Family History of Essential Hypertension Versus Obesity as Risk Factors for Hypertension in Adolescents
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Family history of hypertension and obesity are both risk factors for hypertension. Hypertension and obesity share several physiopathologic abnormalities and are frequently associated. However, not all obese people are hypertensive. Renal handling of sodium has been proposed as a physiopathogenic mechanism of essential hypertension and obesity. This study was conducted in obese adolescents to evaluate the role of a family history of hypertension versus obesity in the renal handling of sodium. Fractional excretion of lithium (FELi) and uric acid (FEUA) were measured in 46 obese adolescent offspring of hypertensive parents (OH: body mass index [BMI], 29.5 ± 0.6 kg/m², age 14.2 ± 0.3 years, 22 males); eight obese offspring of normotensive parents (ON: BMI, 30.7 ± 1.7 kg/m², 14.8 ± 0.8 years, four males), and in 34 lean adolescent offspring of hypertensive parents (LH: BMI, 20.5 ± 0.5 kg/m², 14.3 ± 0.3 years, 24 males). FELi in OH was 16.5% ± 1.3%, in ON it was 22.4% ± 2.3%, and in LH it was 14.4% ± 1.2% (P < .05). FEUA in OH was 8.5% ± 0.8%, in ON it was 14.8% ± 3.6%, and in LH it was 7.9% ± 0.8% (P < .01). Plasma renin activity (PRA) and aldosterone (PA) were measured in OH and LH; PRA was 5.3 ± 0.4 and 4.5 ± 0.4 ng/mL/h, respectively (P = NS), and PA was 366 ± 36 and 242 ± 32 pg/mL, respectively (P < .05). In summary, adolescents with a family history of hypertension, regardless of their body mass, have a diminished FELi and FEUA. Obese adolescents also have higher plasma levels of aldosterone than lean ones. In conclusion, the family history of hypertension would be related to the increased renal proximal sodium reabsorption whereas obesity would be related to increased distal sodium reabsorption mechanisms, such as aldosterone. Both mechanisms could explain the higher prevalence of hypertension in obese offspring of hypertensive parents. Am J Hypertens 1999;12:260–263 © 1999 American Journal of Hypertension, Ltd.

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versus obesity in the renal handling of sodium in normotensive obese adolescents with and without a family history of hypertension.

MATERIALS AND METHODS

Forty-six obese adolescent offspring of hypertensive parents (OH) (mean age ± SEM: 14.2 ± 0.3 years, 22 males, body mass index [BMI]: 29.5 ± 0.6 kg/m²), eight obese adolescent offspring of normotensive parents (ON) (14.8 ± 0.8 years, 4 males, BMI: 30.8 ± 1.7 kg/m²), and 34 lean adolescent offspring of hypertensive parents (LH) (14.3 ± 0.3 years, 24 males, BMI: 20.5 ± 0.5 kg/m²) were included in the study. All subjects were studied at the Hypertension and Lipid Clinic of our Medical Center, were healthy, and were taking no medication. All adolescents were normotensive according to the Task Force and their blood pressures were similar. Blood pressure of parents was assessed personally by one of the authors. Procedures were explained carefully to both parents and children, and informed consent was obtained from parents.

All subjects came to the clinic after an overnight fast and having received 300 mg/m² of lithium carbonate at 10 PM the night before. At 6 AM they emptied their bladders completely and collected urine up to 12 AM for measurement of sodium, potassium, creatinine, uric acid, and lithium. At 9 AM a blood specimen was obtained in the sitting position, for measurement of lithium, creatinine, uric acid, sodium, potassium, renin, aldosterone, and lipids. Patients received an oral water load (20 mL/kg + diuresis) throughout the study. Sodium, potassium, and creatinine were measured by an automated method (Beckman Instruments, Fullerton, CA). Lithium was measured by atomic absorption spectrophotometry (Perkin Elmer, Norwalk, CT) and renin and aldosterone by radioimmunoassay.

Statistical Analysis  Comparisons between groups were calculated with analysis of variance and unpaired t test. A P value < .05 was accepted as significant. Findings are expressed as mean ± SEM.

RESULTS

Clinical characteristics of the groups are shown in Table 1. All adolescents had normal renal function evaluated through creatinine clearance, urea, and urine analysis, and there were no significant differences between groups. Creatinine clearance in OH was 127 ± 9 mL/min, in ON it was 134 ± 18 mL/min, and in LH it was 133 ± 15 mL/min (P = NS). Fractional excretion of lithium in OH was 16.5% ± 1.3%, in ON it was 22.4% ± 2.3%, and in LH it was 14.4% ± 1.2%; P < .05 (Figure 1). Fractional excretion of uric acid in OH was 8.5% ± 0.8%, in ON 14.8% ± 3.6%, and in LH 7.9% ± 0.8%; P < .01 (Figure 2). Urinary sodium excretion was similar in the three groups: 203 ± 13 mEq/day in OH; 237 ± 21 mEq/day in ON, and 185 ± 10 mEq/day in LH. Plasma renin and aldosterone were evaluated in obese and lean offspring of hypertensive parents. In OH plasma renin activity was 5.3 ± 0.4 ng/mL/h and in LH 4.5 ± 0.4 ng/mL/h (P = NS), and plasma aldosterone was 366 ± 36 ng/mL in OH and 242 ± 32 ng/mL in LH (P < .05) (Figure 3).

