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Coronary Artery Disease

Gender differences in blood thrombogenicity in hyperlipidemic patients and response to *pravastatin* $\hat{\sim}\dagger$

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Abstract

Thrombotic risk in hyperlipidemic women and its response to lipid therapy is unknown. We prospectively studied 28 men and 29 women with high low-density lipoprotein (LDL) cholesterol during 6 months of therapy with pravastatin. Women had significantly higher high-density lipoprotein (HDL) cholesterol ($54.2 \hat{\pm} 1.7$ vs $39.5 \hat{\pm} 2.2$ mg/dl, $p < 0.01$), lower prevalence of coronary artery disease (41% vs 67%, $p = 0.04$), and otherwise similar baseline characteristics compared with men. Both genders achieved a 33% reduction in LDL at 6 weeks ($188 \hat{\pm} 6$ to $133 \hat{\pm} 5$ mg/dl) and maintained similar LDL levels throughout the study. Systemic hemostatic markers and thrombus formation under dynamic flow conditions were evaluated at baseline, and at 3 and 6 months of follow-up. Prothrombin fragment $F_{1,2}$, a marker of thrombin generation, was higher in

women versus men at baseline ($2.4 \hat{\pm} 0.2$ vs $1.4 \hat{\pm} 0.3$ nmol/L, $p = 0.02$). The levels decreased in women to $2.0 \hat{\pm} 0.3$ nmol/L at 3 months and to $1.6 \hat{\pm} 0.2$ nmol/L at 6 months ($p < 0.045$, analysis of variance), whereas it remained unchanged in men. Plasminogen activator inhibitor-1 significantly decreased at 3 and 6 months of follow-up: by 12.6% and 18.7%, respectively, in women, and by 18.8% and 23.5%, respectively, in men. Similarly, tissue plasminogen activator decreased significantly by 7.4% in women and 11.8% in men at 6 months compared with baseline. Fibrinogen showed an increase in both genders at follow-up. Thrombus formation was similar at baseline between the 2 genders, and decreased at 3 and 6 months compared with baseline by 12.5% and 29.5% in women, and by 18.6% and 19.4% in men ($p < 0.04$ at 6 months vs baseline in both men and women). Other markers, including C-reactive protein, fibrinopeptide A, D-dimer, and factor VIIa, did not differ between genders and did not change with therapy. Thus, despite higher HDL, and lower incidence of coronary disease, women with high LDL had a comparable thrombotic and/or fibrinolytic profile to men and even evidence of increased thrombin generation at baseline. Blood thrombogenicity was reduced with pravastatin in both genders; in addition, thrombin generation was gradually reduced in women to a level similar to that of men by 6 months of follow-up.



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