Letter by Tsuda Regarding Article, “Low Plasma Arginine:Asymmetric Dimethyl Arginine Ratios Predict Mortality After Intracranial Aneurysm Rupture”

To the Editor:

We read with great interest the article by Staalsø et al pertaining to the relationship between asymmetrical dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide (NO) synthase, and survival in patients with aneurysmal subarachnoid hemorrhage. The results of their study demonstrated that a low arginine:ADMA ratio in the first week after subarachnoid hemorrhage predicted mortality rate in the first 30 days. The arginine:ADMA ratio was negatively correlated with the serum NO-metabolite levels. In addition, the arginine:ADMA ratio was higher in good grade patients, but did not change significantly overtime. The authors proposed that plasma arginine:ADMA ratio might be associated with the pathophysiology in the subacute phase after subarachnoid hemorrhage, affecting the mortality rate possibly through modulation of cerebral blood flow. Evidence indicates that NO may actively participate in neuroprotection in cerebral ischemia. In a study presented previously, we investigated the relationship between NO and membrane fluidity (a reciprocal value of membrane microviscosity) of red blood cells by means of an electron spin resonance method. Reduced membrane fluidity of red blood cells might cause a disturbance in the blood rheological behavior and microcirculation, which could contribute, at least in part, to the pathophysiology of circulatory disorders. We demonstrated that an NO donor increased membrane fluidity of red blood cells and improved the rigidity of cell membranes in hypertensive and normotensive subjects. In the separate series of the study, we reported that reduced membrane fluidity of red blood cells was associated with decreased NO-metabolites and increased ADMA levels in plasma. The findings might support the hypothesis that NO would be a defense against vascular complications in circulatory disorders, which would be in accordance with the present result of Staalsø et al.

Recently, it has been shown that not only ADMA, but also its analogue symmetrical dimethylarginine (SDMA) might have a pivotal role in the progression of stroke. It was reported that higher SDMA levels in the cerebrospinal fluid were correlated with a poor outcome at 3 months after stroke onset. Worthmann et al demonstrated that an increase of both plasma ADMA and SDMA levels within the first 72 hours after the onset of ischemic stroke may predict a poor outcome. In this context, it is strongly suggested that both ADMA and SDMA could be the biomarkers referring to endothelial dysfunction and disturbed cerebrovascular circulation. Therefore, we would like to know whether SDMA alone, or in combination with ADMA and arginine, might have a predictive value for the outcome of subarachnoid hemorrhage in the study of Staalsø et al. It would be important to assess more precisely the relationships between endogenous NO synthase inhibitors and circulatory dysfunction in the brain, and their role in determining the outcome of cerebrovascular disorders.

Disclosures

None.

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