23, 24). We found (in TEE of control) that hypertensive patients treated with anti-HTA and statins (group A) showed significantly more AA plaques reduction 20/38 or 52.6%, compared to hypertensive statins (group A) showed significantly more AA plaques reduction 20/38 or 52.6%, compared to hypertensive patients treated with anti-HTA but without statins 1/24 or 4.1%. AA plaque reduction of group A of 52.6% was not treated for long time).

Our results support the finding that systolic and diastolic BP (6). The results of our study group of patients, followed for 12 months, show that all patients (group A and group B) had significantly BP reduction. The highest decrease of high blood pressure was achieved in patients of group A with AA plaque reduction (rA); systolic/diastolic BP was 138.2 ± 3.21 / 89.17±3.20, respectively, followed by patients of the same group but without AA plaque reduction (nrA); systolic/diastolic BP was 140.1 ± 3.38 / 90.95±2.94, respectively, and finally significantly reductions of BP but not as in group A (two subgroups of group A) had patients of group B without AA plaque reduction (nrB); systolic/diastolic BP was 143.39 ± 2.12 / 93.28±3.32, respectively. Reduction of BP (systolic and diastolic) was more significantly lower in patients of group A subgroup rA as compared to patients with no AA plaque reduction rB vs. nrB. Systolic, but not diastolic; BP reduction was also significantly lower in group A with no AA reduction compared to group B with no AA plaque reduction nrA vs. nrB.

But, reduction of BP was always much more in group A with antihypertensive and statin, than in group B with antihypertensive without statins. BP reduction was more in group A with AA reduction subgroup rA than in group A without AA plaque reduction subgroup nrA; both subgroups were treated with antihypertensives and statins but, BP reduction was more in group with AA plaques reduction; we suppose that this is because of pleiotropic effects of statins (13, 14, 15, 16) and their effect in improvement of arterial compliance (2, 17).

5. CONCLUSION

Hypertensive patients with presence of AA plaques treated with antihypertensins and statins have more BP reduction compared with hypertensive patients treated with antihypertensins alone. Atherosclerotic plaque reduction, as a result of statins treatment, has much more reduction effect on lowering of BP (addition to antihypertensins) than if reduction of atherosclerotic plaques was not achieved despite treatment with statins (addition to antihypertensins).

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