HMG-CoA Reductase Inhibitor Use in the Aged
A Review of Clinical Experience

Caroline J. Lintott and Russell S. Scott
Lipid and Diabetes Research Group, Hagley, Christchurch Hospital, Christchurch, New Zealand

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Summary

While the benefit of cholesterol-lowering in the elderly has yet to be proven in clinical trials, individuals at high risk of coronary events who otherwise enjoy a good quality of life, should not be denied cholesterol-lowering therapy on the basis of age alone. Moreover, hypolipidaemic drugs are already extensively used in the aged. The HMG-CoA reductase inhibitors lovastatin, simvastatin and pravastatin are potent well tolerated hypolipidaemic therapies in young subjects. Although there have been few studies on their use in elderly subjects, the available data suggest the efficacy and safety of HMG-CoA reductase inhibitors is similar to that established for younger age groups.
1. Delayed Cardiovascular Mortality in the Aged

The use of hypolipidaemic drugs in the aged remains an area of controversy (Bilheimer 1991; Denke & Grundy 1990; Tikkanen & Tilvis 1991), since clinical trials to assess the benefits of pharmacological reduction of cholesterol, in terms of mortality, morbidity, and quality of life, for those aged over 60 years have not been performed.

Nonetheless, hypolipidaemic drugs are used extensively in the aged. A national study in the US from 1978 to 1988, using data from the National Disease and Therapeutic Index, showed that cholesterol-lowering drugs are prescribed primarily to individuals ≥ 60 years of age. Of the estimated 13 million individuals receiving hypolipidaemic treatment in 1988, 59% were aged ≥ 60 years (Wysowski et al. 1990).

Despite the lack of proven benefit, use of hypolipidaemic drugs in the elderly may be expected to increase even further. Firstly, the proportion of the population which is aged is increasing dramatically in most developed countries. In the US, the population aged > 65 years is expanding at 2.5 times the rate of the remaining population, and will total more than 30 million by the year 2000, when nearly two-thirds of American men will be in this age group (Kashyap 1989). Thus, the number of potential candidates for drug intervention is increasing.

In the past, atherosclerotic disease has been incorrectly considered an inevitable concomitant of aging; those surviving into old age were considered a genetically resistant residual population, following the premature deaths of high risk individuals. However, over the last 20 years a significant decline in cardiovascular mortality amongst those aged ≥ 65 years has been observed in more than 20 countries (Simons 1989). Even in those aged ≥ 75 years, reductions in mortality exceeded 20% for men from Israel, Yugoslavia, Australia, the US, Canada, Bulgaria, Italy, and Austria. The same trend was observed for women in these countries. While the reduction could be attributed to such factors as a reduction of serum cholesterol levels or smoking prevalence, the limited data on cardiovascular risk factors in these age groups allow only speculation on possible causes. It does indicate, however, that cardiovascular mortality in the aged can be significantly delayed. It has also been argued that since heart disease represents the major disease in the aged, lowering cholesterol levels will also lead to compression of morbidity, such as angina (Fries et al. 1989). With the average life expectancy for a 65-year-old person now ranging from 15 to 20 years in most developed countries, preventive healthcare may have considerable beneficial effect on elderly populations. The epidemiological evidence from a number of longitudinal studies, demonstrating that hypercholesterolaemia remains a risk factor for atherosclerosis into old age (Agner & Hansen 1983; Benfante & Reed 1990; Harris et al. 1988), may result in increased demand for treatment of elevated cholesterol levels in the aged.

In addition, elderly patients are being referred with increasing frequency for angioplasty and coronary artery surgery. In the US, the number of patients aged ≥ 65 years undergoing coronary artery bypass surgery rose 215% between 1981 and 1985 (Anderson et al. 1989). Angiographic studies in younger populations have shown that aggressive cholesterol-lowering by drug therapy can both slow the rate of progression or even lead to regression of coronary atherosclerosis following coronary bypass surgery (Blankenhorn et al. 1987), and prevent restenosis after successful coronary angioplasty (Sahni et al. 1991). Although, progression of atherosclerosis tends to be slow in patients aged > 65 years, extrapolation of the benefits of hypolipidaemic therapies seen in younger patients following these cardiovascular procedures may lead to their increasing utilisation in older patients following surgical treatment of their atherosclerotic heart disease.

Finally, because of the large number of persons at risk of cardiovascular events in the > 65 years age group, the short term potential benefit of hypolipidaemic drug treatment, expressed as numbers of cardiovascular events prevented annually per 1000 persons treated, is potentially greater in