

Re-Evaluation of Efficacy of Moderate-Intensity Statins in Korean Patients with Type 2 Diabetes Mellitus


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Statins are competitive inhibitors of 3-hydroxy-3-methylglutaryl-coenzyme A reductase, a rate-limiting enzyme in the cholesterol biosynthesis pathway [1]. Inhibiting cholesterol synthesis reduces secretion of apo-lipoprotein B-containing lipoproteins from the liver and upregulates low density lipoprotein (LDL) receptor activity, resulting in lower plasma LDL cholesterol (LDL-C).

Many clinical trials have consistently demonstrated that lowering LDL-C levels with statins is associated with reduced cardiovascular disease (CVD) event rates [2-5]. Type 2 diabetes mellitus (T2DM) is a risk factor for macrovascular diseases, and controlling dyslipidemia is important for the prevention of CVD. The third report from the National Cholesterol Education Program-Adult Treatment Panel recommends reducing LDL-C levels to <100 mg/dL for primary prevention, and <70 mg/dL for secondary prevention [6]. However, the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines does not recommend a specific target level of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults, but rather recommends the use of a specific statin dose based on its lipid-lowering efficacy from the results of previous clinical trials [7]. However, the treatment guidelines for dyslipidemia from the Korean Diabetes Association suggest an LDL-C target level [8], which has made treatment guidelines for dyslipidemia controversial. One of these debates concerns the appropriate statin and dose to lower lipid levels. Significant ethnic differences and heterogeneity exist in the response to statin, and statin efficacy in Asian populations differs

from that in Caucasians. A lower statin dose than that used in Caucasian populations can be used to achieve a similar therapeutic effect in Asian populations. Japanese patients who received 5 mg of simvastatin daily for 6 months decreased their LDL-C level by 26%, which was similar to the effect of 20 mg of simvastatin daily in Western studies [9]. Another Asian study showed that patients who received 10 mg of atorvastatin or simvastatin reduced their LDL-C levels by 42.5% and 34.8%, respectively [10]. However, higher doses are required for similar LDL-C reductions in Caucasians. Few studies have compared the efficacy among statins in Korean patients [11]. Committee of clinical practice guideline [8] reported that a moderate-intensity statins was sufficient to achieve the target LDL-C level recommended by the Korean Diabetes Association. Kong et al. [12] supported the difference in statin efficacy in Korean when compared to Caucasian. Kong et al. [12] evaluated the efficacy of the moderate-intensity statins among Korean patients with T2DM. The study results showed that about 92.1% of patients with T2DM taking a moderate-intensity statin achieved the target LDL-C level (<100 mg/dL). Furthermore, after treatment with moderate-intensity statins for 6 months, 38.3% of the patients had reductions in their LDL-C levels by between 30% and 50%, and 42.3% of the patients had a reductions in their LDL-C levels by greater than 50% from their baseline levels [12]. These LDL reductions were higher than those observed in Caucasians [13]. As mentioned by the authors, the discrepancy in the efficacy of statins between Asians and Caucasians has been reported previously. A genetic differ-

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ence in statin metabolism could explain this ethnic difference in LDL-lowering efficacy of statins [14]. Polymorphisms in the cytochrome P450 family of enzymes or drug target receptors are associated with differences in drug pharmacokinetics and pharmacodynamics [14]. Actually, some Asians metabolize statins slower, leading to higher plasma statin concentration [15,16]. These differences in drug pharmacokinetics and pharmacodynamics could result in inter-subject variability within the same ethnic group. Kong et al. [12] also showed that 19.4% of participants achieved < 30% reduction in their LDL-C levels after taking a moderate-intensity statins, whereas others achieved a greater reduction in their LDL-C levels. Although differences in age, comorbid conditions, physical activity, or socioeconomic status may lead to a different statin efficacy, the difference in drug response could cause this difference in statin efficacy [15,16].

The different responses to statins raise concerns about an increased risk for adverse events, because most adverse effects from statins are dose-related [14,15]. However, no increase in the frequency of adverse events has been reported in Asian patients taking lower or higher doses of a statin [17,18]. Kong et al. [12] also reported few adverse events including musculoskeletal and hepatic adverse events during the use of a moderate-intensity statins.

The 2013 ACC/AHA guidelines use the 10-year atherosclerotic CVD risk for choosing the initial statin and dose [7]. Dyslipidemia-related mortality and the reduction in CVD frequency after dyslipidemia differ between Asians and Caucasians [19,20]. The ACC/AHA guidelines recommended the use of a moderate- to high-intensity statins in patients with T2DM. However, studies based on the ACC/AHA guidelines included a limited number of Asian subjects. Many studies have reported differences in statin efficacy, and Kong et al. [12] also showed that the LDL-lowering effects of statin in Korean differ from those in Caucasians, indicating that a lower intensity statin could be sufficient to reduce CVD risk in Korean subjects. Further studies are needed to develop guidelines that reflect the actual CVD risk in Korean subjects with dyslipidemia and the appropriate statin for reducing their CVD risk.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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