

DRUG TREATMENT OF HYPERLIPIDA-EMIA-A CONTROVERSY

Pages with reference to book, From 75 To 75

Drug treatment of Hyperlipidaemia still remains a debatable subject. Most of these drugs produce unsuspected side effects thus giving a point of controversy. The primary treatment of hyperlipidaemia is dietary for a minimum of three months. If at the end of this period the plasma lipid values fail to reach the normal level then drug therapy is considered.

Clofibrate, a branched, chained fatty acid ester is widely used for hypertriglyceridaemia. Many patients with combined hyperlipidaemia also respond. Clofibrate causes a decrease in VLD production and accelerates its catabolism to LDL (Grundy et al., 1972). The endogenous triglycerides are synthesized slower by the liver and those made are broken down faster. Side effects of clofibrate appear as occasional nausea and diarrhoea. A few cases of myalgia leading to a raised CPK value have been noted. Litho-genic bile has been reported in a few patients (Coronary Drug Project Research Group, 1975; Committee of Principal Investigators, 1978). This causes cholelithiasis and other diseases of the biliary tract. Clofibrate enhances the effect of coumarin derivatives. A close monitoring of both drugs is therefore necessary. The daily recommended dose of clofibrate is 2 Gm in divided doses.

Cholestyramine and cholestipol are high molecular weight anion exchange resins. They bind bile acids in the gastro-intestinal tract which in turn interrupts the entero-hepatic circulation.

Bile acids are the end product of cholesterol metabolism. Their increased faecal excretion leads to a rapid conversion of cholesterol to bile acids resulting in a fall in blood cholesterol level (Glueck et al., 1972; Witztum et al., 1976). Cholesterol absorption is also slightly decreased when the drug is taken before meals (Davidson et al., 1979). These resins tend to produce constipation and their taste is also rather unpleasant. The daily dose ranges between 12G to 36G.

Nicotinic acid belonging to the B-complex family has also been tried in large doses to lower plasma lipids. The mechanism of action of nicotinic acid is unknown. But it has been noted that nicotinic acid decreases lipolysis and the production of triglycerides in the liver, and increases the faecal excretion of cholesterol end products. This altogether brings about a lowering of serum cholesterol by 8% to 16% and serum triglycerides by 20% to 30%. Side effects are intense due to which patient acceptance is poor. Intense cutaneous flushing and Pruritus occur in almost all patients. Anorexia, nausea, vomiting, diarrhoea and activation of peptic ulcer have also been reported. It potentiates the action of vasodilators and hyperuricaemic diuretics. The dosage used is from 300 mg to 3 Gm a day in divided doses.

Neomycin-a broad spectrum aminoglycoside antibiotic is poorly absorbed from the gastro-intestinal tract. It decreases cholesterol absorption and increases faecal cholesterol end product excretion. It acts by decreasing the 7 alpha-dehydroxylase activity in the intestinal flora and also interferes with micelle formation in the lumen of the gastro-intestinal tract. Transitory diarrhoea or abdominal cramps are side effects produced by Neomycin. It cannot be used in renal insufficiency as the small amount absorbed is excreted via the kidneys. Ototoxicity has been reported rarely and steatorrhoea, renal damage, enterocolitis and moniliasis occurs when a dose of 12 Gm daily or higher is used. Digoxin absorption is interfered by simultaneous administration. The action of coumarin anticoagulants is potentiated by Neomycin. The daily dose varies from 1.5G to 2Gm.

Probucol, a substitute dithioacetal has been used in moderate hypercholesterolaemia. Its mode of action remains unknown. It is speculated that the drug decreases cholesterol bio-synthesis. The side effects noted are few including diarrhoea and flatulence. Cardiac arrhythmias have been noted in large doses tried in animals. The usual daily dose is 500 mg twice daily.

In spite of the plasma lipid lowering property of all these drugs one has to weigh carefully the benefits

against the side effects.

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