UPIDS IN LIVER DISEASE

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Liver plays a central role in lipid metabolism as indicated by the alterations in the concentration and composition of various lipid fractions that occur in liver disease[1]. The cause of these changes is multifactorial and reflects complex biosynthetic, enzymatic and catabolic derangements. The profound abnormalities in lipid metabolism which occur in patients with liver disease could be of considerable biological importance and may explain some of the general metabolic disturbances seen in severe liver disease. Hypercholesterolaemia and hypertriglyceridaemia, common in hepatocellular disease, are usually transient and levels return to normal with resolution of the disease[2]. The most characteristic abnormality in plasma lipids is a decrease in the concentration of cholesterol esters as a result of lecithin cholesterol acyl transferase (LCAT) deficiency. This is possibly due to inadequate synthesis or loss of the enzyme secondary to hepatocyte necrosis[3] and results in changes in most lipoprotein fractions, which become deficient in cholesterol esters and enriched in triglycerides and phospholipids[4]. The apolipoprotein composition and content of the lipoprotein particles is also abnormal[4]. In the high density lipoprotein (HDL) fraction there may be a marked decrease in the levels of apoprotein A-I and apoprotein A-Il with an increase in apoprotein-E and apoprotein- C. The very low density lipoproteins (VLDL) are correspondingly depleted in these apoproteins. The increased levels of plasma triglycerides are usually found in lipoproteins isolated in the low density lipoprotein (LDL) density range. Triglycerides rich LDL particles may accumulate because a reduced number of cholesterol esters are available for transfer from HDL. Impaired lipolysis or ineffective remnant clearance by the injured liver has also been implicated[5]. As these particles are too small to scatter light, plasma remains clear despite moderate hypertriglyceridaemia. In cholestatic liver disease, there is a marked elevation of plasma cholesterol and phospholipids and the appearance in cholestatic plasma of a variety of unusual lipoproteins, including the classic cholestatic lipoproteins, lipoprotein-X (Lp-X) [6-8]. Lp-X is a bilamellor nesicular structure containing phospholipid and free cholesterol complexed with albumin and C. apoproteins on the surface. The origin of Lp-X remains unclear but may be due to regurgitation of biliary lipids with interaction of bile and serum constituents, particularly albumin[9]. In patients with early and intermediate histologic stages of primary biliary cirrhosis, mild elevations of VLDL and LDL concentration were often noted. In contrast patients with advanced disease had marked elevations in LDL levels with the presence of Lp-X and a significant decrease in HDL. Mean plasma apolipoprotein B and C-II concentrations were increased in both groups. Apolipoprotein A-I and A-Il values were divergent, with the former subjects having increased values and the latter with decreased values[10]. Apolipoprotein E was also increased in later stages of the disease[10,11] while altered cholesterol esterification was only observed in patients with advanced disease[9]. Although lipoprotein abnormalities are very sensitive indicators of fundamental hepatic metabolic defects, the biochemical changes are not usually of any diagnostic significance. Alcohol, drugs or viral infections may produce hepatocellular dysfunction with similar changes in lipoprotein composition attributable to a decrease in plasma LCAT activity. It has been suggested that the degree of LCAT deficiency may be of some prognostic -significance since patients with low activity appear to have a greater impairment of hepatic function and therefore, a worse prognosis than patients with lesser degrees of impaired LCAT activity[12,13]. FIDL cholesterol may serve as a useful marker of primary biliary cirrhosis disease progression because it falls to low levels as the disease advances, Lipoprotein-X is present consistently in cholestasis but is of no diagnostic value in distinguishing between intra and extrahepatic cholestasis.

The profound abnormalities in lipid metabolism which occur in patients with liver disease may be of considerable biological importance and may explain some of the general metabolic disturbances seen in severe liver disease.

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