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Response to letter by Hadjiev et al

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Letters to the Editor

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We thank Hadjiev and colleagues for their interest in our article.

They seem to suggest that adverse effects are more common with rosuvastatin than with other statins. We think the adverse effects they mention are class effects and that differences among statins are related to potency of statins. Indeed, this was the conclusion of a recent meta-analysis of head-to-head trials of atorvastatin and rosuvastatin.[1] We do not have complete data on adverse effects of statins in our study population but estimate that approximately 10% of our patients have myalgias or myopathy with statins. This adverse effect is probably due to depletion of intramuscular ubiquinone (coenzyme Q10) by statins in people predisposed to myopathy because of an inherited disorder of mitochondrial function[2,3]; myalgias may improve with coenzyme Q10 supplementation.[3,4] Similarly, the increase in incident diabetes with statins was shown in the meta-analysis to which they refer[5] to apply to all statins with little heterogeneity among statins. The apparent excess with rosuvastatin to which Hadjiev et al refers may have been due to the larger sample size of the Jupiter study, which at 17 802 was the biggest of the studies included in that meta-analysis, but the relative potency of statins may also be the key issue here. Thus, the use of statins involves a tradeoff between benefits and adverse effects.

With regard to the question of intracerebral hemorrhage from statins, it should be said that this is probably a myth. In a meta-analysis of 90 056 patients on statins,[6] there was no increased risk of intracerebral hemorrhage with statins. The excess risk reported in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial[7] to which they refer was probably not causally related to statin use, because there was no association of intracerebral hemorrhage with lower low-density lipoprotein. Because the control group was a placebo, the low-density lipoprotein should have been lower on 80 mg atorvastatin had the patients been taking it. This means that patients who had intracerebral hemorrhage were noncompliant with their statin therapy; the most likely explanation for the intracerebral hemorrhages was that they were also noncompliant with their antihypertensive therapy.

With regard to calcium channel antagonists, there was no significant difference between the two eras in the proportion of patients taking these drugs at baseline (8.2% before versus 8.8% since 2003; $P=0.31$). We suspect that addition of ezetimibe, particularly in patients with plaque progression who were intolerant of high-dose statin, may account for some of our findings (unpublished data; ezetimibe became available in Canada in June 2003).

The reasons for plaque progression despite good control of traditional risk factors probably include as yet unknown factors that are mainly genetic. Plaque measurement can be used to quantify the extent to which patients have plaque that is not explained by traditional risk factors. That approach can markedly increase statistical power for genomewide association studies[8] and lead to new therapeutic targets and new therapies for atherosclerosis. However, until then, all that is available is more intensive application of therapies now in existence: if all one has is a hammer, everything is a nail (in this case, low-density lipoprotein).

Patients with plaque progression despite already low levels of low-density lipoprotein and control of traditional risk factors such as smoking and blood pressure can only be identified by measuring the burden of atherosclerosis. Treating atherosclerosis without measuring plaque burden would be like treating hypertension without measuring blood pressure.

Disclosures

None.

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