Combination Treatment to Prevent Atherosclerosis

To the Editor:

Strazzullo et al\(^1\) demonstrated that systolic blood pressure (SBP) was significantly lower in patients on statins than in those on placebo or control hypolipidemic drug (mean difference: −1.9 mm Hg; 95% CI: −3.8 to −0.1 mm Hg). The effect was greater when the analysis was restricted to studies with a baseline SBP >130 mm Hg (ΔSBP: −4.0 mm Hg; 95% CI: −5.8 to −2.2 mm Hg). There was a trend for lower diastolic blood pressure (DBP) in patients receiving statin therapy compared with control at −0.9 mm Hg (95% CI: −2.0 to 0.2 mm Hg) overall and −1.2 mm Hg (95% CI: −2.6 to 0.1 mm Hg) in studies with a baseline DBP >80 mm Hg. In general, the higher the baseline blood pressure, the greater the effect of statins on blood pressure (\(P=0.066\) for SBP and \(P=0.023\) for DBP).

Even this well-performed meta-analysis study demonstrated significant heterogeneity between studies (both \(P<0.01\) for SBP and DBP) because they were carried out in a variety of settings with different methods, particularly blood pressure measurement, small or very small sample size, effects of concomitant antihypertensive therapy, and using various criteria and different comparative groups. These factors can greatly affect the interpretation of the results. In addition, this kind of meta-analysis has some flaws, because it assembles data from secondary sources (published articles) rather than the primary data set. For example, this meta-analysis study quoted our article.\(^2\) It reported that simvastatin increased SBP by 5 mm Hg and DBP by 4 mm Hg. But in fact, simvastatin decreased SBP by 3 mm Hg (\(P=0.058\)) and DBP by 3 mm Hg (\(P=0.052\)). The baseline SBP and DBP were 145 and 90 mm Hg, and in a different study of ours in patients with type 2 diabetes,\(^3\) simvastatin increased SBP by 1 mm Hg (\(P=0.659\)) and DBP by 0 mm Hg (\(P=0.827\)). The baseline SBP and DBP were 134 and 80 mm Hg. Thus, the use of statins may significantly improve blood pressure control in subjects with both hypercholesterolemia and uncontrolled hypertension.

Hypercholesterolemia and hypertension are both associated with endothelial dysfunction, and their coexistence is associated with an increased incidence of cardiac events in epidemiological studies. In pigs with both hypercholesterolemia and hypertension, the vasodilator response of coronary arteries to bradykinin and calcium ionophores was significantly impaired, and increased oxidative stress was observed when compared with only hypercholesterolemia or hypertension alone. These results suggest that hypercholesterolemia and hypertension have synergistic deleterious effects on coronary endothelial function that are associated with increased oxidative stress.\(^4\) In clinical studies, combined therapy significantly reduced plasma malondialdehyde, monocyte chemotactrant protein-1, and C-reactive protein levels more than monotherapy.\(^2,3\) The additive beneficial effects of combined therapy are consistent with previous experimental\(^6\) and clinical studies.\(^7\) Thus, there is a scientific rationale for recommending a combination of statins and angiotensin-converting enzyme inhibitors or angiotensin II type-1 receptor blockers to prevent atherosclerosis and coronary heart disease even in patients with controlled hypertension.\(^8\)

Disclosures

None.

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