Obesity and dietary fat modulate HDL function in adolescents: results from a cross-sectional analysis and a randomized, placebo-controlled, crossover trial

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The athero-protective potential of high-density lipoprotein (HDL) is partially attributable to its role as a cholesterol acceptor in reverse cholesterol transport (RCT). RCT removes excess cholesterol from lipid-laden arterial macrophages and delivers it to the liver for excretion. The influence of obesity and dietary fat on the capacity of HDL to facilitate cholesterol efflux has not yet been described in an adolescent cohort.

Cholesterol efflux from macrophages was determined as a metric of HDL function in a cross-sectional cohort of lean, overweight and obese adolescents (n=82). Cholesterol efflux was assessed by incubating plasma HDL with 3H-cholesterol labelled J774 macrophages for 4h, from which ABCA1-dependent and ABCA1-independent efflux capacities were quantified. The effects of LC n-3 polyunsaturated fatty acid (PUFA)-rich supplementation and a monounsaturated fatty acid (MUFA)-rich control supplement on efflux capacity were examined after an 8-wk randomized controlled crossover trial in overweight and obese adolescents (n=52). Cholesteryl ester fatty acid composition was assessed as a biomarker of dietary fat intake.

Cross-sectional analysis demonstrated a stepwise decrease in total cholesterol efflux with increasing weight status, attributable in part to reduced HDL cholesterol concentration. While HDL cholesterol concentration was a significant determinant of ABCA1-dependent efflux in lean adolescents, this relationship was attenuated in overweight and obesity, indicative of reduced HDL function and quantity. Relative to lean adolescents, ABCA1-dependent efflux was impaired in overweight and obese adolescents with low cholesteryl ester n-3 PUFA status. However, overweight and obese adolescents with high cholesteryl ester n-3 PUFA content demonstrated preserved HDL function, despite reduced HDL cholesterol concentration. Both LC n-3 PUFA-rich and MUFA-rich supplementation enhanced ABCA1-dependent efflux in overweight and obese adolescents with impaired HDL function at baseline, independently of changes in HDL cholesterol or apolipoprotein A1 concentrations.

We report for the first time, impaired cholesterol efflux capacity in overweight and obese adolescents, attributable in part to reduced HDL cholesterol concentration. However, both LC n-3 PUFA-rich and iso-energetic MUFA-rich supplementation partially rescued HDL function despite obesity. These novel findings illustrate the potential to attenuate cardiovascular disease risk in overweight and obese adolescents through dietary fat modification.

This trial was registered at clinicaltrials.gov as NCT01665742.

Funding: This research was funded by The National Children’s Research Centre, Ireland. HMR & FCM are supported by Science Foundation Ireland Principal Investigator Programme (11/PI/1119) and Wellcome Trust Career Development Fellowship (097311/Z/11/1). Intervention products were provided by Smartfish, Oslo, Norway and Best Formulations, CA.