

Is It Time for a Combination Antihyperglycemic-Statin Pill?

Jennifer B. Marks, MD, FACP, FACE, CDE, Editor

Cardiovascular disease (CVD) associated with type 2 diabetes is undoubtedly multifactorial, with significant risk attributable to oft-associated conditions hypertension and dyslipidemia and, to an as yet undefined extent, hyperglycemia. However, recently published results from the data analysis of the diabetic subgroup of the Heart Protection Study (HPS),¹ summarized by Ronald B. Goldberg, MD, in the “Landmark Studies” department of

this issue (p. 151), clearly highlight the tremendous risk for CVD conferred by diabetes regardless of other risk factors.

The nearly 6,000 diabetic individuals in this study are in a category of patients who may or may not have been considered candidates for statin therapy by their own physicians. Yet those individuals randomized to simvastatin had significantly reduced vascular event rates compared with a placebo group, regardless of the presence of a number

of other CVD risk factors, including vascular disease, hypertension, longer duration of diabetes, or older age. Most remarkably, benefit was demonstrated even in patients whose LDL cholesterol levels were < 116 mg/dl at study entry.

Current treatment guidelines for diabetes management do not generally recommend initiation of a statin unless LDL levels are elevated > 129 mg/dl, although it remains a treatment option with LDL levels in the range of

100–129 mg/dl.² Even in high-risk patients with diabetes, the utilization of statins in clinical practice is not the norm. According to the most recent National Cholesterol Education Program Adult Treatment Panel report, fewer than half of those who qualify for lipid-lowering treatment are receiving it, and less than one-third of those achieve their LDL goal.²

Was the benefit of simvastatin to patients in the HPS a result of aggressive LDL-lowering or some extra lipid-lowering effect of the statins? Do the results suggest that it is time to rethink what defines CVD risk in diabetic individuals and how that risk can most effectively be reduced? The results of the HPS strongly suggest that we should be more aggressive with our

diabetic patients and give serious consideration to initiating statin therapy irrespective of LDL level, particularly since, by definition, these patients have a condition with equal risk to that of established CVD.

Is it time for a combination anti-hyperglycemic-statin pill?

To paraphrase Dr. Goldberg's comments about lowering cholesterol, we just don't really know "how low to go." Is 99 mg/dl low enough? Perhaps not. For that matter, do we really know how low blood pressure levels or hemoglobin A_{1c} results should be? Perhaps we've not been aggressive enough toward reducing all of our patients' modifiable risk factors for CVD. Perhaps the answer is as simple as, "the lower the better."

REFERENCES

¹The Heart Protection Study Collaborative Group: MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5,963 people with diabetes: a randomized placebo-controlled trial. *Lancet* 361:2005–2016, 2003

²National Institutes of Health: Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Bethesda, Md., National Institutes of Health, 2001. NIH Publ. No. 01-3670

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