

# Abstract

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## Factorial study of the effect of n-3 fatty acid supplementation and atorvastatin on the kinetics of HDL apolipoproteins A-I and A-II in men with abdominal obesity.

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**BACKGROUND:** Disturbed HDL metabolism in insulin-resistant, obese subjects may account for an increased risk of cardiovascular disease. Fish oils and atorvastatin increase plasma HDL cholesterol, but the underlying mechanisms responsible for this change are not fully understood.

**OBJECTIVE:** We studied the independent and combined effects of fish oils and atorvastatin on the metabolism of HDL apolipoprotein A-I (apo A-I) and HDL apo A-II in obese men.

**DESIGN:** We conducted a 6-wk randomized, placebo-controlled, 2 x 2 factorial intervention study of the effects of fish oils (4 g/d) and atorvastatin (40 mg/d) on the kinetics of HDL apo A-I and HDL apo A-II in 48 obese men with dyslipidemia with intravenous administration of [d3]-leucine. Isotopic enrichments of apo A-I and apo A-II were measured with gas chromatography-mass spectrometry with kinetic parameters derived from a multicompartmental model (SAAM II).

**RESULTS:** Fish oils and atorvastatin significantly decreased plasma triacylglycerols and increased HDL cholesterol and HDL2 cholesterol ( $P < 0.05$  for main effects). A significant ( $P < 0.02$ ) main effect of fish oils was observed in decreasing the fractional catabolic rate of HDL apo A-I and HDL apo A-II. This was coupled with a significant decrease in the corresponding production rates, accounting for a lack of treatment effect on plasma concentrations of apo A-I and apo A-II. Atorvastatin did not significantly alter the concentrations or kinetic parameters of HDL apo A-I and HDL apo A-II. None of the treatments altered insulin resistance.

**CONCLUSIONS:** Fish oils, but not atorvastatin, influence HDL metabolism chiefly by decreasing both the catabolism and production of HDL apo A-I and HDL apo A-II in insulin-resistant obese men. Addition of atorvastatin to treatment with fish oils had no additional effect on HDL kinetics compared with fish oils alone.

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