Statins and Gender-Related Difference in Endothelial Function in Cerebral Small Vessel Disease

To the Editor:

We read with great interest the article by Dr Lavallée and colleagues dealing with the effect of the high dose of statin administration on cerebral vasoreactivity in patients with cerebral small vessel disease. The results of their study demonstrated that 3-month treatment with 80 mg atorvastatin per day did not significantly improve brachial and carotid artery endothelium-dependent vasodilatory responses in patients with recent lacunar stroke. The authors also indicated that the same dose of atorvastatin markedly reduced the low-density lipoprotein cholesterol and high-sensitivity C-reactive protein in these patients. The authors propose that, despite a significant reduction in low-density lipoprotein cholesterol and high-sensitivity C-reactive protein, there is no positive evidence indicating that a high dose of statin might restore the cerebral microvasculature endothelial dysfunction in patients with cerebral small vessel disease.

Numerous studies have shown that estrogen may have beneficial effects on circulatory functions. One of the mechanisms underlying the protective effect of estrogen may be the enhancement of nitric oxide production. There is evidence showing that vascular endothelial function is markedly influenced by estrogen which is converted from testosterone by aromatase, and improved by hormone replacement therapy in postmenopausal women.

In an in vitro study presented earlier, we demonstrated that 17β-estradiol increased membrane fluidity (a reciprocal value of membrane microviscosity) of erythrocytes and improved the rigidity of cell membranes in postmenopausal women through the nitric oxide-dependent mechanism. Because abnormalities in membrane microviscosity could cause a disturbance in rheological behavior and microcirculation, estrogen deficiency could be involved in the pathogenesis of vascular complications in women. Recently, the role of estrogen in male physiology has also become evident, and normal physiological estrogen, which is converted from testosterone by aromatase, may confer cardiovascular benefits for men.

In this context, we speculate that changes in nitric oxide production by sex hormones might modify the effects of statin on endothelial function in patients with lacunar stroke. It was demonstrated that when a low dose of simvastatin was administered to the hypercholesterolemic patients, the incidence of the coronary events was lower in women than in men. Therefore, we would like to know whether gender difference might be related to the magnitudes of the restored endothelial function by the statin in the present study of Dr Lavallée and colleagues. It would be important to assess more precisely the relationships among the statin effect, sex hormone status, and nitric oxide production as well as their contribution to the improvement of endothelial function in patients with cerebral small vessel disease.

Disclosures

None.

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