Asymmetric Dimethylarginine and DDAH1 Transcript Variants in Cardiovascular and Cerebrovascular Diseases

Kazushi Tsuda¹

To the Editor: We read with great interest the article “Correlations of DDAH1 Transcript Variants With Human Endothelial Asymmetric Dimethylarginine Metabolizing Activity”¹ by Sun and colleagues, which deals with the relationship between the activity of asymmetric dimethylarginine (ADMA; an endogenous nitric oxide synthase inhibitor) and its degradation enzyme (dimethylarginine dimethylaminohydrolase 1 (DDAH1)) transcript variants in humans. The results of their study demonstrated that mRNA expression levels of DDAH1 transcript variant DDAH1-V3 correlated significantly with that of both DDAH1-V2 and DDAH1-V1 in human umbilical vein endothelial cells. In peripheral blood mononuclear cells from healthy subjects, significant correlation was observed between DDAH1-V2 and DDAH1-V3. In addition, the authors indicated positive pairwise correlations between mRNA levels of DDAH1 transcripts in peripheral blood mononuclear cells from patients with acute ischemic stroke and acute myocardial infarction. However, only mRNA expression level of the DDAH1-V1 transcript correlated significantly with intracellular ADMA-metabolizing activity in human umbilical vein endothelial cells. The authors proposed that DDAH1-V1 transcript might be responsible for ADMA metabolism.

Current evidence indicates that ADMA might actively participate in the pathophysiology of cardiovascular and cerebrovascular diseases. In a study presented previously, we demonstrated that plasma ADMA levels were significantly higher in hypertensive subjects than in normotensive subjects.² In contrast, plasma nitric oxide (NO) metabolite levels were decreased in hypertensive subjects compared with normotensive subjects. Furthermore, we showed that impaired membrane microviscosity of red blood cells might be associated with increased ADMA and decreased NO metabolite levels, suggesting that ADMA could contribute, at least in part, to the microcirculatory disorders in hypertension.² Worthmann et al.³ demonstrated that an increase of plasma ADMA within 72 hours after onset of ischemic stroke might predict a poor outcome. It was also reported that higher levels of ADMA were strongly associated with lower levels of high-density lipoprotein cholesterol in patients with myocardial infarction.⁴ Because DDAH1 degradation of ADMA might help against cardiovascular disease in which ADMA levels are elevated,⁵ we would like to know whether plasma ADMA levels might be altered in patients with ischemic stroke and myocardial infarction during the clinical stages of the diseases and whether mRNA expression levels of DDAH1 transcript variants might precede or correlate with the changes in plasma ADMA levels in these patients in the study of Sun and colleagues. It would be important to assess more precisely the relationships between plasma ADMA levels and DDAH1 transcript variants and their role in the progression of endothelial dysfunction in cardiovascular and cerebrovascular diseases.

DISCLOSURE

The author declared no conflict of interest.

REFERENCES


Correspondence: Kazushi Tsuda (tsudak@mail.wakayama-med.ac.jp).

¹Cardiovascular Medicine, Cardiovascular and Metabolic Research Center, Kansai University of Health Sciences, Osaka, Japan.

Initially submitted November 16, 2013; date of first revision November 22, 2013; accepted for publication November 25, 2013; online publication January 27, 2014.
doi:10.1093/ajh/hpt242

© American Journal of Hypertension, Ltd 2014. All rights reserved. For Permissions, please email: journals.permissions@oup.com