Response to Letter by Tsuda

We thank Dr Tsuda for the interest in our article on the effects of acute ADMA infusion on vascular stiffness and cerebral perfusion and for expanding the discussion on ADMA beyond the well established effects of ADMA on different vascular beds in humans.\(^1\) Although not part of our study, the interaction between corpuscular blood components and the endothelium are important because they influence the microcirculation. Preclinical and clinical data suggest that ADMA is able to influence properties and behavior of corpuscular blood components. Dr Tsuda and his group showed that elevated ADMA levels in hypertensive men are associated with lower membrane fluidity of erythrocytes.\(^2\) Kang et al\(^3\) reported that ADMA is metabolized in human erythrocytes. In a very elegant study Billecke et al\(^4\) recently analyzed in detail how the whole blood, a 5-kg constantly moving tissue (in a 70-kg human), contributes to the regulation of ADMA levels. Rat erythrocytes were not only able to hydrolyze ADMA but also to liberate large amounts of ADMA. But also white leukocytes are affected by ADMA. When Chan et al cocultured monocytes with ADMA, exposed endothelial cells became hyperadhesive.\(^5\) These data suggest that ADMA may simultaneously increase vascular adhesion and vasoconstriction with adverse consequences on vascular patency.

A secondary analysis of our data, which Dr Tsuda asked for, showed that there was a weak correlation between baseline total cerebral blood flow and baseline ADMA levels \(r^2=0.261, P=0.025\) and a stronger correlation between ADMA and baseline augmentation index \(r^2=0.316, P=0.015\). The limited number of subjects studied does not, however, allow a meaningful multivariate analysis so that this univariate analysis should be interpreted cum grano salis. ADMA has an irresistible appeal as a biomarker for cardiovascular risk and unifying mediator of atherosclerosis and beautifully fits in our current understanding of the pathophysiology of this multifaceted disease. There is, however, the ultimate test ADMA has to take: reducing ADMA should ideally translate into decreased morbidity and mortality, a lesson the rise and fall of acknowledgement of homocysteine as a cardiovascular risk factor should have taught us.

Disclosures

None.

Jan T. Kielstein, MD
Department of Nephrology
Medical School
Hannover, Germany
Stanford University
School of Medicine

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Jan T. Kielstein, Frank Donnerstag, Sandra Gasper, Jan Menne, Danilo Fliser, Anousheh
Kielstein, Jens Martens-Lobenhoffer, Fortunato Scalera, Stefanie M. Bode-Boger and John
Cooke

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