Asymmetric Dimethylarginine and Hypertension in Cerebral Small Vessel Disease

To the Editor:

We read with great interest the recent article by Khan et al dealing with the relationship between the endogenous nitric oxide (NO) synthase inhibitor, asymmetric dimethylarginine (ADMA), and cerebral small vessel disease (SVD). The results of their study demonstrated that the plasma ADMA levels were elevated in SVD and significantly correlated with leukoariosis severity. They also indicated that there was no correlation between plasma ADMA and homocysteine levels. The authors proposed that ADMA might be independently associated with SVD and mediate small perforator damage, contributing leukoariosis.

Many studies have focused on the vascular protective effects attributable to NO and have shown that hypertension as well as vascular dysfunction may be associated with impaired NO metabolism. In the separate series of the study, the colleagues of the authors directly demonstrated that intravenous infusion of ADMA decreased heart rate and cardiac output, and increased mean blood pressure in humans. It was also shown that ADMA increased systemic vascular resistance and blood pressure in a dose-dependent manner in healthy volunteers. However, it was demonstrated that inhibition of NO bioavailability by ADMA and a subsequent reduction in endothelial function might contribute to the increase in blood pressure during salt intake in normotensive postmenopausal women not receiving estrogen. In a study presented recently, we showed that the plasma ADMA levels were increased in hypertensive subjects compared with normotensive subjects, suggesting that the higher plasma ADMA levels might be accompanied by hypertension and vascular dysfunction. In addition, we demonstrated that membrane fluidity of erythrocytes (a reciprocal value of membrane microviscosity) in hypertensive subjects was associated with decreased NO metabolite and increased ADMA levels in plasma. The findings might suggest that NO and ADMA might have a crucial role in the regulation of rheologic behavior of cell membranes. The reduction in membrane fluidity of erythrocytes by ADMA might cause a disturbance in the microcirculation, which would contribute, at least in part, to the circulatory disorders.

In this context, it can be speculated that in SVD patients with higher ADMA levels, hypertension-induced endothelial dysfunction might be more pronounced. Although the authors mentioned that the prevalence of hypertension and other vascular risk factors was not different between SVD and control groups, we would like to know whether the magnitude of blood pressure might be correlated with the plasma ADMA levels or leukoariosis severity in SVD patients. It would be important to assess more precisely the mechanisms underlying the ADMA effects and their contribution to the pathophysiology of SVD.

Disclosures

None.

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