The official journal of the Japan Atherosclerosis Society and
the Asian Pacific Society of Atherosclerosis and Vascular Diseases

Editorial

J Atheroscler Thromb, 2019; 26: 406-407. http://doi.org/10.5551/jat.ED107

Cholesterol and Inflammation in Stroke Recurrence

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See article vol. 26: 432-441

It has been widely understood that the clinical event risk in atherosclerotic cardiovascular disease (ASCVD) is associated with the serum levels of both low-density lipoprotein (LDL) cholesterol and C-reactive protein (CRP). Inflammatory process is involved in the initiation of atherosclerosis and in the instability of atherosclerotic plaque. Lipid lowering therapy may reduce both LDL cholesterol and CRP levels and can suppress the clinical events of ASCVD. In Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER) trial, rosuvastatin reduced the cardiovascular event in the group with lower levels of both LDL cholesterol and CRP to a greater extent than in the group with higher levels[1, 2]. Similar cumulative effect was reported in Improved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) trial, which investigated the effect of simvastatin and ezetimibe combination therapy on cardiovascular events in acute coronary syndrome[3]. In these studies, stroke was also suppressed by LDL cholesterol and CRP lowering therapies[4, 5].

Recently, the Japan statin treatment against recurrent stroke (J-STARS), a multicenter randomized trial, showed that pravastatin could reduce recurrent stroke in patients with a history of atherothrombotic infarction[6]. Additionally, it was also revealed that CRP level was decreased by statin treatment[7]. The question that arises is regarding the association of CRP reduction with the suppression of stroke recurrence independent of LDL cholesterol in patients with prior stroke and whether this association is similar to that in other high-risk patients. Kitagawa *et al*. have reported regarding this point in this issue[8]. They investigated the effect of the level of LDL cholesterol and CRP on recurrent stroke and transient ischemic attack (TIA) in 1077 subjects participating in J-STARS. All patients were divided into lower (<120 mg/dL) or higher LDL cholesterol group and lower (<1 mg/L) or higher CRP group. The lower LDL cholesterol group and the lower CRP group showed 29% and 32% reduction in recurrent stroke and TIA than the higher group, respectively. These two factors contributed to stroke recurrence independently. Patients with both lower LDL cholesterol and CRP showed 51% reduction in recurrent stroke and TIA than patients with both higher LDL cholesterol and CRP. These results clearly demonstrated the cumulative effect of lowering the levels of LDL cholesterol and CRP on prevention of stroke recurrence.

The next clinical question to be clarified is the establishment of the optimal target value for the levels of LDL cholesterol and CRP in the lipid-lowering therapy for the prevention of stroke recurrence. Intensive lipid-lowering therapy may be recommended in high risk ASCVD. Proprotein convertase subtilisin/kexin type 9 inhibitors can be used to achieve lower LDL cholesterol level[9]. It should be assessed whether the intensively lower LDL cholesterol level can contribute to better outcomes in patients with prior stroke. Anti-inflammatory drugs, such as anti-interleukin 1β antibody canakinumab, may be utilized to suppress the remaining inflammation. Canakinumab can prevent cardiovascular events in patients with prior myocardial infarction and sustained higher CRP level, regardless of LDL cholesterol level[10]. It has not been assessed yet whether anti-inflammatory drugs can contribute to prevent stroke recurrence in patients with high CRP level even if LDL cholesterol level is markedly low. Regarding the levels of LDL cholesterol and CRP, is "the lower, the better" to prevent stroke recurrence? Can treatment for dual target add to the benefits? Further assessment is required to answer these clinical questions.

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Received: December 1, 2018 Accepted for publication: December 3, 2018

Conflict of Interest

Yoshiki Yagita reports honoraria from Daiichi Sankyo Co., Ltd and Sanofi K.K., and research grant from Bayer Yakuhin, Ltd,

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