Do Statins Reduce the Risk for Diabetes by Improving Exercise Capacity?

To the Editor:

In the January 23, 2001, issue of Circulation, Freeman et al1 undertook a retrospective analysis of data from the West of Scotland Coronary Prevention Study (WOSCOPS) and showed that assignment to pravastatin therapy resulted in a 30% reduction (P=0.042) in the hazard of developing diabetes. They suggested that lowering plasma triglyceride levels may favorably influence the development of diabetes and speculated that the antinflammatory properties of pravastatin in combination with its endothelial effects may also play a part. In an accompanying editorial, Haffner suggested that the perceived benefit of such an intervention “is likely to be markedly underestimated.”2

It should be noted, however, that the absolute risk reduction in this post hoc analysis was only 0.86% (2.76% in the pravastatin group and 1.90% in the placebo group). As such, 116 subjects would need to be treated for 5 years to prevent 1 case of diabetes. Moreover, the authors’ Kaplan-Meier plots showing the percentage of patients developing diabetes (Figure, D) are nearly parallel after 3 and a half years,3 which suggests that treatment may only delay the development of diabetes for about 1 year.

Lack of exercise is a powerful predictor of risk for diabetes.3 Increases in physical activity have been shown to prevent progression to diabetes.4 Thus, one alternative explanation for the modest but unexpected effect found by Freeman et al1 is the impact that statin therapy has on patients’ capacity for physical activity. Angina and other cardiac end points, such as heart failure, have a significant impact on exercise capacity. Improvements in such end points have been shown to result in increased exercise tolerance. A recent meta-analysis of clinical outcomes in 17 statin treatment trials shows an odds benefit ratio of 0.70 (95% CI, 0.65 to 0.76) for angina.5

We would suggest that such clinical improvements underlie the reduced risk for diabetes seen by Freeman et al.3 The practical implication of this is that the antidiabetic properties of statin therapy may be a result of the drug’s capacity for improving clinical outcomes in heart disease, rather than any pleiotropic effect specific to pravastatin.

Ehud Ur, MD, FRCP
Allan Shlossberg, MD, FRCP
Division of Endocrinology and Metabolism
Dalhousie University
Suite 048, 7 North Victoria Building
1278 Tower Rd
Halifax, Nova Scotia B3H 2Y9
Canada


Response

We welcome the contribution of Drs Ur and Shlossberg to our discussion on the impact of pravastatin on the prevention of new type 2 diabetes mellitus. As we clearly indicated in our article,1 our conclusions were based on a post hoc analysis of the West of Scotland Coronary Prevention Study (WOSCOPS) database. As such, our aim in publishing was to raise the possibility that pravastatin may have an important preventive effect on the development of this serious condition, in addition to its now well-known effects on the reduction of cardiovascular and cerebrovascular disease risk. In so doing, we hoped to open the debate and stimulate further, more definitive research in this area.

The importance of lifestyle factors on the development of type 2 diabetes in high-risk individuals should not be forgotten.2 Drs Ur and Shlossberg suggest that an indirect effect of statin therapy may have been to allow patients treated with pravastatin in WOSCOPS to maintain higher levels of physical activity. This possible mechanism of action cannot be excluded by our current analyses, and it deserves further examination, as do the other possible mechanisms of action that we have put forward relating to the lipid-lowering effects of the drug and its effects on endothelial function and inflammatory processes. Only in detailed prospective studies can the potentially beneficial effects of pravastatin be examined fully.

Currently, we are conducting the Prospective Study of Pravastatin in the Elderly at Risk (PROSPER).3 Analyses of this study will allow further evaluation of the different hypotheses that have been generated to explain the important observation in WOSCOPS that subjects receiving pravastatin therapy experienced a statistically significant reduction in their risk of developing type 2 diabetes mellitus during the course of the study. We look forward to continuing this debate when further data are available at the conclusion of PROSPER in 2002.

D.J. Freeman
Department of Biological Sciences
University of Durham
Durham, UK

J. Norrie
I. Ford
Robertson Centre for Biostatistics
University of Glasgow
Glasgow, UK

N. Sattar
C.J. Packard
J. Shepherd
Department of Pathological Biochemistry
Glasgow Royal Infirmary University NHS Trust
Glasgow, UK

R.D.G. Neely
Department of Clinical Biochemistry
Dryburn Hospital
North Durham Healthcare NHS Trust
Durham, UK

S.M. Cobbe
A.R. Lorimer
P.W. Macfarlane
Department of Medical Cardiology
Glasgow Royal Infirmary
Glasgow, UK

C. Isles
Department of Medicine
Dumfries and Galloway Royal Infirmary
Dumfries, UK


Do Statins Reduce the Risk for Diabetes by Improving Exercise Capacity?
Ehud Ur and Allan Shlossberg

Circulation. 2001;104:e104-e105
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/104/20/e104

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/