Acta Pharmaceutica Turcica
XLI (3) (97-99) 1999

LIPOPROTEIN Lp(a) AS A RISK FACTOR FOR CORONARY HEART DISEASE

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Lipoprotein lp(a) structuire

Originally described by Berg in 1963 (1), lipoprotein Lp(a) consists of a LDL bound by a disulfide bond to apo(a) (2). The gene encoding apo(a) is located on chromosome 6q and is linked to that gene encoding plasminogen (*1).

Lp(a), atherrogenesis and thrombogenesis

Apo(a) has a high degree of homology to plasminogen (2) and competes with the binding of plasminogen to U937 monocyte-like cells and vascular endothelial cells (3,4). Histological studies have localized Lp(a) in the arterial intima, atherosclerotic plaque and in saphenous vein coronary artery bypass grafts (5-8,9,10). Lp(a) also promotes atherosclerosis by enhancing oxidation of LDL, formation of oxygen free radicals in human monocytes and inducing smooth muscle cell proliferation in arterial intima (11-13). Lp(a) is thought to promote migration of smooth muscle cells from the media to the intima by decreasing the concentration of the transforming growth factor-B, a migration inhibitor(14).

Factors regulating plasma lp(a) levels

Genetic factors related to the size of apolipoprotein(a) gene are responsible for the production of Lp(a) from the liver (15,16). Lipoprotein Lp(a) levels therefore differ by race(17). Other factors responsible for raised Lp(a) levels are acute myocardial infarction, in response to pregnancy, advanced malignant neoplasms, and nephrotic syndrome (18-25).

Measurement of lp(a) levels

Previously measured by electrophoresis, Lp(a) levels are now determined by the enzyme linked immunoabsorbent (ELISA) method(26,27).

Lipoprotein lp(a) excess and CHD

Several retrospective studies (28-41) have suggested excess lipoprotein Lp(a) levels to be a strong and independent risk factor for coronary heart disease (CHD). A study of familial lipoprotein disorders found Lp(a) excess as the most common disorder in patients with premature CHD(42). Results from retrospective studies have been contradictory due to a number of methodological and statistical limitations like inadequate sample storage temperatures, inadequate Lp(a) measurements, small sample size and wide confidence intervals (43). The propective studies of the 1990's have clarified the association of excess Lp(a) levels and CHD risk(44-51). The results of these studies suggest that the Lp(a) level is a strong predictor of premature CHD, especially in patients with concomitant hypercholesterolemia.

Screening for lipoprotein lp(a) excess

Lp(a) levels are mainly related to heredity and presently screening cannot be advised for all racial groups (52,53). Screening is recommended only for patients with premature atherosclerosis, a strong family history of premature atherosclerotic vascular disease not explained by other dyslipidemias, or patients with hypercholesterolemia who are refractory to cholesterol-lowering therapy with a statin or a bile acid sequestrant (43). Screening may also be considered for patients with coronary allograft vasculopathy (52), patients who have undergone percutaneous transluminal angioplasty (PTCA) (54,55), and patients who have undergone coronary artery bypass graft (CABG) (56).

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Treatment options for lp(a) excess

Lifestyle modifications, diet and exercise have no effect on Lp(a) levels. Pharmacological therapy is generally indicated for at risk patients. Pharmacological agents lowering the Lp(a) levels include benzafibrate (fibric acid derivative), nicotinic acid (3-4g/d), neomycin sulphate (2g/d), angiotensin converting enzyme (ACE) inhibitors, and estrogen replacement therapy (43).

Conclusion

Lipoprotein Lp(a) excess is an important and strong risk factor for premature CHD in men and women. Screening and treatment should be limited to patients at high risk for the complications of CHD. Smoking, hypercholesterolemia and hypertansion remain by far the most important risk factors for coronary heart disease.

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Accepted: 14.12.1998