Asymmetric Dimethylarginine and Hypertension in Carotid Artery Disease

To the Editor:

We read with great interest the recent article by Maas and colleagues1 dealing with the relationships between endogenous nitric oxide (NO) synthase inhibitor, asymmetrical dimethylarginine (ADMA), and carotid artery intimal media thickness. The results of their study demonstrated that higher plasma concentrations of ADMA were associated with greater internal carotid artery/bulb intima media thickness but not with greater common carotid artery intima media thickness in a large community-based sample. The authors proposed that ADMA might promote subclinical atherosclerosis in a site-specific manner and serve as a biomarker for carotid artery disease.

Numerous 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. It was demonstrated that intravenous infusion of ADMA decreased heart rate and cardiac output and increased mean blood pressure in humans.2 It was also shown that ADMA increased systemic vascular resistance and blood pressure in a dose-dependent manner in healthy volunteers.3 On the other hand, Scuteri et al4 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,5 suggesting that the higher plasma ADMA levels might be accompanied by hypertension and vascular dysfunction. In addition, we showed 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.6 The findings might suggest that NO and ADMA might have a crucial role in the regulation of rheological behavior of cell membranes. The reduction in membrane fluidity of erythrocytes by ADMA could cause a disturbance in the microcirculation, which might contribute to the pathophysiology of circulatory disorders.

In this context, it can be speculated that in subjects with carotid artery disease with higher ADMA levels, hypertension-induced endothelial cell dysfunction might be more pronounced. Although the authors analyzed the role of ADMA in carotid atherosclerosis after adjusting the systolic blood pressure, we would like to know whether the magnitude of blood pressure and the indices of endothelial functions such as plasma and urinary NO metabolites or flow-mediated dilatory responses of the brachial artery might be related to the plasma ADMA levels or carotid artery disease severity in the study of Maas and colleagues. It would be important to assess more precisely the mechanisms underlying the ADMA effects and their contribution to the pathophysiology of carotid artery atherosclerosis.

Disclosures

None.

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*Stroke*. 2009;40:e703; originally published online October 29, 2009; doi: 10.1161/STROKEAHA.109.563973

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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