

SY5 NEW HYPOLIPIDEMIC AGENTS

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Many lipoprotein and nonlipid parameters have been identified as risk factors for coronary artery disease. Lipoprotein parameters include elevated Lp(a), increased triglyceride, reduced HDL, oxidized LDL, whereas nonlipid parameters are increased levels of homocysteine and fibrinogen, decreased endothelial-derived nitric oxide production. Among these parameters, lipoproteins remain the primary target for promoting the development of new therapeutic agents for the prevention of coronary artery disease. A new group of lipid lowering agents that are currently introduced for clinical use is HMG CoA reductase inhibitors, simvastatin, pravastatin, fluvastatin, atorvastatin and cerivastatin. The newer synthetic HMG CoA reductase inhibitors, atorvastatin and cerivastatin are more potent on a milligram basis, exhibit improved activity for reducing lipoproteins and improving tissue selectivity. As the result of HMG CoA reductase inhibition, the reduced intrahepatic cholesterol synthesis induces upregulation of LDL receptor in the liver, thereby enhancing removal of LDL and VLDL remnant particles from circulation. They also modestly increase HDL. In addition, the statins posses other pharmacological effects that are categorized as antiatherosclerotic and antithrombogenic effects (regulate coronary arterial tone by improving endothelial dysfunction, interfere with smooth muscle cell proliferation and migration, inhibit monocyte-macrophages and their inflammatory cytokine activity, diminish proinflammatory component, inhibit platelet activating factors and platelet aggregation, reduce fibrinogen level). Another group of lipid lowering agent is fibric acid derivatives. Fibrates are more capable in reducing VLDL and are recommended for the treatment of hypertriglyceridemia. But, newer fibric acid derivatives (bezafibrate, fenofibrate) could also lower serum LDL to levels comparable to the level that achieved by statins. Moreover, fenofibrate was demonstrated to reduce proinflammatory mediators (cytokines, TNF- α and IFN- γ) and fibrinogen levels. These fibrates as well as gemfibrozil also increase HDL level. Other lipid lowering agent that are recently available are colesevelam (bile acid sequestrant) In addition to these agents, there are many lipid lowering agents that are under clinical evaluation, ciprofibrate and lifibrol (the fibrates), rosuvastatin, nisvastatin (HMG CoA reductase inhibitors), tiqueside and pamaqueside (synthetic saponin as bile acid sequestrant), acylCoA:cholesterol acyltransferase inhibitors (ACAT inhibitors).