



LETTER TO THE EDITOR

Benefits of LDL cholesterol reduction in the secondary prevention of ischemic stroke New evidence[☆]**Beneficios de la reducción del colesterol LDL en la prevención secundaria del ictus isquémico. Nuevas evidencias**

We read with interest the excellent manuscript published in your journal by Climent et al.¹ on lipid-lowering therapy in the secondary prevention of ischaemic cerebrovascular disease.

This review addresses the relationship between hypercholesterolaemia, cerebrovascular disease and mortality, as well as the effect of lipid-lowering treatment on reducing the risk of cerebrovascular disease. The authors conducted a review of statin intervention studies, most notably Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL),² which was the first clinical trial designed to confirm the benefits of statin therapy in the secondary prevention of stroke. A post hoc analysis of this study showed that patients with LDL cholesterol (LDL-C) <70 mg/dL had a 28% lower relative risk of stroke than patients with LDL-C levels above 100 mg/dL.³ They also reviewed subsequent clinical trials with combined therapy⁴ and the evidence of the beneficial effects of treatment with the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors in cardiovascular prevention.^{5–7}

Following the online publication of this review, new evidence has emerged that highlights the importance of LDL-C reduction in the secondary prevention of stroke. First, a new post hoc analysis of the SPARCL⁷ study showed that the number of reduced successive events in the atorvastatin-treated group was more than double the observed reduction in first events (164 and 390 events respectively, HR: .68, 95% CI .60–.77. About 20 events per 100 participants were avoided during the six years of follow-up. This reinforces the idea that the lower the LDL-C the better.^{8,9} Secondly, the results of the Treat Stroke to Target Trial have just been

published.^{10,11} In this clinical trial, conducted in France and South Korea, 2860 patients with ischaemic stroke in the previous three months or transient ischaemic attack (TIA) in the previous 15 days were included and randomly assigned to two different therapeutic objectives: in one arm the therapeutic objective was to achieve a reduction in LDL-C to below 70 mg/dL, and in the other to a therapeutic range of 90–110 mg/dL. All patients received either statin, ezetimibe or both. The average follow-up was 3.5 years, and the study was discontinued prematurely for administrative reasons (lack of funding). The mean LDL-C levels in both groups at the end of follow-up were 65 mg/dL and 96 mg/dL, respectively. The primary composite objective (major cardiovascular events, including ischaemic stroke, myocardial infarction, new symptoms requiring urgent coronary or carotid revascularization and vascular mortality from any cause), was observed in 121 patients (8.5%) in the group with lower LDL-C, and in 156 (10.9%) in the group with higher LDL-C: adjusted HR .78 (95% CI .61–.98), $p = .04$. It is important to note that the incidence of intracranial haemorrhage and newly diagnosed diabetes was not different between the two groups. The authors conclude that a reduction in LDL-C of less than 70 mg/dL over 5.3 years prevents one vascular event in four with an NNT of 30, and without an increased risk of intracranial haemorrhage. This last aspect has been a concern when intensifying lipid-lowering treatment in stroke subjects, although in previous studies no relationship has been observed between the level of LDL-C achieved with treatment and this complication.

The study provides relevant information for clinical practice, and confirms that we can and should reduce LDL-C in non-cardioembolic ischaemic stroke below 70 mg/dL, without fear of inducing haemorrhagic stroke. Whether further decreases in LDL-C translate into greater clinical benefit, as in heart disease, is yet to be resolved.^{5,6}

Conflict of interests

The authors have no conflict of interests to declare.

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