Letter

Diabetes Metab J 2011;35:86-87
doi: 10.4093/dmj.2011.35.1.86
pISSN 2233-6079 · eISSN 2233-6087

dmj
DIABETES & METABOLISM JOURNAL

A Retrospective Study on the Efficacy of a Ten-Milligram Dosage of Atorvastatin for Treatment of Hypercholesterolemia in Type 2 Diabetes Mellitus Patients (*Korean Diabetes J* 2010;34:359-67)

Eun-Jung Rhee

Division of Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea

Hypercholesterolemia is a major cardiovascular risk factor. Type 2 diabetes patients tend to have high risk for cardiovascular disease not just due to hypercholesterolemia, but also due to dyslipidemia composed of hypertriglyceridemia and low high density cholesterol lipoprotein cholesterol (HDL-C) levels caused by insulin resistance [1]. Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (statin) is the drug of choice for the treatment of hypercholesterolemia. The American Diabetes Association recommends lowering low density lipoprotein cholesterol (LDL-C) levels to less than 100 mg/dL in diabetes patients, preferably through statin administration [2].

In the last issue of *Korean Diabetes J*, Kim et al. [3] reported a retrospective study of the efficacy of 10 mg atorvastatin in 105 Korean type 2 diabetes patients. They found that the response rate to 10 mg atorvastatin was 74.3% in the first 6 months of treatment, and that the response rates in three subgroups of responder groups divided by dosage were in compliance with the dosage. Interestingly, the average LDL-C levels and body mass indexes (BMIs) of the responder group were significantly lower than those of the non-responder group. In non-responders, when the dosage was doubled to 20 mg, the response rate increased from 28.6% to 50%. Kim et al. therefore found that 10 mg atorvastatin, which is one of the most often prescribed statin dosage regimens in Koreans, significantly lowered LDL-C levels in type 2 diabetes patients within 6 months. They showed that the baseline risk factors that correlated with the response were LDL-C levels and BMI, which supports reflects the association of obesity with statin response in their study sample. They also showed that the response rate for the 5-year follow-up period was 71.4% in a small proportion of the patients followed up, although the absolute number of patients was too small to draw any conclusions.

Although it yielded interesting results, the study by Kim et al. left several questions to be answered. First of all, their study lacks power because it did not include actual drug compliance in considerations of efficacy. This may decrease confidence regarding their results, since adherence and persistence are strongly associated with the effects of statin and hence, with clinical outcomes [4]. For example, in diabetes patients with and without cardiovascular disease, nonadherence (<80%) resulted in significantly increased risks of hospitalization (odds ratio [OR], 1.39) and all-cause mortality (OR, 2.07) [5]. Not taking adherence and compliance into consideration makes the results of their study tenuous.

Kim et al. recommended that although three quarters of

Corresponding author: Eun-Jung Rhee
Division of Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, 108 Pyeong-dong, Jongno-gu, Seoul 110-746, Korea
E-mail: hongsiri@hanmail.net

their patients showed efficacy under 10 mg fixed dose regimens of atorvastatin with lowered LDL-C levels in 6 months, significant numbers of patients required higher starting and maintenance dosages. As they mentioned in their discussion, pharmacogenetic differences in drug response may exist between different populations. Asian patients frequently have heightened responses to therapeutic drugs [6]. As a consequence, recommended drug doses are often lower in Asian countries. Among the explanations cited as the reasons for the differences is their smaller body size; but body size appears to have little effect on statin response in Asians [7]. The results of Kim et al.'s study must be interpreted considering population-specific differences in drug metabolism [6]. In addition, the size of the whole study sample was relatively small, and so was the number of patients followed up for 6 months. This could be one of the biggest pitfalls in making the conclusion from the study. The authors also did not consider switching to other statins as an alternative for non-responders. Certainly, structural differences in different statins affect their efficacy for the prevention of cardiovascular disease, since the LDL-C lowering effect is not the only anti-atherosclerotic effect of statin [8]. Before considering elevation of statin dosage in non-responders, these other factors should be considered.

