Correspondence

Letter by Tsuda Regarding Article, “Plasminogen Activator Inhibitor-1 Antagonist TM5441 Attenuates No\textsuperscript{-}Nitro-L-Arginine Methyl Ester–Induced Hypertension and Vascular Senescence”

To the Editor:

We read with great interest the article by Dr Boe and colleagues\textsuperscript{1} dealing with the effect of the plasminogen activator inhibitor-1 (PAI-1) antagonist TM5441 in a mouse model with nitric oxide (NO)-deficiency. The results of their study demonstrated that TM5441 attenuated the development of hypertension and cardiac hypertrophy in mice that had received \textsuperscript{\textomega}nitro-L-arginine methyl ester (L-NAME). In addition, TM5441-treated mice had a significant reduction in periaortic fibrosis. Furthermore, the authors showed that TM5441 prevented the decrease in telomere length induced by L-NAME treatment. The authors proposed that PAI-1 inhibition might improve NO production and bioavailability and be a novel approach in preventing vascular aging and hypertension.

Evidence indicates that PAI-1 might strongly be related to leptin, which is expressed in adipose tissue. It was reported that plasma PAI-1 levels were associated with plasma leptin levels, and further demonstrated that leptin per se potentially increased plasma PAI-1 levels in obese subjects.\textsuperscript{2} Recently, Valle Jiménez et al\textsuperscript{3} showed that changes in plasma leptin levels might independently predict changes in plasma PAI-1 levels in obese children. On the other hand, Frühbeck et al\textsuperscript{4} demonstrated that leptin infusion increased blood pressure in rats under NO synthase inhibition, and suggested that leptin might have a balanced effect on blood pressure with a pressor response attributable to sympathetic activation and a depressor response attributable to NO release. In a study presented previously, we also showed that the relaxing effect of leptin on blood vessels was partially mediated by the NO-dependent mechanism.\textsuperscript{5} In this context, we speculate that leptin-induced NO might actively participate in the homeostasis of not only blood pressure but also vascular tone. Therefore, we would like to know whether plasma leptin levels might be altered by the treatment of the PAI-1 antagonist TM5441, and whether leptin-induced NO might relate, at least in part, to the preventing effect of the PAI-1 antagonist against hypertension and vascular damages in the study of Dr Boe and colleagues. Further studies should be required to assess more precisely the interactions of PAI-1 and other adipokines such as leptin, and the mechanisms underlying the preventing effect of the PAI-1 antagonist against vascular disease and arteriosclerosis.

Disclosures

None.

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References


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