Plasma Brain Natriuretic Peptide and N-Terminal Proatrial Natriuretic Peptide Levels in Obese Patients: A Cause or Result of Hypertension?

To the Editor:

We read with great interest the paper by Wang et al. indicating that obese subjects had lower brain natriuretic peptide (BNP) and N-terminal proatrial natriuretic peptide (N-terminal proANP) levels than did lean subjects in a large sample population of the Framingham Heart Study. They speculated that lower BNP levels might result from increased receptors in adipose tissue and that lower natriuretic peptide levels might predispose obese patients to hypertension.

Their results are interesting; however, we question the hypotheses derived from their cross-sectional, observational study. In that study, not only BNP, but also N-terminal proANP was decreased in obese patients, strongly suggesting decreased release of natriuretic peptides from the heart. In addition, a higher proportion of overweight and obese patients received antihypertensive therapy, as compared with patients who had a normal body mass index. The production of natriuretic peptide is known to be affected by medical treatment, including antihypertensive drugs and statins. Furthermore, whether very small differences in natriuretic peptide levels (<5 ng/L) between obese and lean subjects contribute to the development of hypertension is questionable, despite evidence showing that complete gene disruption of the natriuretic peptide system causes hypertension in mice.

Confirmation of the effects of obesity on plasma natriuretic peptide levels would require prospective and interventional studies examining whether reduction in body weight modifies natriuretic peptide levels. We recently investigated the effects of a hypocaloric diet on plasma natriuretic peptide levels in 12 obese patients with essential hypertension (age, 48 to 81 years; body mass index, 26 to 34 kg/m²). A standard diet of 2000 kcal/d was given for 1 week, followed by a hypocaloric diet of 850 kcal/d for 3 weeks. Sodium intake remained constant. The patients lost 3.7±0.2 (mean ± SE) kg of body weight during the hypocaloric diet period (P<0.0001), accompanied by a reduction in systolic blood pressure (10.3±3.6 mm Hg, P=0.02). Plasma BNP and ANP levels decreased significantly from 22.7±5.7 to 16.7±4.5 ng/L and from 22.2±5.0 to 13.4±2.1 ng/L, respectively (P=0.04 for each). McMurray and Vesely also confirmed a dramatic fall in plasma ANP levels after 12 weeks of weight reduction in both obese normotensive and hypertensive subjects. Messaoudi et al. reported that a very low-calorie diet with a constant sodium intake decreased plasma ANP levels in 12 obese subjects over the course of 8 days.

Taken together, these observations suggest that obesity may be associated with plasma volume expansion accompanied by elevated natriuretic peptide levels. Even in obese patients with hypertension, natriuretic peptides may protect against further elevation of blood pressure rather than contribute to the pathogenesis of hypertension.

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Response

We appreciate the interest of Dr Minami and colleagues in our study. We agree that the lower plasma N-terminal proatrial natriuretic peptide levels in obese individuals may implicate nonclearance mechanisms, as N-terminal proatrial natriuretic peptide does not bind to the clearance receptors. We chose to mention both clearance and synthetic/secretory mechanisms because the reduction in plasma natriuretic peptide levels in obese individuals may be multifactorial. We disagree, however, that our findings could be explained by use of antihypertensive medications, for two reasons. First, our primary analyses adjusted for the use of antihypertensive therapy as a covariate. Second, exclusion of individuals on antihypertensive medications did not affect our results.

We agree that the cross-sectional nature of our investigation prevents us from knowing whether a lower plasma natriuretic peptide level precedes or follows obesity. Although several small series suggest that plasma natriuretic peptide levels may go down after weight loss,1–3 these observations are confounded by concomitant reductions in plasma volume and blood pressure, themselves strong determinants of natriuretic peptide levels. Thus, the decrease in natriuretic peptide levels observed in these studies may be the consequence of reductions in plasma volume and blood pressure, rather than changes in adiposity. Dr Minami and colleagues correctly point out that prospective or interventional studies will be necessary to elucidate the complex relations of obesity, natriuretic peptide levels, and hypertension.

Dr Minami and colleagues note that obesity is associated with plasma volume expansion and hypertension. Obesity is also associated with increases in left ventricular wall thickness and dimensions.4 The aforementioned associations would lead to higher plasma natriuretic peptide levels in obese individuals. They fail to explain the primary and somewhat paradoxical finding of our study—that obese individuals have lower plasma natriuretic peptide levels than nonobese individuals.5 Additional studies are certainly needed to understand the mechanisms underlying this observation and the physiological consequences, if any.

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