![Figure 1](image-url)  Fractional excretion of lithium in obese adolescents, offspring of normotensive parents (ON), offspring of hypertensive parents (OH), and in lean adolescent offspring of hypertensive parents (LH).
DISCUSSION

Family history of hypertension and obesity are both major risk factors for hypertension. Although hypertension and obesity share several physiopathologic abnormalities and are frequently associated,1–4 to our knowledge, no study has looked at the role that a family history of hypertension could play in the abnormalities found in obese individuals.

In this study, we found that obese as well as lean adolescent offspring of hypertensive parents have a diminished fractional excretion of lithium, that is, an increased fractional proximal tubular sodium reabsorption, whereas obese adolescents with no family history of essential hypertension have a normal fractional excretion of lithium. In addition, a diminished fractional excretion of uric acid was present only in both groups of offspring of hypertensive parents, supporting an abnormality at the proximal segments of the renal tubules.

In most patients with hypertension, no specific renal disease can be identified, at least in the early stages of hypertension. Direct evidence that abnormalities of kidney function play a causal role in animal models of genetic hypertension comes from kidney cross-transplantation studies in which transplantation of kidneys from hypertensive donors into normotensive controls raised blood pressure in the recipient rats.9–11 These observations in rats may be relevant to the pathogenesis of human essential hypertension, and support the view that essential hypertension is caused by some type of renal defect. Guyton was one of the first to point out the important role of the kidney in the genesis and maintenance of hypertension, suggesting that hypertension would be a necessary consequence of a reduced ability of the kidney to excrete a sodium overload to promote natriuresis and maintain a normal sodium balance.5 Studies in animal models of hypertension showing abnormalities in the renal sodium excretion and in the pressure-natriuresis curve preceding the development of hypertension support the genetic hypothesis of hypertension.12,13 We have also been able to show a reduced ability of the kidney to excrete sodium in normotensive adolescents, offspring of hypertensive parents, in whom we reported an increased fractional proximal renal sodium reabsorption, evaluated through the fractional excretion of lithium.7

In this study there was very little difference in blood pressure between the three groups. The finding of an increased fractional proximal sodium reabsorption in offspring of hypertensive parents could reflect an abnormality preceding the development of high blood pressure. Blood pressure follow-up of these subjects will be of special interest and will provide useful information.

Obesity is believed to be a major cause of human essential hypertension. Several studies have provided important information about the pathogenesis of weight-related increases in blood pressure in obese dogs— involving renal and hemodynamic alterations associated with marked sodium retention—which include hyperinsulinemia, increased renin-angiotensin system, and sympathetic nervous activity.14,15

A potential cause of the increased fractional tubular sodium reabsorption found in this study is activation of the renin-angiotensin system. Evidence of an activation of the renin-angiotensin system in normotensive offspring of hypertensive parents comes from a previous report in which converting enzyme inhibitors were able to normalize the diminished fractional excretion of lithium in the evaluated group.16 In fact, both lean and obese offspring of hypertensive parents showed higher plasma renin activity levels when compared with our normal population.17 Previous studies of the renin-angiotensin system in obesity have yielded conflicting results. Rocchini et al found no change in plasma renin activity but an increase in
aldosterone levels in both obese dogs and obese adolescents. Tuck et al reported increased levels of renin and aldosterone in obese subjects, and Hall found twofold increases in plasma renin activity in obese dogs.

As mentioned earlier, both lean and obese offspring of hypertensive parents had increased plasma renin activity, suggesting that this finding could be related to the family history of hypertension. The obese group, however, also showed significantly higher plasma aldosterone levels than lean adolescents, suggesting that there may be another underlying stimulus of the system in obesity. The elevated level of plasma aldosterone found in obesity could be another sodium-retention mechanism, acting at distal levels of the tubules and contributing to the development of hypertension in obesity.

Therefore, our findings show that normotensive adolescents with a family history of hypertension, regardless of their body mass index, have a diminished fractional excretion of lithium and uric acid, suggesting that an abnormality in the proximal renal tubule would be related to the family history of hypertension. On the other hand, obese adolescents, regardless of their family history of hypertension, have higher plasma levels of aldosterone, suggesting that an increased distal sodium reabsorption is present in obesity.

In conclusion, a family history of hypertension may be relevant to the development of hypertension in obese adolescents. Both mechanisms of increased renal sodium reabsorption could account for the higher prevalence of hypertension in obese subjects.

REFERENCES