Increased Cholesteryl Ester Transfer Protein Activity in Impaired Glucose Tolerance: Relationship to High Density Lipoprotein Metabolism

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Aim. To investigate the mechanisms and dynamics of cholesteryl ester (neutral lipid) transfer protein activity in subjects with impaired glucose tolerance.
Methods. Eighty six Caucasian subjects were recruited by advertisement from the local population between January 1998 and December 1999. The activity of cholesteryl ester transfer protein in 44 non-obese subjects with impaired glucose tolerance (plasma triglycerides 1.56±0.64 mmol/L; high density lipoprotein (HDL) cholesterol 0.96±0.25 mmol/L; and plasma insulin 78±8 pmol/L) and in 42 normoglycemic controls (plasma triglycerides 0.88±0.41 mmol/L; HDL cholesterol 1.48±0.29 mmol/L; and plasma insulin 38±14 pmol/L) was measured with a new fluorometric assay.
Results. Cholesteryl ester transfer protein activity was increased in subjects with impaired glucose tolerance by 47% (39.5±7.8 vs 26.8±6.8 nmol/mL × h-1; t-test, $p<0.05$). Linear regression analysis showed that cholesteryl ester transfer protein activity in subjects with impaired glucose tolerance significantly correlated with the following parameters: plasma triglycerides ($r=0.614$, $p<0.05$), HDL-triglycerides ($r=0.595$, $p<0.05$), percentage of HDL-triglyceride ($r=0.667$, $p<0.05$), percentage of HDL cholesterol ester ($r=-0.751$, $p<0.01$), percentage of HDL phospholipid ($r=0.648$, $p<0.05$), 2-h-insulin ($r=0.668$, $p<0.05$), and 2-h-proinsulin ($r=0.658$, $p<0.01$). In a subgroup of 13 subjects with impaired glucose tolerance, cholesteryl ester transfer protein activity correlated with HDL apoA-I fractional catabolic rate ($r=0.701$, $p<0.01$). In normoglycemic subjects, significant correlations were found only between cholesteryl ester transfer protein activity and percentage of HDL-triglycerides ($r=0.541$, $p<0.05$), percentage of HDL cholesteryl ester ($r=-0.639$, $p<0.01$), 2-h-proinsulin ($r=0.642$, $p<0.05$), and HDL apoA-I fractional catabolic rate ($n=10$, $r=0.587$, $p<0.05$).
Conclusion. Cholesteryl ester transfer is important for HDL composition and HDL catabolism both in normoglycemic subjects and subjects with impaired glucose tolerance. Under insulin resistant conditions, increased cholesteryl ester transfer protein activity modulates HDL metabolism more drastically than in normoglycemic conditions. This modulation may be explained by increased availability of triglyceride-rich lipoproteins for neutral lipid exchange in subjects with impaired glucose tolerance.

Key words: apolipoproteins; carrier proteins; glucose intolerance; hyperlipidemia; insulin resistance; lipoproteins, HDL; metabolism