

HYPOLIPIDEMIC DRUGS - THE PROMISE OF STATINS

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Abstract : The introduction of statins has changed the management scenario of hyperlipidemia; apart from therapeutic efficacy their preventive role is now being recognised. Numerous studies have proven that they not only lower cholesterol but also reduce the risk for cardiovascular events and total mortality. Trials done with patients in secondary prevention (who are at higher risk) show a greater benefit than those in primary prevention. Statins seem to exert pleiotropic effects beyond cholesterol lowering on various parameters like endothelial dilation, VSMC proliferation etc. Increasing HDL-cholesterol has become an important new target for lipid modulating therapeutic approaches. Although statins have been proven to be efficient in Type-2 diabetics, fibrates may be considered, too, for treating this population; Some of the new treatment approaches have been covered in this overview.

INTRODUCTION

The introduction and the clinical evaluation of statins as therapeutic agents has hanged the current scenario of management of hyperlipidemia and the focus is on prevention. Among lipid risk factors the evidence strongly indicates that LDL cholesterol is the most important contributor. In high risk patients the focus is on rather how much LDL cholesterol lowering should be done and what target levels should be achieved?

STATINS

Statins are the most frequently prescribed and the most efficacious drugs to lower cholesterol. Numerous studies¹⁻⁵ have proven that they do not only lower cholesterol but also lower the risk for cardiovascular events and total mortality. In patients of existing atherosclerotic disease as well in asymptomatic high risk patients they exert their beneficial actions. The benefit of the therapy with statins depends on the total risk for cardiovascular disease of the patient and is independent of age and sex¹. The global risk for cardiovascular disease or death may be calculated according to the PROCAM score or the ESC score. Since the basal risk of premenopausal women is substantially lower than that of men of comparable age, only postmenopausal women have a similar benefit as men from such a therapy. Trials done with patients in secondary prevention (who are at higher risk) show a greater benefit than those in primary prevention.

Do all Statins have equal efficacy?

Statins are pharmacologically diverse group of drugs that share the ability to inhibit hydroxymethylglutaryl coenzyme A (HMG CoA) reductase, the enzyme which controls the rate-limiting step of cholesterol synthesis. The currently available statins are *lovastatin*, *simvastatin*, *pravastatin*, *atorvastatin*, *rosuvastatin* and *pitavastatin*.

The CURVES study has investigated the cholesterol lowering effect of five statins Fluvastatin 20mg/day and atorvastatin 10mg/day lowered LDL cholesterol 17% & 38% respectively. Similar data were obtained in the STELLAR study with pravastatin at 10 mg/day to 55% and rosuvastatin at 40 mg/day. Table 1 gives the relative cholesterol lowering efficiency, reported in various studies.

The Multifarious Role of Statins

The pleiotropic effects of statins may also be responsible for the beneficial effects which have been observed in a wide range of

other diseases, including multiple sclerosis, neurodegenerative disorders such as Alzheimer's disease, the prevention of bone fractures, and even in the reduction in the incidence of some types of cancer. Certainly more evidence is needed to prove these benefits, but statins seem to exert other effects beyond cholesterol lowering which has been summarised in Table-2.

Table1.: Mean cholesterol lowering by Statin in various strokes

	Mean cholesterol lowering (mmol/L)
4S (7)	1.7
PROSPER (8)	1.3
GREACE (9)	2.4
LIPID (10)	1.0
CARE (11)	1.1
LIPS (12)	1.0
HPS (13)	1.5 (re-adjusted)
WOSCOPS (13)	1.4
ALERT (14)	1.2
AFCAPS/TexCAPS (15)	1.0
ASCOT (16)	1.0
TNT (17)	0.6

Table2.: Pleiotropic Effects of Statins on Various Parameters of Endothelial Dysfunction

Parameter	Lovastatin	Pravastatin	Simvastatin	Fluvastatin	Atorvastatin
Endothelial dilation	↑	↑	↑, neutral	↑	↑
LDL oxidation resistance	↑	↑	↑	↑	↑
VSMC proliferation	↓	Neutral	↓	↓	↓
VSMC apoptosis	↑	Neutral	↑	↑	↑
Platelet aggregation	↑	↓	Neutral	↓	↓
CRP	↓	↓	↓	↓	↓

Statins also differ with respect to pharmacokinetic properties which may explain differences in drug-drug interactions, tolerability, and safety. In principle statins show little undesired effects and are considered very safe drugs, but some combinations of Statins and other drugs should be avoided. Among these are in particular

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