Abstract


Oxidized type IV hypertriglyceridemic VLDL-remnants cause greater macrophage cholesteryl ester accumulation than oxidized LDL.

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OBJECTIVE: We have previously shown that very low density lipoproteins (VLDL, Sf 60-400) from subjects with type IV hyperlipoproteinemia (HTG-VLDL) will induce appreciable cholesteryl ester accumulation in cultured macrophages (J774A.1). The present study examined whether copper-mediated oxidative modification of HTG-VLDL and their remnants would further enhance cholesteryl ester accumulation in J774A.1 cells.

METHODS AND RESULTS: Incubation with oxidized VLDL-remnants caused the greatest increase in cellular cholesteryl ester concentrations (54-fold) relative to control cells (P = 0.001). HTG-VLDL and VLDL-remnants each induced similar increases in cholesteryl ester levels (32.3- and 35.8-fold, respectively; both P = 0.001), whereas incubation with oxidized HTG-VLDL brought about only a 20.6-fold increase in cholesteryl ester concentrations (P = 0.014). The increase in cellular cholesteryl ester concentrations induced by oxidized VLDL-remnants was significantly higher (P < or = 0.04) than that induced by all other lipoproteins tested including low density lipoprotein (LDL) and oxidized LDL which caused a 6.7- and a 35.1-fold increase (P < or = 0.0002 for both), respectively. Unlike HTG-VLDL and to a lesser extent VLDL-remnants, uptake of oxidized VLDL and oxidized VLDL-remnants did not require catalytically active, cell secreted lipoprotein lipase. Co-incubation with polyinosine, which blocks binding to the type I scavenger receptor, completely inhibited the cholesteryl ester accumulation induced by oxidized HTG-VLDL, oxidized VLDL-remnants and oxidized LDL (P < or = 0.02).

CONCLUSION: We conclude that oxidation of VLDL-remnants significantly enhances macrophage cholesteryl ester accumulation compared to either HTG-VLDL, VLDL-remnants, or oxidized LDL. Uptake of oxidized VLDL and oxidized VLDL-remnants does not require catalytically active lipoprotein lipase, and involves a receptor that can be competed for by polyinosine.

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