Prevalence and risks of undertreatment with statins

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Abstract

Statins are prescribed worldwide for patients with coronary heart disease (CHD) and also for those at risk of developing atherosclerotic vascular disease. This article looks at the prescribing of statins in the UK demonstrating how they are underprescribed in this country, how ineffective doses of statins are used due to many doctors not understanding how to implement guidelines, and how the greatest reductions in CHD risk are achieved by the greatest reductions in cholesterol.

Key words: statins, cholesterol, coronary heart disease, guidelines.

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Introduction

The directive for statin use in the UK and worldwide is prescription for practically all patients with overt coronary heart disease (CHD) and also for those patients at risk of developing atherosclerotic vascular disease, as guided by risk tables, up to about the age of 80. Secondary prevention of further cardiovascular events in a patient with existing CHD is the first target being addressed nationally.

Patients on statins: still too few

Statin prescribing has improved lately, but not all that much. In hospitals in 1998, the Prospective Registry of Acute Ischaemic Syndromes in the UK (PRAIS-UK) study showed that of 1,046 patients admitted with an acute coronary syndrome, 44% were on a statin at six months post-discharge.[1] The larger Healthwise I, also carried out in 1998, showed that in general practice, of 24,431 patients with CHD only 16% were on a statins.[2] The British Regional Heart Study showed that by 2000, 29% of the 646 men with CHD surveyed were on statins.[3]

Healthwise II, the follow-up study of CHD patients in general practice, was presented last month at the British Cardiac Society in Glasgow.[4] This studied 11,996 individuals with CHD, from 1999 until the end of November 2002. It found that 34% of patients received a statin in 1999 compared to 46.2% who were prescribed statins in 2000. By 2001, 49.4% of the patients were receiving statin therapy; and by the end of November 2002, 53.2% of the study population had finally been prescribed statins.

November 2002 was also the fifth anniversary of the Standing Medical Advisory Committee which indicated that all CHD patients should be on statins. Healthwise II shows how slow implementation has been – almost half of all CHD patients remain untreated, despite overwhelming evidence of benefit.

Cholesterol levels achieved with statins – not low enough

Clinical trials have shown that substantial cholesterol lowering saves lives. But what is actually happening in practice in the UK? This has been surveyed in several large recent databases. The Healthwise II study showed that the mean cholesterol level of the 11,996 CHD patients studied fell from 5.1$\pm$1.1 mmol/L at the start of the study to 4.8$\pm$1.1 mmol/L at the end of 2002.[4] Both the joint British Guidelines and the National Service Framework for Coronary Heart Disease (NSF for CHD), however, state that an achieved cholesterol of < 5 mmol/L, plus a reduction in cholesterol of at least 30% from the initial level, are both required. The mean cholesterol in the 1998 Healthwise I study among the 14,265 patients who had a cholesterol check was 5.9 mmol/L. To reduce this by 30% would mean that the target total cholesterol was 4.13 mmol/L. Healthwise II shows, however, that achieving a cholesterol level which scrapes under 5.0 mmol/L seems to be how the guidelines are being implemented. Doctors are aiming for a total cholesterol < 5 mmol/L for their patients, either not understanding or ignoring both the evidence and guidelines which recommend that a fall of 30% should be achieved.

This is confirmed in the Performance for Life survey of over 14,000 patients with CHD (Brady A and Ford I, data on file, University of Glasgow). In this ongoing survey of general practitioner statin prescribing, as part of the study, patients' cholesterol levels are recorded and titrations of statin doses noted. With patients followed from 1999–2003 it is seen that when patients were first commenced on a statin, a significant proportion did not reach the target cholesterol level of $\leq$ 5.0 mmol/L, the target set out in the NSF for CHD. Up-titration and changes in statin used resulted in modest increases in patients reaching target. A substantial number of patients do not achieve a fall in total cholesterol of 30%, even after months on therapy (data on file).

