STATINS FOR THE PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE

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ABSTRACT

Reducing high blood cholesterol, a risk factor for cardiovascular disease (CVD) in people with and without a past history of CVD is an important goal of pharmacotherapy. Statins are the first-choice agents. Previous reviews of the effects of statins have highlighted their benefits in people with CVD. The case for primary prevention was uncertain when the last version of this review was published (2011) and in light of new data an update of this review is required.

INTRODUCTION

Reducing high blood cholesterol, a risk factor for cardiovascular disease (CVD) events in people with and without a past history of CVD is an important goal of pharmacotherapy. Statins are the first-choice agents. Previous reviews of the effects of statins have highlighted their benefits in people with CVD. The case for primary prevention was uncertain when the last version of this review was published (2011) and in light of new data an update of this review is required.

OBJECTIVE

To assess the effects, both harms and benefits, of statins in people with no history of CVD.

SELECTION, METHOD AND CRITERIA

To avoid duplication of effort, we checked reference lists of previous systematic reviews. The searches conducted in 2007 were updated in January 2012. We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (2022, Issue 4), MEDLINE OVID (1950 to December Week 4 2011) and EMBASE OVID (1980 to 2012 Week 1).There were no language restrictions.

We included randomized controlled trials of statins versus placebo or usual case control with minimum treatment duration of one year and follow-up of six months, in adults with no restrictions on type of cholesterol - total, low density lipoprotein (LDL) or high density lipoprotein (HDL) cholesterol levels. Of these 10% or less had a history of CVD.

BODY

Cardiovascular disease (CVD) encompasses a wide range of disease including coronary heart disease (eg. heart attack, angina), cerebrovascular disease (ischaemic and haemorrhagic stroke), raised blood pressure, hypertension, rheumatic heart disease and heart failure. In the context of this review the major causes of CVD are unhealthy diets, tobacco use and physical inactivity (WHO 2008).

CVD is ranked as the number one cause of mortality and is a major cause of morbidity world - wide accounting for 17 million deaths i.e 30% of total deaths. Of these, 7.6 million are due to heart attacks and 5.7 million due to stroke (WHO 2008). Over 80% of CVD deaths occur in low- and middle-income countries (WHO 2008). In developing countries, it causes twice a many deaths as HIV, malaria and tuberculosis combined (Gaziano 2007). It has been estimated that between 1990 and 2020, the increase in ischaemic heart disease alone will increase by 29% in men and 48% in women in developed countries and by 120% in women and 127% in men in developing countries (Yusuf 2001). CVD imposes high social costs, including impaired quality of life and reduced economic activity and accounts for a large share of health service resources (Gaziano 2007).

CVD is multi-factorial in its causation and lifestyle changes are the basis of any treatment strategy, with patients often requiring behavioral counseling. Those unable to achieve or maintain adequate risk reduction through lifestyle changes alone or those at high risk may benefit from pharmacotherapy. High blood cholesterol (hypercholesterolaemia) is a risk factor for both fatal and non-fatal CVD events in people with and without a past history of CVD (Prospective Studies Collaboration 2007), and lowering cholesterol, in particular low density lipoprotein (LDL) cholesterol, is an important target of pharmacotherapy. Statins are the first-choice agents for LDL cholesterol reduction.

Since the relation between blood cholesterol and cardiovascular risk is continuous (Chen 1991), there is no definite threshold to initiate treatment. If a threshold for 'high' cholesterol is set at over 3.8 mmol/L, (146.9 mg/dL) this would contribute 4.4 million deaths worldwide and 40.4 million disability-adjusted life years (DALYs) (Ezzati 2002). Furthermore, the average level of blood cholesterol within a population is an important determinant of the CVD risk of the population. Differences in average levels of blood cholesterol between populations is largely determined by differences in diet eg countries with higher dietary saturated fat intake and a lower ratio of polyunsaturated to saturated fatty acids have higher than average cholesterol levels (Davey Smith 1992).

CONCLUSION

Implications for practice

The totality of evidence now supports the benefits of statins for primary prevention. The individual patient data meta-analysis now provide strong evidence to support their use in people at low risk of cardiovascular disease. Further cost-effectiveness analysis are needed to guide widening their use to these low risk groups.

Implications for research

In addition to the cost-effectiveness analysis referred above, it will be useful to study the effects of public health interventions that attempt to alter diet and physical activity patterns and compare their effects with statins in robust randomized trials. This is based on the recent evidence of large independent survival benefits of physical fitness in those taking statins in a large prospective cohort study (Kokkinos 2012).

Relevant interventions might include nutrition education, exercise prescription, physical education curriculums that may be effective in changing lifestyle behaviors. (Jepson 2000) Studies of patient experiences and views on long-term use of statins are also needed to improve adherence to treatment. It is likely that further trials will be conducted in younger adults with adverse risk factor profiles which are associated with higher lifetime CVD risk (Berry 2012) and also in children (de Ferranti 2008). It is important that these trials examine comprehensively potential adverse effects of statins and quality of life, reporting on them in an unbiased way.

ACKNOWLEDGEMENTS

I am thankful to my mentor Dr.JP Singh for his support and guidance in writing this article review, along with them my friend Dr.Rakhi, Dr.Nitin. Dr.Jeetentra, for their constant support and guide.

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