Response to “Plasma Homocysteine Levels and Endothelial Dysfunction in Cerebro- and Cardiovascular Diseases in the Metabolic Syndrome”

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To the Editor: Tsuda commented on our recently published study in which we reported data obtained in 562 essential hypertensive patients showing that elevated plasma homocysteine levels are associated with the metabolic syndrome. We reported also that increasing homocysteine levels are associated with progressively greater prevalence of coronary heart and cerebrovascular disease. In another study, we have demonstrated that plasma homocysteine is directly related with the carotid artery intima-media thickness in patients with high blood pressure, suggesting a contribution of homocysteine to the earliest stages of the atherosclerotic process. In his letter, “Plasma Homocysteine Levels and Endothelial Dysfunction in Cerebro- and Cardiovascular Diseases in the Metabolic Syndrome,” Tsuda indicates the possibility that endothelial dysfunction and impaired nitric oxide bioavailability might mediate the unoward vascular effects of homocysteine. In fact, experimental studies have suggested many mechanisms that might explain the contribution of elevated circulating homocysteine to promotion of atherogenesis and progression of vascular damage. Among these mechanisms, endothelial damage with impaired endothelial vasodilatory response, proliferation of vascular smooth muscle cell, activation of monocytes and prothrombotic mediators, and lipid peroxidation might play a prominent role. These mechanisms might result from multiple biochemical reactions that are triggered by homocysteine and include auto-oxidation through the production of reactive oxygen species, nitrosylation by binding to nitric oxide, inhibition of transmethylation, and protein homocysteinylation. All these mechanisms are currently under debate and will deserve further investigation.

Therefore, we agree with the comments of Tsuda, although in our study we did not have the opportunity to assess any of the markers of endothelial dysfunction and nitric oxide bioavailability in a reasonable number of patients, taking into account the large sample of recruited subjects and also considering that such assessments were beyond the scopes of our study. Inclusion of such assessments in future studies will surely provide important insight into the mechanisms that cause vascular damage in subjects with elevated plasma homocysteine.

DISCLOSURE

The authors declared no conflict of interest.

REFERENCES