CORRESPONDENCE

Predictors of Change in Low-Density Lipoprotein Size During Lipid-Lowering Treatment in Type 2 Diabetes

FIBRATES (alone or combined with statins) have proved to be effective in increasing low-density lipoprotein (LDL) size in type 2 diabetes.[1] Because the methods used for its measurement are time-consuming and require specialized personnel, we aimed to find predictors of change in LDL size that could easily be measured during treatment with fibrates.

Forty-three type 2 diabetic patients (70.5% male; age, 57.4 ± 8.8 years; hemoglobin A_{1c} [HbA_{1c}], 6.9% ± 0.6%) were given 12 weeks of atorvastatin (mean dose, 14.5 mg/d) and gemfibrozil (1,161 mg/d) in a randomized, cross-over study, and thereafter, combined treatment. Triglyceride, total cholesterol (c) (enzymatic methods), LDLc (Friedewald/ultracentrifugation), high-density lipoprotein (HDL)c (direct method), non-HDLc, apolipoprotein B (apoB) (immunoturbidimetry), and LDL size (gradient polyacrylamide gel electrophoresis) were measured/calculated at baseline and after each treatment, as previously described.[1] Bivariate correlations and multivariate analysis were performed to find predictors of change in LDL size during treatment with the fibrate (alone or with the statin).

During fibrate treatment, bivariate analysis showed changes in HDLc ($r = 0.543$, $P < .0005$), LDLc/apoB ($r = 0.416$, $P = .006$), triglyceride ($R = -0.444$, $P = .003$), and very-low-density lipoprotein (VLDL)c ($R = -0.398$, $P = 0.008$) to be predictors of LDL size increment. In multivariate analysis, however, only the increment in HDLc remained predictive. No significant predictors were found during combined treatment. When both treatments were analyzed together, both bivariate and multivariate analysis showed that only the change in HDLc ($r = 0.344$, $P = .001$) predicted change in LDL size.

Women showed good correlation between change in LDL size and change in triglyceride ($R = -0.508$, $P = .011$), HDLc ($r = 0.421$, $P = .04$), and LDLc/apoB ($r = 0.450$, $P = .027$) in bivariate analysis, but only with the latter in multivariate analysis. Men showed correlation between change in LDL size and HDLc increment only ($r = 0.358$, $P = .005$), both in bivariate and multivariate analysis.

Because the components of diabetic dyslipidemia are metabolically intertwined and have a high statistical colinearity, it is difficult to decide which of them best represents the change in LDL size. Although triglyceride concentration plays a decisive role in the modification of LDL phenotype, its biologic variability limits its value as a predictor.[2] HDLc has been related to triglyceride in a comparable fashion as HbA_{1c} is related to glucose, and it has a lower variability, as is the case for LDLc/apoB ratio, a previously known marker of LDL size.[2-4] The lack of predictive factors during combined therapy may be due to the different effect both drugs have on diabetic dyslipidemia, both increasing HDLc but only fibrates modifying LDL size.[1]

In conclusion, during treatment with fibrates, HDLc increment seems to be the most robust predictor of change in LDL size, although it only explains about one third of the variability of this change.

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