Another interesting result of Kim et al.'s study was that the average BMI of the responder group was significantly lower than that of the non-responder group. Several previous studies showed the effect of obesity on HDL-C levels [9-11]. However, there are few studies exploring the direct effects of obesity on the LDL-C lowering action of statin. The poor response to statin therapy in patients with high BMIs might not be due simply to greater fat mass, but also due to higher insulin resistance and more severe dyslipidemia leading to high triglyceride and apolipoprotein B levels. Comparisons of the LDL-C lowering effects of statin between groups with high and low BMIs should be performed alongside concurrent analyses of triglyceride and HDL-C levels.

Although their results require further discussion, Kim et al.'s study is important because the LDL-C lowering effects of 10 mg atorvastatin regimens, which is one of the most often prescribed statin regimens in Korea, was assessed for relatively long duration of follow-up period in Korean type 2 diabetes patients. I greatly appreciate the efforts of the authors in performing such an interesting study and in publishing their work in this journal.

REFERENCES

1. Dunn FL. Management of dyslipidemia in people with type 2 diabetes mellitus. Rev Endocr Metab Disord 2010;11:41-51.
2. American Diabetes Association. Standards of medical care in diabetes--2009. Diabetes Care 2009;32 Suppl 1:S13-61.
3. Kim DK, Lee SR, Kim MS, Bae SH, Hwang JY, Kim JM, Suh SH, Lee HJ, Park MK, Kim DK. A retrospective study on the efficacy of a ten-milligram dosage of atorvastatin for treatment of hypercholesterolemia in type 2 diabetes mellitus patients. Korean Diabetes J 2010;34:359-67.
4. Simpson RJ Jr, Mendys P. The effects of adherence and persistence on clinical outcomes in patients treated with statins: a systematic review. J Clin Lipidol 2010;4:462-71.
5. Ho PM, Rumsfeld JS, Masoudi FA, McClure DL, Plomondon ME, Steiner JF, Magid DJ. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. Arch Intern Med 2006;166:1836-41.
6. Liao JK. Safety and efficacy of statins in Asians. Am J Cardiol 2007;99:410-4.
7. Morales D, Chung N, Zhu JR, Sangwatanaroj S, Yin WH, Lee K, Davies MJ, Shah A, Loeys T, Bilheimer D. Efficacy and safety of simvastatin in Asian and non-Asian coronary heart disease patients: a comparison of the GOALLS and STATT studies. Curr Med Res Opin 2004;20:1235-43.
8. Arnaboldi L, Corsini A. Do structural differences in statins correlate with clinical efficacy? Curr Opin Lipidol 2010;21: 298-304.
9. Goldberg RB, Guyton JR, Mazzone T, Weinstock RS, Polis AB, Tipping D, Tomassini JE, Tershakovec AM. Relationships between metabolic syndrome and other baseline factors and the efficacy of ezetimibe/simvastatin and atorvastatin in patients with type 2 diabetes and hypercholesterolemia. Diabetes Care 2010;33:1021-4.
10. Shear CL, Franklin FA, Stinnett S, Hurley DP, Bradford RH, Chremos AN, Nash DT, Langendorfer A. Expanded Clinical Evaluation of Lovastatin (EXCEL) study results. Effect of patient characteristics on lovastatin-induced changes in plasma concentrations of lipids and lipoproteins. Circulation 1992;85: 1293-303.
11. Simon JA, Lin F, Hulley SB, Blanche PJ, Waters D, Shiboski S, Rotter JI, Nickerson DA, Yang H, Saad M, Krauss RM. Phenotypic predictors of response to simvastatin therapy among African-Americans and Caucasians: the Cholesterol and Pharmacogenetics (CAP) Study. Am J Cardiol 2006;97:843-50.