Asymmetric Dimethylarginine and Cerebrovascular Disorders in Humans

To the Editor:

We read with great interest the recent article by Dr Kielstein and colleagues1 dealing with the cerebrovascular effects of the endogenous nitric oxide (NO) synthase inhibitor, asymmetric dimethylarginine (ADMA), in humans. The results of their study demonstrated that systemic infusion of ADMA increased arterial stiffness and decreased total cerebral perfusion independent of blood pressure changes. The authors proposed that ADMA modulated vascular compliance and decreased cerebral blood flow and might be involved in the pathogenesis of cerebrovascular diseases in humans.

There is evidence that ADMA may actively participate in the regulation of vascular functions. It was shown that intravenous infusion of ADMA decreased heart rate and cardiac output and increased mean blood pressure in humans.2 In the separate series of the study,3 Dr Kielstein and colleagues also demonstrated that infusion of ADMA caused a decrease in cardiac output with compatible decrease in effective renal plasma flow in healthy volunteers. In addition, ADMA increased systemic vascular resistance and blood pressure in a dose-dependent manner.3 Dr Kielstein proposed that ADMA might have definite effects on cardiovascular and renal function in human subjects. On the other hand, 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.4 Similarly, it was reported that there was a significant inverse correlation between plasma ADMA and flow-mediated dilatation of the brachial artery, indicating that ADMA might be related to a decline in endothelial vasodilator function.5 In a study presented earlier, we showed that NO-induced improvement of membrane fluidity of red blood cells (RBCs; a reciprocal value of membrane microviscosity) was counteracted by ADMA.6,7 In addition, we showed that amelioration in membrane fluidity of RBCs was associated with higher NO metabolite and lower ADMA levels in plasma.8 The findings might suggest that NO and ADMA might have a crucial role in the regulation of rheologic behavior of cell membranes and microcirculation. The reduction in membrane fluidity of RBCs by ADMA could cause a disturbance in the blood rheologic behavior and in the microcirculation, which might contribute to the pathophysiology of circulatory disorders. In this context, it can be speculated that in humans with higher ADMA levels, endothelial dysfunction is more pronounced. Therefore, we would like to know whether endothelial function (flow-mediated dilatation of the brachial artery) or plasma NO metabolite levels might be correlated with the changes in the cerebral blood flow and the augmentation index in the study of Dr Kielstein and colleagues. The precise role of ADMA in the pathogenesis of cerebrovascular diseases is still unclear. It would be important to assess more precisely the mechanisms underlying the ADMA-effects and their contribution to the pathophysiology of cerebrovascular diseases in human subjects.

Disclosures

None.

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