COMMENTS AND RESPONSES

Comment on: Gaillard et al. HDL Dysfunctionality (Paraoxonase) Is Worse in Nondiabetic, Postmenopausal African American Than in White Women. Diabetes Care 2011;34:e19

We read with interest the recent study by Gaillard et al. (1) focused on relationships between paraoxonase (PON1) activity and oxidized LDL and cardiovascular disease (CVD) risk factors in nondiabetic, postmenopausal women. Higher CVD mortality and morbidity in the presence of higher HDL cholesterol is a frequent occurrence in African American women compared with white women. The authors reported the ethnic HDL–related dysfunction (as measured by PON1) in nondiabetic women. They concluded that this paradox may be caused by enhanced LDL oxidation associated with HDL dysfunctionality (lower activity of PON1) in a group of African American women.

PON1 is a structural enzyme of HDL that binds to apolipoprotein (apo) A1 (apoA1) and is able to protect LDL from oxidative modification by hydrolyzing lipid peroxides. The protective role of PON1 against oxidation of LDL as well as HDL has been supported by several observations (2,3). Oxidative modification of lipoproteins is associated with initiation and progression of atherosclerosis. Activity of HDL-associated PON1 may be a major contributor to the antiatherogenicity of HDL. Therefore, altered activity of PON1 may predict vascular disease status in humans (4).

In our pilot study, we investigated relationships between PON1 activity and lipid risk markers in 75 nondiabetic subjects (mean age 42.6 ± 7 years) who had no history of CVD and were not taking antihypertensive or antihyperlipidemic medication. The participants (white population) were divided into 4 subgroups (on the basis of lipid parameter levels): normocholesterolemic (NC) men and women and hypercholesterolemic (HC) men and women. Although we recorded no significant differences in levels of HDL cholesterol and apoA1 among these groups, serum PON1 activity was lower in the HC groups ($P < 0.05$) compared with the NC groups. We found positive correlations between PON1 activity and HDL cholesterol ($r = 0.455$, $P < 0.05$) and apoA1 ($r = 0.697$, $P < 0.05$) in NC women. PON1 did not correlate with HDL cholesterol and apoA1 in HC women.

In conclusion, we suggest that low serum activity of PON1 and altered associations between PON1 activity and HDL as well as apoA1 may deteriorate the beneficial functions of HDL and result in the higher susceptibility of LDL to oxidative modification and, therefore, a possible higher risk of initiation and progression of atherosclerosis. The factors modifying serum PON1 activity are unclear and require further evaluation. Our results supporting the findings of the study by Gaillard et al. (1) might contribute to explaining the possible role of altered activity of PON1 and its relationship to some lipid risk markers in the pathogenesis of atherosclerosis.

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