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LETTER TO THE EDITOR

Fluvastatin/fenofibrate vs. simvastatin/ezetimibe in patients with metabolic syndrome: different effects on LDL-profiles

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In a recent article in this journal, Winkler *et al.* [1] report on a study comparing the different effects of fluvastatin/fenofibrate (F/F) (80/200 mg) and simvastatin/ezetimibe (S/E) (10/10 mg) on plasma lipids in patients with the metabolic syndrome, including 27% of patients with type 2 diabetes mellitus. In their final conclusion, the authors state that the combination of fluvastatin and fenofibrate appears to be better suited to address the characteristic dyslipidaemia in the metabolic syndrome. This conclusion is based on the more pronounced effect of F/F on triglycerides in the subgroup of patients with higher levels of small dense LDL (sdLDL) >250 mg L^{-1} and the smaller LDL radius in the F/F group. However, S/E in this study was more effective than F/F treatment in lowering LDL-C and ApoB-100. This difference was more pronounced in patients with elevated sdLDL (0·4 mmol L^{-1} difference), which was the majority (68%) of the study population. Both treatments were equally effective in lowering sdLDL irrespective of sdLDL baseline levels.

In their discussion, the authors state that F/F treatment is superior to S/E treatment in patients with metabolic syndrome. We firmly disagree with this statement, which is not supported by the data presented in this or other studies.

Lowering of plasma LDL-C concentrations is the primary target for lipid treatment, also in patients with elevated sdLDL [2]. In the TNT trial, lowering LDL to 1·9 mmol L^{-1} with a statin in patients with coronary artery disease and metabolic syndrome was associated with a HR 0·71 (95% CI 0·61–0·84) for major cardiovascular events at 5 years compared with LDL-C lowering to 2·6 mmol L^{-1} [3]. As shown in the CARDS study, in patients with type 2 diabetes mellitus, statin treatment lowers LDL-C, ApoB, triglycerides and increases HDL-C, and is associated with a lower incidence of cardiovascular disease during 4 years follow-up [4]. These beneficial effects on cardiovascular morbidity and mortality are mainly a result of effective LDL-C lowering.

The authors are correct in stating that currently there is no trial available showing the effect of a combination of simvastatin and ezetimibe on cardiovascular outcome or mortality. However, there is also no study published on the effect of F/F on cardiovascular outcome. Treatment with a fibrate, whether or not in combination with a statin, in patients with type 2 diabetes is proven not to be effective in reducing cardiovascular events [5].

In the light of the overwhelming evidence for LDL-C lowering on cardiovascular disease prevention, it seems prudent to focus on treatment strategies that are highly efficacious in lowering LDL-C in patients at elevated risk for cardiovascular events. Many patients with metabolic syndrome have an increased risk for cardiovascular diseases and deserve optimal lipid-lowering therapy.

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