Can Pravastatin Reduce Risk of Diabetes?

Freeman DJ, Norrie J, Sattar N, et al. Pravastatin and the development of diabetes mellitus: evidence for a protective treatment effect in the West of Scotland Coronary Prevention Study. Circulation 2001;103:357–62.

Study Overview

Objective. To determine if pravastatin use is associated with reduced risk of developing diabetes mellitus.

Design. Observational study.

Setting and participants. 5974 patients selected from the 6595 participants of the West of Scotland Coronary Prevention Study (WOSCOPS) [1], a randomized controlled trial designed to determine whether primary prevention with pravastatin could decrease cardiovascular events in men with risk factors for heart disease. Members of the WOSCOPS cohort were aged 45 to 65 years, had hypercholesterolemia and no history of myocardial infarction or organ transplantation at baseline. For the current study, subjects were chosen who did not self-report diabetes and had a baseline plasma glucose level of less than 7.0 mmol/L.

Main outcome measures. Development of diabetes, as defined by at least 2 fasting plasma glucose levels of 7.0 mmol/L or more and one glucose measurement of 2.0 mmol/L or more above baseline. Patients were evaluated at 6-month intervals. Researchers also considered baseline patient characteristics, including body mass index (BMI), high-density lipoprotein (HDL) cholesterol levels, age, smoking status, alcohol use, hypertension, white blood cell (WBC) count, and plasma triglyceride levels.

Main results. 139 out of 5974 patients developed diabetes during the 5-year study period. Predictors of diabetes in the univariate analysis were BMI, HDL cholesterol, total cholesterol, log WBC, log triglyceride, baseline glucose, and systolic blood pressure; age, alcohol intake, and smoking status were not significant predictors. Pravastatin treatment was associated with a 30% reduced risk of developing diabetes (95% confidence interval [CI] 0.50 to 0.98; $P = 0.036$). When a multivariate analysis was performed, BMI, log triglyceride, and baseline glucose remained significant predictors but systolic blood pressure and log WBC were no longer statistically significant. Risk reduction with pravastatin remained at 30% (95% CI 0.50 to 0.99, $P = 0.042$).

Conclusion

By lowering plasma triglyceride levels, pravastatin therapy may favorably influence the development of diabetes. The role of other mechanisms, such as the agent's anti-inflammatory properties in combination with its endothelial effects, remains unclear.

Commentary

Statins have recently been examined for their potential benefits beyond lipid lowering; these benefits may include reducing risk for osteoporosis [2] and Alzheimer's disease [3]. Freeman and colleagues' work is the first large-scale, long-term study to look at diabetes development in patients treated with a statin. Sheu et al [4], who suggested that pravastatin did not improve glycemia and may have actually worsened glycemic control, conducted a very small study with short-term follow-up. Other research has examined the rate of cardiovascular events in diabetic patients who received pravastatin, but investigators did not look at diabetes development in the pravastatin group [5].

Among the strengths of Freeman and colleagues' study were its duration (patients were followed for an average of 3.5 to 6.1 years), use of a standard screening technique to diagnose diabetes, and well-conducted multivariate analysis. Some weaknesses lay in the fact that study results were based on secondary data analysis. Important risk factors were not measured by investigators, including family history of diabetes and use of medications that may affect glycemia (eg, β blockers and diuretics). Also, the authors did not mention angiotensin-converting enzyme (ACE) inhibitor use, which may be significant because a recent study has found that ACE inhibitors may induce hypoglycemia [6]. While numerous studies have shown that exercise improves glycemic control, exercise is not considered among Freeman et al's baseline patient characteristics. Unfortunately, number needed to treat could not be calculated because the authors did not provide an expected rate of events in patients not receiving pravastatin. Despite these shortcomings, which the authors acknowledge in their discussion, the study generates an interesting hypothesis that is worth pursuing. Further, study results confirm that characteristics traditionally considered risk factors (BMI, HDL cholesterol level, total cholesterol, WBC, baseline glucose, systolic blood pressure) can predict development of diabetes. Whether the treatment effect of pravastatin is unique to the agent or is similar to all statins remains to be determined in future research.

Applications for Clinical Practice

It is still too soon to recommend using statins for diabetes prevention. However, the possibility that pravastatin may reduce risk of developing diabetes merits further investigation.

References

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