Leptin and Nitric Oxide in Blood Pressure Regulation in Humans

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To the Editor: We read with great interest the article "Leptin in Association With Common Variants of *MC3R* Mediates Hypertension" by Alsmadi and colleagues[1] dealing with the relationship between polymorphisms of leptin gene and blood pressure levels in humans. The results of their study demonstrated that the *MC3R* missense variant (rs3827103) might be associated with systolic blood pressure in Kuwaiti natives. The N-terminal variant (rs3746619) was in linkage disequilibrium with the rs3827103 variant. The AA halotype of rs3746619–rs3827103 was significantly associated with systolic blood pressure. Furthermore, the authors showed that, in individuals who habor these variants, the plasma leptin levels were correlated with systolic blood pressure. The authors proposed that, because leptin might increase sympathetic nerve activity, the *MC3R* variants in association with leptin levels might mediate hypertension in humans.

Previous studies showed that acute administration of leptin increased plasma nitric oxide (NO)–metabolite concentration in a dose-dependent manner in the rats.[2,3] It was demonstrated that leptin infusion increased blood pressure under NO synthase inhibition and decreased blood pressure with pharmacologically induced ganglionic blockade in the rats.[2] One hypothesis is 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.[2] In regard to this issue, we showed that the relaxing effect of leptin on blood vessels was partially mediated by an NO-dependent mechanism.[4] Furthermore, it was demonstrated that plasma leptin levels were positively correlated with plasma NO metabolites in the overall analysis of normotensive and hypertensive subjects.[5] In this context, it is strongly suggested that leptin-induced NO might have a crucial role in the homeostasis of blood pressure and vascular tone. Therefore, we would like to suggest that plasma leptin levels and *MC3R* variants of leptin might partially be related to endothelial function or plasma NO metabolites in the populations in the study of Alsmadi and colleagues. Further studies should be required to assess more precisely the associations of leptin with both sympathetic nerve activation and NO release and their integrated effects on blood pressure in humans.

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DISCLOSURE

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