Adiposity, the Sympathetic Nervous System, and Childhood Primary Hypertension

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Why is it important to understand the pathophysiologic mechanisms underlying primary hypertension in childhood? Two answers immediately come to mind: first, the number of children and adolescents with primary hypertension seems to be increasing; and second, hypertensive children are likely to become hypertensive adults who in turn will be at risk for adverse cardiovascular outcomes. So, despite recent analyses questioning the value of routine assessment of blood pressure in childhood, many feel that with better understanding of the pathophysiology of childhood primary hypertension, it could be possible to develop better strategies to prevent adult cardiovascular disease.

Thus, the study of Niemirska et al in this issue of Hypertension is notable. Using advanced Fourier analysis of ambulatory blood pressure monitoring studies in a small group of adolescent boys with primary hypertension, they demonstrated that abnormalities of cardiovascular rhythms present at the diagnosis of hypertension persisted despite successful blood pressure reduction, and that improvements in blood pressure and heart rate were related to reductions in visceral fat. These findings support the central role of the sympathetic nervous system in the pathophysiology of childhood hypertension and underscore the importance of visceral adiposity as not only an influence on sympathetic nervous system activity but also as a potential target for prevention of adult cardiovascular disease.

Sympathetic nervous system abnormalities are well described in animal models of hypertension and can be seen clinically as well, even in hypertensive children and adolescents. Most mechanistic studies have focused on activation of the sympathetic nervous system as manifested by increased sympathetic nerve activity; such activation seems to be mediated at least in part by cytokines, such as leptin, that are produced by visceral fat (as summarized in the Figure). Although invasive studies of sympathetic nerve activity have not been done in children, clinical studies have demonstrated that obese hypertensive children and adolescents have higher heart rates and increased blood pressure variability on ambulatory blood pressure monitoring than lean hypertensive subjects, both of which are considered indirect markers of increased sympathetic nervous system activity. The correlation between the reduction in heart rate and reduction in visceral fat demonstrated by Niemirska et al is consistent with the animal studies demonstrating modulation of sympathetic nervous system activity by visceral fat.

Ambulatory blood pressure monitoring has also been used to explore more subtle alterations of blood pressure regulation that are seen in pediatric primary hypertension. In a cross-sectional study, hypertensive adolescents were shown to have abnormal blood pressure rhythmicity compared with normotensive patients of similar age, and the abnormalities were more pronounced in obese hypertensive subjects compared with lean hypertensive subjects. The latter finding again suggests that visceral adiposity plays an important modulatory function on the abnormalities of the sympathetic nervous system that are present in primary hypertension. However, the lack of change in the rhythmicity abnormalities with antihypertensive treatment in the present study suggests that some abnormalities in sympathetic nervous system function in primary hypertension may be independent of adiposity. Further study will be needed to determine whether other interventions might be able to reverse these abnormalities.

A unique feature of the study of Niemirska et al is that they were able to analyze longitudinal data, including repeated ambulatory blood pressure monitoring and repeated assessments of visceral fat, obtained before and after antihypertensive treatment. The same group of investigators had previously demonstrated in a larger group of hypertensive adolescents that improvements in hypertensive target organ damage after treatment were related to reductions in visceral fat as reflected by decreased waist circumference. The present study strengthens the emerging body of evidence that childhood primary hypertension is related to visceral adiposity. Indeed, other investigators have demonstrated that a significant correlation exists between the degree of obesity and the level of blood pressure elevation in both hypertensive and normotensive pediatric patients.

The childhood obesity epidemic has had significant effects on the epidemiology of childhood primary hypertension. Although the increasing numbers of obese, hypertensive youth suggest that an epidemic of adult cardiovascular disease is imminent, there is also reason to be hopeful that such an outcome can be averted. The 2 studies conducted by the group in Warsaw clearly show that lifestyle modification, if successful as evidenced by decreased visceral fat, can ameliorate the adverse effects of obesity on the cardiovascular system in hypertensive children and adolescents (Figure). These data support the recommendation of the National High Blood Pressure Education Task Force and others that a combination of nonpharmacological and pharmacological measures.
should be used to treat obesity-related hypertension in the young. Although quantification of visceral fat mass is expensive and impractical to implement on a large scale, tracking of waist circumference could be added to the follow-up care of hypertensive children, as it was decreased waist circumference that clearly correlated with reductions in hypertensive target organ damage.8

Additionally, these results point the way toward primary prevention of at least some cases of adult cardiovascular disease. Effective treatment of childhood obesity, instituted before the development of complications such as hypertension, might reduce the influence of visceral fat on sympathetic nervous system function, or perhaps prevent it entirely. Public health measures intended to combat childhood obesity, such as the Let’s Move campaign (http://www.letsmove.gov/), should be supported by pediatricians and others interested in the prevention of hypertension and its complications. We are unlikely to put ourselves out of business entirely, but perhaps we would then have more time to investigate other aspects of hypertension that have so far eluded our understanding.

Disclosures

None.

References

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