Cardio DIGEST
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Editorial

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HDL-C rise: The effect on cardiovascular events

The use of statin therapy to modify lipid levels is now well established in terms of its effect on reducing cardiovascular (CV) risk, particularly in people with a high baseline risk of cardiovascular disease (CVD). Dyslipidaemia management in such individuals has predominantly focused on reducing low-density lipoprotein cholesterol (LDL-C) levels.

Outcomes from large-scale trials of statin therapy in various patient groups have revealed a relative reduction in the risk of CVD ranging from 16–37% (Hee et al, 2012)– consequently, a significant residual risk of CVD remains. A proposed explanation for this residual risk is the presence of low HDL-C and elevated triglyceride levels in people with atherogenic dyslipidaemia – the latter have also been recognised in epidemiological studies as an independent risk factor for CV mortality and morbidity.

"Following statin therapy, further reduction of cardiovascular disease risk in people whose low-density lipoprotein cholesterol is at the recommended targets may be achieved by raising high-density lipoprotein cholesterol and/or lowering triglycerides."

Data from epidemiological analyses have suggested that there is an inverse relationship between high-density lipoprotein cholesterol (HDL-C) levels and CVD risk – this was also reported in statin trials in individuals when target LDL-C was reached (Emerging Risk Factors Collaboration, 2009). Consequently, it has been proposed that, following statin therapy, further reduction of CVD risk in people whose LDL-C is at the recommended targets may be achieved by raising HDL-C and/or lowering triglycerides. Not only has this hypothesis not been examined in large-scale trials, but smaller studies have also failed to demonstrate a significant impact of HDL-C rise on the occurrence of CV events.

In the ACCORD (Action to Control Cardiovascular Risk in Diabetes) lipid study, adding fenofibrate to simvastatin yielded no significant effect on CVD risk in people with T2D, although some positive features were noted in those who had atherogenic dyslipidaemia (ACCORD Study Group, 2010). In the FIELD (Fenofibrate Intervention and Event Lowering in Diabetes) study, treatment with fenofibrate compared with placebo resulted in a non-significant 11% relative risk reduction in primary CV outcomes, including major coronary events, death and non-fatal myocardial infarction. A pre-specified sub-group analysis revealed a significant reduction in the composite of total CV events (coronary events, stroke, coronary and carotid revascularisation; 11%, $P=0.035$) (Sacks, 2008). More recent analyses of the FIELD study outcome data did not support treatment with fenofibrate differently based on the presence or absence of prior CV events (Tonkin et al, 2012). Other epidemiological data from recent studies do not provide evidence in support of a significant benefit of increasing HDL-C independent of the effect on lowering LDL-C, when corrected for traditional CV risk factors.

In conclusion, current evidence suggests that, except for specific individual patients –particularly those with an atherogenic lipid profile – additional therapy in an attempt to increase HDL-C should not be routine. Current ongoing trials of other newer therapies that target HDL-C may provide us with further important evidence.

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