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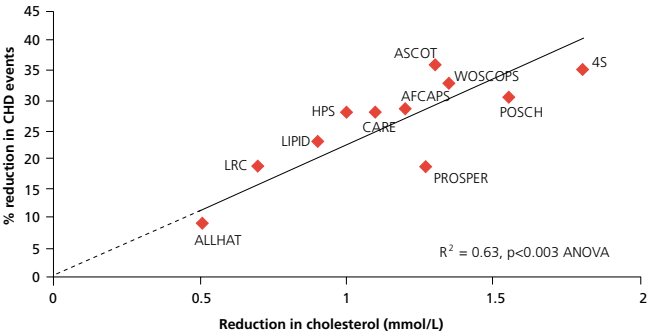
Figure 1. Reduction in CHD events with lipid-lowering therapy



Key: CHD = coronary heart disease; LRC = Lipid Research Council; LIPID = Long term Intervention with Pravastatin in Ischaemic Disease; HPS = Heart Protection Study; CARE = Cholesterol And Recurrent Events; AFCAPS = Air Force Coronary Atherosclerosis Prevention Study; WOSCOPS = West of Scotland Coronary Prevention Study; ASCOT = Anglo-Scandinavian Cardiac Outcomes Trial; 4S = Scandinavian Simvastatin Survival Study; POSCH = Program on the Surgical Control of the Hyperlipidemias; PROSPER = PROspective Study of Pravastatin in the Elderly at Risk; ALLHAT = Antihypertensive and Lipid Lowering treatment to present Heart Attack Trial

Key messages

- UK guidelines recommend that target cholesterol levels of < 5.0 mmol/L plus a reduction in cholesterol of at least 30% from the initial level should be achieved in at-risk patients
- A study of statin prescribing in general practice has shown that underprescribing of statins leaves one in four coronary heart disease patients failing to meet a total cholesterol below 5.0 mmol/L
- Two in three patients in the study failed to achieve a fall in total cholesterol of 30%
- The greater the reduction in cholesterol, the greater each individual patient benefits

Thus, while statin prescribing is improving, we are nowhere near reaching defined targets.

Benefits of statins are related to cholesterol lowering – lower is better

Statins save lives by lowering cholesterol. There has been much discussion about pleiotropic effects, i.e. the effects of statins on endothelial function, inflammatory markers and so on. But the view of ourselves and also of the Oxford Triallists is that while pleiotropic mechanisms certainly exist and may be important, the principal benefit of statins is in lowering low-density lipoprotein and, therefore, total cholesterol. Figure 1 shows a novel analysis of the data which supports this. All of the major statin trials are represented, together with the Lipid Research Council and the Program on the Surgical Control of the Hyperlipidemias (POSCH) trials for illustration.

Each trial position on the graph is represented by the effects on cholesterol lowering compared to placebo in that trial, plotted against the reduction in CHD events for that particular study. It is clear that the greatest reduction in events is related closely to the degree of cholesterol lowering. This is reinforced by the recent data from the Antihypertensive and Lipid-Lowering treatment to prevent Heart Attack Trial (ALLHAT), where 10,355 patients were randomised to 40 mg of pravastatin or placebo. There are criticisms of this trial, one of which is that the difference in achieved cholesterol levels between the groups was modest. This resulted in only a 9% reduction in CHD event rate in the active therapy group compared to 'usual care.' This confirms the concerns that a small reduction in cholesterol with inefficient use of statins confers little benefit for the individual. It is also clear from figure 1 that the greater the reduction in cholesterol with statins, the greater the benefit for the patient.

Some epidemiologists have argued that a small reduction in cholesterol across a population will make a worthwhile difference to CHD event rates. While this might be true, it seems clear that, when treating individuals, the greatest reduction in risk we can offer is by lowering cholesterol as much as possible. This is achievable with statin therapy in 2003. We believe that an increased awareness of the clear benefits of aggressive cholesterol lowering should be more widespread. This requires increased public awareness, as well as an improvement in the performance of doctors. All the databases described above show the modest achievements to date in British statin prescribing.

We should ask ourselves in clinic when discussing treatments with our individual patients, shall I lower their CHD risk a little or a lot? We now have the drugs to do this.

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