Statins: the high risks of discontinuation and large benefits of continuation

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In their mini-review/short communication in this issue of the Archives of Medical Science, Dr. Paraskevas et al. [1] draw proper attention to the consequences of statin discontinuation. They focus primarily on the cerebrovascular disease but their conclusion that absolute benefits of discontinuation are small and the absolute risks are high is consistent with a large and robust totality of evidence.

The Cholesterol Treatment Trialist’s Collaboration [2, 3] published two worldwide and comprehensive meta-analyses of randomized data. The first, among about 90,000 participants in 14 randomized trials, showed that statin therapy produced statistically significant and clinically important reductions in myocardial infarction, stroke, cardiovascular death and total mortality and a remarkable safety profile. The second, among 170,000 participants in 26 randomized trials, showed that further reductions by statins in low density lipoprotein (LDL) cholesterol safely produce definite further reductions in the incidence of myocardial infarction, stroke and revascularization. Specifically, each 1.0 mmol/l reduction in LDL cholesterol produces a statistically significant and clinically important reduction in the annual rate of these major vascular events by just over 20%. There was no evidence of any threshold within the cholesterol range studied, suggesting that reduction of LDL cholesterol by 2-3 mmol/l would reduce risk by about 40-50%. Thus, the recent randomized trials of statins using higher doses against lower doses as the active comparator arm have contributed importantly relevant information to two long standing hypotheses [4]. The first is that lower is better and the prior totality of evidence included basic research and observational epidemiological studies, including in rural China where the average total cholesterol is less than 3.7 mmol/l and those with total cholesterol levels that are 10% lower had significantly decreased risks of occlusive vascular events [5]. The second is that there is no threshold and the meta analysis of the data from randomized trials with active comparators in secondary prevention contribute importantly relevant data to this hypothesis. In terms of primary prevention the JUPITER trial also contributes the most importantly relevant data as the randomized population had no prior events and a 10 year risk of a first CHD event of 16-18% [6]. Further, at baseline the LDL was about 3.0 and subjects assigned to 20 mg rosuvastatin achieved a greater than
50% reduction in LDL to about 1.4. The trial was terminated early after a median treatment and follow up of about 1.9 years due to a 44% statistically significant reduction in the primary composite endpoint. In JUPITER there were also statistically significant reductions in MI, stroke, and revascularizations and this was the first primary prevention trial to demonstrate a statistically significant and clinically important reduction in total all cause mortality. It seems most plausible that the large reductions in LDL to levels far below those that had ever been studied in primary prevention were critical components of the favorable outcomes.

In conclusion, in this issue of the *Archives of Medical Science*, Dr. Paraskevas et al. contribute an added dimension to the risks of discontinuation of statins. The risks are high of statin discontinuation so any decision to do so should be made by the individual health care provider and each of his or her patients. The general goal should be to avoid discontinuation of statins whenever possible.

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