Lipoproteins and Coronary Artery Disease

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Coronary artery disease (CAD) is the single most important disease entity in terms of both mortality and morbidity and is a leading cause of death[1]. plaque within the coronary arteries due to multifactorial vascular alterations, results in coronary atherosclerosis[2].

Epideni iological studies have demonstrated that major risk factors such as dyslipidaemia, hypertension, diabetes mellitus and the use of tobacco products act in a synergestic manner[3]. Other risk factors include physical inactivity, obesity, family history of CAD, age gender, hemostatic factor, horn ocystoin em ia, alcohol consumption and psychological factors[4]. Risk factor reduction is the primary clinical approach for preventing CAD morbidity and mortality.

Raised serum concentration of cholesterol, low density lipoprotein cholesterol (LDL-C) and low serum concentration of high density lipoprotein cholesterol (HDL-C) are all associated with an increased risk of coronary atherosclerosis[5,6]

Plasma lipids are important substrates for energy metabolism, membrane integrity and steroid synthesis. They are transported through the plasma compartment as lipoproteins, complex with soluble molecules and are separated into five major classes by the content of triglycerides, cholesterol, cholesterol esters, phospholipids and apolipoprotein. The major plasma lipoproteins are chylomicrons, very low density lipoprotein (VLDL), intermediate density lipoprotein (IDL), low density lipoprotein (LDL) and high density lipoprotein (HDL)[4].

In dyslipidaemia, circulating levels of lipids or lipoprotein fractions are abnormal because of genetic and/or environmental conditions that alter the production, catabolism or clearance of plasma lipoproteins from the circulation[4].

Lipoprotein a (LP a), discovered by Berg[7] in 1963 has been shown in a number of clinical studies to be an independent risk factor for CAD[8]. Structurally it is identical to LDL with the addition of a single Apo (a) molecule attached by a disulfide bond to the apo B-100[9-12]. The mechanism by which LP(a) may increase risk for CAD is complex. It has been demonstrated to be deposited in the arterial walls, particularly in areas with atherosclerotic plaque and apo(a) has been found co-lacalized with fibrinogin in the arterial walls[13]. It is mainly synthesized by the liver14 and with the physiological role still unknown, it is speculated that it delivers cholesterol to cells at wound sites[15].

High density lipoprotein has been proposed to play a pivotal role in retarding foam cell formation by removing excess cholesterol from peripheral cells and transporting the cholesterol back to the liver, where it is secreted as free cholesterol or bile acids.

Diminished HDL levels alter the equilibrium of cholesterol deposition by reducing cholesterol removal and transport back to the liver which promotes lipid accumulation in peripheral cells. Patients with low HDL levels have been characterized by several genetic defects in apo lipo-protein Al Epiderniological studies have established a strong inverse association of HDL-C concentration with CHD[18,19].

Genetic diseases that alter expression of the LDL receptor or one of the apolipoprotein molecule can severely affect cholesterol metabolismt&u.

Familial hypercholesterolem ia established the importance of LDL levels in atherogenesis and has been characterized by four classes of mutations in the LDL receptor gene[16,17].

An earlier study[20] reported sign ifcantly increased concentration of total cholesterol, LDL-C, apo B and Lp(a) and decreased concentration of HDL-C and Apo Al in CHD patients than in control subjects.

Ratios between various serum concentrations of lipids or apo lipoproteins have been proposed as risk markers of CUD. Best ratios for the detection of risk of CUD are LDL-C/HDL-C and HDL-

C/cholesterol[21].

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