Pravastatin
A Reappraisal of its Pharmacological Properties and Clinical Effectiveness in the Management of Coronary Heart Disease

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Pravastatin is an HMG-CoA reductase inhibitor which lowers plasma cholesterol levels by inhibiting de novo cholesterol synthesis.

Pravastatin produces consistent dose-dependent reductions in both total and low density lipoprotein (LDL)-cholesterol levels in patients with primary hypercholesterolaemia. Favourable changes in other parameters such as total triglyceride and high density lipoprotein (HDL)-cholesterol levels are generally modest. Combination therapy with other antihyperlipidaemic agents such as cholestyramine further enhances the efficacy of pravastatin in patients with severe dyslipidaemias.

Available data suggest that pravastatin is effective in elderly patients and in patients with hypercholesterolaemia secondary to diabetes mellitus or renal disease.

The benefit of cholesterol-lowering in terms of patient outcomes is currently an area of considerable interest. Recently completed regression studies (PLAC I, PLAC II, KAPS and REGRESS) show that pravastatin slows progression of atherosclerosis and lowers the incidence of coronary events in patients with mild to moderately severe hypercholesterolaemia and known coronary heart disease. Large scale primary (WOSCOPS) and secondary (CARE) prevention studies, moreover, demonstrate that pravastatin has beneficial effects on coronary morbidity and mortality. In WOSCOPS, all-cause mortality was reduced by 22%.

Pravastatin is generally well tolerated by most patients (including the elderly), as evidenced by data from studies of up to 5 years in duration. As with other HMG-CoA reductase inhibitors, myopathy occurs rarely (<0.1% of patients treated with pravastatin); approximately 1 to 2% of patients may present with raised serum levels of hepatic transaminases.

Thus, with its favourable effects on cardiovascular morbidity/mortality and total mortality, pravastatin should be considered a first-line agent in patients with elevated cholesterol levels, multiple risk factors or coronary heart disease who are at high risk of cardiovascular morbidity.

Pravastatin inhibits HMG-CoA reductase, the enzyme which catalyses the rate-limiting step within the cholesterol biosynthetic pathway. By inhibiting de novo cholesterol production and reducing intracellular cholesterol stores, pravastatin stimulates the synthesis and activity of low density lipoprotein (LDL) receptors, thereby enhancing the clearance of atherogenic LDL-cholesterol. In vitro and in vivo data indicate that pravastatin exhibits hepatocellular tissue selectivity, with greatest inhibition of cholesterol synthesis occurring in the liver.

In hypercholesterolaemic patients, pravastatin produces consistent changes in total cholesterol, LDL-cholesterol, high density lipoprotein (HDL)-cholesterol and triglyceride levels; its effects on lipoprotein(a) are, however, variable.

Hypercholesterolaemic patients treated with pravastatin 10 to 20 mg/day also show decreases in apolipoprotein B (the major component of LDL) of 12 to 30%. Other major proteins found in HDL (apolipoprotein A1 and AII) increase by 12