Matters of Controversy Regarding Lipid Therapy for Japanese Patients with Coronary Artery Disease

Maki Komiyama¹, Hiromichi Wada² and Koji Hasegawa²

Key words: lipid disorder, coronary artery disease


The efficacy of lowering serum low-density lipoprotein-cholesterol (LDL-C) for the primary and secondary prevention of arteriosclerotic cardiovascular disease (CVD) has been confirmed, and the Japan Atherosclerosis Society Guidelines recommend an LDL-C level of less than 100 mg/dL for coronary disease patients. Meanwhile, it has been shown that more intensive lowering of LDL-C further reduces the occurrence of ischemic cardiac events (1). Accordingly, in the United States lipid-control guidelines of the National Cholesterol Program, Adult Treatment Panel III recommend LDL-C reduction up to 70 mg/dL in high-risk cases of ischemic heart disease. In Western countries, however, the number of obese patients is high, and in patients with obesity, there is weakening of statin-induced plaque regression effects (2). In fact, Japanese patients, with their low rate of obesity, demonstrate more favorable reaction characteristics to statins (3). Even at the same cholesterol levels, compared with patients in Europe and North America, Japanese individuals have extremely low rates of myocardial infarction (4). As such, Japanese patients differ in many points from their Western counterparts, and there exists no verification of the effects of aggressive LDL-C lowering up to 70 mg/dL in Japanese individuals. In Japan, there is a need to establish clear and appropriate control targets.

It has been reported that high-density lipoprotein-cholesterol (HDL-C) hypocholesterolemia also heightens the risk of CVD, and even sporadic HDL-C hypocholesterolemia increases CVD risks (5). HDL-C has numerous anti-arteriosclerotic effects, including the following: HDL-C extracts cholesterol from foamy cells and performs reverse cholesterol transport to the liver, HDL-C has anti-inflammatory, anti-oxidative and anti-thrombotic effects and HDL-C repairs endothelial cells and promotes nitric oxide production within endothelial cells, etc. In research reported within this Journal (6), Endo et al. showed that, as the result of a multivariate analysis of risk factors leading to revascularization following percutaneous coronary intervention (PCI), a high LDL-C/HDL-C ratio is the strongest independent factor. That is, by sufficiently lowering the LDL-C/HDL-C ratio, the possibility of suppressing the progression of post-PCI coronary atherosclerosis is suggested. As to the target value for LDL-C/HDL-C ratio control with the purpose of suppression/regression of atherosclerosis, a ratio of 2.0 or lower is recommended for primary prevention, while a ratio of 1.5 or lower is recommended for secondary prevention. Among patients with metabolic syndrome or diabetestes, in many cases, an increased level of small dense LDL is observed due to increased insulin resistance; in such cases, the HDL-C level is low and the LDL-C level does not increase. Further evidence must be established in the future concerning the LDL-C/HDL-C ratio.

The results of the study by Endo et al. also showed that, in patients with diabetes, even when control was performed such that the LDL-C level was <100 mg/dL, the percentage of cases resulting in revascularization was high. Therefore, there is a possibility that controlling the LDL-C value to below 100 mg/dL may not be sufficient in diabetes patients. Another possibility is that residual CVD risks other than LDL-C are not sufficiently controlled. It has been reported that, in patients receiving intensive statin therapy, further increases in the HDL-C level induced by niacin do not elicit incremental clinical benefits (7). Therefore, a distinctive answer must be found as to identifying the target among residual CVD risks factors in high-risk patients, such as those with diabetes. Furthermore, the effects of blood glucose control on CVD have yet to be clearly determined. In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, drastic lowering of blood glucose via intensive therapy increased total mortality (8). At present, it has not been sufficiently established whether blood glucose...
control predominates in major vascular disorders or in total mortality. An absolutely essential task for suppressing the risk of CVD in diabetes patients is to establish total, standardized therapies that include controlling blood pressure, blood glucose and lipids.

The authors state that they have no Conflict of Interest (COI).

References


© 2014 The Japanese Society of Internal Medicine
http://www.naika.or.jp/imonline/index.html