Hypoadiponectinemia and Endogenous Nitric Oxide Synthase Inhibitor in Hypertension

To the Editor:

We read with great interest the article by Xing et al1 dealing with the relationship between adiponectin and vascular insulin resistance in hypertension. The results of their study demonstrated that hypoadiponectinemia induced vascular insulin resistance in young spontaneously hypertensive rats. In addition, the authors indicated that downregulation of APPL1 (an adaptor protein that interacts directly with adiponectin receptors by the phosphotyrosine-binding domain) might partially contribute to vascular insulin resistance by differentially modulating the activation of Akt-dependent nitric oxide (NO) and ERK1/2-dependent endothelin-1 pathways in vascular endothelium in spontaneously hypertensive rats. Furthermore, the authors proposed that supplementation with exogenous adiponectin may have potential therapeutic value in the prevention and alleviation of endothelial dysfunction and vascular insulin resistance in hypertension.

Current evidence indicates that adiponectin may improve NO bioavailability and restore endothelial dysfunction. In a study presented previously, we investigated the relationship between plasma adiponectin levels and plasma NO metabolites in hypertensive subjects.2 It was demonstrated that plasma adiponectin levels were significantly correlated with plasma NO metabolites.2 In the separate series of the study, we reported that reduced membrane fluidity of red blood cells was associated with hypoadiponectinemia in hypertensive subjects.3 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. It might be possible that adiponectin would be a defense against vascular complications in circulatory disorders through increased NO production.

However, it has been shown that, in an in vitro study, adiponectin significantly inhibited the tumor necrosis factor-α-induced asymmetrical dimethylarginine (an endogenous NO synthase inhibitor) accumulation in both human umbilical vein endothelial cells and human coronary artery endothelial cells, which was accompanied by an increase in dimethylarginine dimethylaminohydrolase activity.4 Heilman et al5 also have reported the elevated plasma adiponectin and decreased plasma asymmetrical dimethylarginine levels in children with type 1 diabetes mellitus. In this context, it is strongly suggested that adiponectin would protect against endothelial dysfunction, at least in part, by influencing asymmetrical dimethylarginine metabolism. Therefore, we would like to know whether asymmetrical dimethylarginine might actively participate in hypoadiponectinemia-induced alterations in NO signaling and vascular insulin resistance in the study of Xing et al. It would be important to assess more precisely the relationships between adiponectin and endogenous NO synthase inhibitors and their role in the progression of endothelial dysfunction and insulin resistance in hypertension.

Disclosures

None.

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Hypertension. 2013;62:e4; originally published online June 10, 2013;
doi: 10.1161/HYPERTENSIONAHA.113.01641
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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