Prescribing statins: the real issues

Reassessing the benefits, harms and risk levels of statin therapy

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Patients have been stopping their statins without medical advice, in the wake of a media report in November 2013 in which United States-based commentators criticised the use of statins for various reasons, including their failure to reduce mortality, inappropriate promotion and inappropriate prescription.[1] While rebuttal occurred in subsequent media reporting and by the National Heart Foundation of Australia (NHF), general practitioners continued to see patients who intended to discontinue statin therapy on the basis of the original report.

Statins are effective in lowering levels of low-density lipoprotein cholesterol (LDL-C). Highly supportive evidence for cardiovascular disease (CVD) benefit was summarised in a recent meta-analysis of 169 138 subjects in 26 statin trials (five comparing more with less statin use [39 612 patients] and 21 comparing statin users with controls [129 526 patients]).[2] Overall, there were 15 969 deaths, 24 323 major vascular events and 10 124 cancers.[2] Relative risk reduction in total mortality was 10% per 1 mmol/L reduction in LDL-C over 5 years ($P < 0.001$), due to significant reduction in deaths from coronary disease and other cardiac causes. Stroke mortality was not reduced significantly. The relative risk reduction for major vascular events (non-fatal myocardial infarction, fatal coronary heart disease, coronary artery bypass surgery, percutaneous transluminal coronary angioplasty, and ischaemic stroke) was 21%–22% per 1 mmol/L reduction in LDL-C over 5 years.[2] Similar mortality and major vascular events benefits from statins also occurred in patients at low CVD risk (5-year risk, < 10%).

Rhabdomyolysis is the most serious adverse drug reaction with statins, but it occurs rarely (in around one patient per million prescriptions).[3] However, myalgia with or without elevated creatine kinase levels may occur in up to 10% of patients in clinical practice.[4] Myalgia remains the most important adverse drug reaction related to statin therapy, along with an increased rate of new-onset diabetes mellitus, which may occur in about 6% of patients, most of whom have previous features of the metabolic syndrome.[5] Because new-onset diabetes mellitus is of short duration and increases in blood glucose and glycated haemoglobin levels are small, the CVD benefits of statins are far more likely to outweigh potential risks of new-onset diabetes mellitus, other than perhaps in long-term treatment of patients at low CVD risk.[5]

> “Future trends … are likely to involve greater use in primary prevention … and use in more diverse patient groups”

The Australian Pharmaceutical Benefits Scheme (PBS) reimburses statin prescriptions based on categories of absolute CVD risk and levels of total cholesterol and high-density lipoprotein cholesterol. These criteria differ in some respects from current US and Australian guidelines for statin therapy. In Australia, the National Vascular Disease Prevention Alliance (NVDPA) recommends simultaneous lipid and blood pressure therapy for patients at high absolute CVD risk (5-year CVD risk > 15%), unless contraindicated or clinically inappropriate. Although drug therapy is not routinely recommended for patients with moderate 5-year CVD risk (10%–15%), blood pressure- and/or lipid-lowering agents, in addition to lifestyle advice, should be considered if 3–6 months of lifestyle intervention does not reduce risk; blood pressure is persistently ⩾ 160/100 mmHg; there is a family history of premature CVD; or the patient belongs to a specific population where risk may be underestimated (eg, Aboriginal and Torres Strait Islander, South Asian, Maori and Pacific Islander, Middle Eastern). For all CVD risk categories, withdrawal of therapy may be considered for those with profound lifestyle changes.[6] Previous lipid-management recommendations of the NHF have recently been superceded by the NVDPA guidelines for primary prevention of CVD and the NHF guide for secondary prevention of CVD.[6-8] New US guidelines recommend statins for patients with 10-year CVD risk ⩾ 7.5%, although the validity of risk assessment using these guidelines has been questioned.[9]

Because benefits of statin therapy occur in patients at all levels of CVD risk, long-term cost-effectiveness is a major issue. In 2010–11, about 2.6 million Australians took statins at a cost to the government of $1229.37 million.[10] Although generic statins have cut costs in Australia by around 25%, they remain expensive by international standards. Lower costs may encourage changes to PBS criteria, which would allow the use of statins for primary prevention of CVD in broader groups of patients, as recommended in recent US guidelines.[9] Future trends in statin prescribing in Australia are likely to involve greater use in primary prevention (resulting from lower costs) and use in more diverse patient groups, some of whom may be defined by computed tomography coronary calcium scoring.[11]

CVD benefits as well as regression of coronary atherosclerosis have been described in populations with mean LDL-C levels around 1.6 mmol/L, consistent with the “lower is better” hypothesis and the “treat to target” paradigm for statin therapy. However, for a given reduction in LDL-C, the greatest CVD benefits occur in populations at the highest baseline LDL-C levels and

CVD risk. Therefore, the new US guidelines focus on statin doses for various risk groups, rather than targeting LDL-C levels.[9]

The recent cholesterol debate gives doctors the opportunity to re-evaluate their patients' absolute CVD risk, and to modify statin therapy according to current guidelines. The outcomes should be more rational prescribing and more cost-effective reduction in CVD events in the longer term.

Competing interests: I serve on the lipid advisory boards of Abbott, Amgen, AstraZeneca and MSD (Australia), and am a member of the US National Lipid Association, European Society of Preventive and Rehabilitation Cardiology, Familial Hypercholesterolaemia Australasia Network, Queensland Lipid Group, Australian and New Zealand Familial Hypercholesterolaemia Registry Board, Cardiac Society of Australia and New Zealand Cardiovascular Genetic Diseases Council, and the Queensland Advisory Committee on Genetic Cardiovascular Diseases. I have also received research grants from MSD and the Australian Atherosclerosis Society.

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