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Lipoprotein (a): Genetic marker for atherosclerosis?

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In lipid composition lipoprotein (a), or Lp(a), resembles low-density lipoprotein (LDL), but Lp(a) is denser and larger.[1,2] Its unique immunologic characteristics are due to apolipoprotein (a), or apo (a).[2] Apo (a) has at least seven isoforms, differing in molecular weight by about 50 000.[2] The polymorphism appears to be due to the variable number of repeat units resembling the kringle IV unit of plasminogen in the apo (a) gene,[3,4] a gene that everyone seems to have.[1]

The Lp(a) level is determined usually by immunoassay and sometimes by agarose gel electrophoresis. The amount of cholesterol carried by Lp(a) varies in humans from about 1.3 mmol/L (50 mg/dl) to less than 0.03 mmol/L (1 mg/dl) but is usually low.[5] The isoforms of lowest molecular weight are associated with the highest plasma Lp(a) levels.[1,4] Because the isoforms are inherited there is a strong genetic influence on the Lp(a) mass.[1,5]

Premature cardiovascular disease is strongly associated with an Lp(a) cholesterol level greater than 0.52 mmol/L (20 mg/dl) (20% to 30% of the LDL cholesterol level considered to be a serious risk), or an Lp(a) total mass greater than 1.3 mmol/L.[1] Two mechanisms are postulated. First, the arterial wall may take up or retain Lp(a) more extensively than it does LDL; Lp(a) has a longer half-life than LDL and is not catabolized as effectively. Second, since the kringle units of plasminogen facilitate binding to fibrin and endothelial cell surface receptors, the major risk from Lp(a) may be through competition of apo (a) with plasminogen for binding sites and consequent interference with fibrinolysis.[6]

Association of Lp(a) with other risk factors is not established. The Lp(a) level is independent of the levels of other lipoproteins in healthy populations.[5] However, people with familial hypercholesterolemia have abnormally high levels of Lp(a), no matter which apo (a) isoform they have.[1] An elevated Lp(a) level may be a greater risk factor when associated with an elevated LDL or low HDL level. Lp(a) may provide a common link between genetic predisposition and environmental factors.

Few therapies influence Lp(a). Maneuvers that alter LDL catabolism have little effect on Lp(a). However, combined neomycin and niacin treatment lowers the Lp(a) level,[7] consistent with the apparent effect of the synthetic rate on the Lp(a) concentration.

The most appropriate approach, particularly in people with a strong family history of premature coronary heart disease, is to determine if the Lp(a) total mass exceeds 1.3 mmol/L. If it does, the focus should probably be on reducing other risk factors, lipoprotein abnormalities and lipoprotein synthesis.

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