Sodium Excretion and Racial Differences in Ambulatory Blood Pressure Patterns

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The influence of Na⁺ excretion and race on casual blood pressure and ambulatory blood pressure patterns was examined in a biracial sample of healthy, normotensive children and adolescents (10–18 years; n=140). The slopes relating 24-hour urinary Na⁺ excretion to systolic blood pressure were different for both black and white subjects for casual blood pressure (p<0.001) and blood pressure during sleep (p<0.03). For casual blood pressure, the slope was significant for black subjects (β=0.17; p<0.001) but not for white subjects. For blood pressure during sleep, the slope was again significant for black subjects (β=0.08; p<0.01) but not for white subjects. Na⁺ excretion was also related to awake levels of systolic blood pressure for black subjects (β=0.08, r=0.36; p<0.01), although the slopes for both black and white subjects were not significantly different. Further analyses indicated the results were not due to racial differences in 24-hour urinary K⁺ excretion. However, plasma renin activity was marginally related to Na⁺ excretion in white subjects (r=0.22; p<0.06) but not black subjects, a finding that is consistent with previous studies. Na⁺ excretion was not associated with diastolic blood pressure or heart rate in either group under any condition. The results of this study support research that has demonstrated a stronger relation between Na⁺ handling and casual blood pressure in black subjects and extend these findings to blood pressure while the subject is both awake and asleep. (Hypertension 1991;18:813–818)

Recent studies in both adolescents¹ and adults²,³ demonstrated that black subjects as a group had a “blunted” nocturnal decline in blood pressure (BP). Research has shown that Na⁺ intake is a primary determinant of BP in a significant percentage of both the hypertensive⁴,⁵ and normotensive⁶,⁷ populations, a characteristic referred to as “salt sensitivity.” Furthermore, the prevalence of salt sensitivity has been found to be greater in the black population than in the white population.⁴,⁸ Therefore, the purpose of the present study was to examine the effect of sodium excretion (UₙaV) and race on casual BP and ambulatory BP patterns in healthy black and white adolescents. In addition, K⁺ excretion (UₖV)⁹–¹¹ and plasma renin activity (PRA)¹²–¹⁶ were measured to determine the role of these factors that are known to influence Na⁺ homeostasis and BP control.

Methods

Subject Characteristics and Casual Measurements

The protocol was approved by the Institutional Committee on Human Research and the Clinical Research Center Scientific Advisory Board. Written, informed parental consent was obtained before testing. The subjects were 199 healthy, normotensive children and adolescents recruited from churches, schools, and social organizations as described in detail.¹⁷ Of these, 19 subjects (10%) were excluded from the analyses due to questionable 24-hour recordings (see below); 40 subjects (20%) were excluded due to inadequate 24-hour urine collections (see below). Excluded subjects were similar in age, gender, BP, heart rate (HR), body surface area (BSA), and PRA to subjects included in the analyses. Health status was evaluated based on the subject’s medical history and a brief physical examination to rule out the presence of cardiovascular or other abnormalities. The demographic characteristics and casual measurements from the subjects included in the analyses are provided in Table 1.

Casual Blood Pressure and Heart Rate

Casual BP and HR measurements were obtained with the Dinamap BP monitor (model 1846SX, Critikon, Tampa, Fla.) before the ambulatory BP re-
The procedures for urine collections and analyses have been described in detail. In brief, the subjects were seated, and the ambulatory BP recording procedures used in our laboratory have been described in detail. In brief, the subject was seated, and the ambulatory BP recording (model 5200, Spacelabs Inc, Redlands, Wash.) was applied and calibrated. The functioning of the recorder was demonstrated to the subject, and the details of the protocol described. The subject was instructed to wear the monitoring device for at least 20 hours of the day. The subject was then instructed to resume his or her normal daily activities and to return the following day for the removal of the recording procedure. The casual measurements were the average of three readings taken in the seated position after 5 minutes of sitting quietly.

Ambulatory Blood Pressure Recordings

The ambulatory BP recording procedures used in our laboratory have been described in detail. In brief, the subject was seated, and the ambulatory BP recording (model 5200, Spacelabs Inc, Redlands, Wash.) was applied and calibrated. The functioning of the recorder was demonstrated to the subject, and the details of the protocol described. The subject was instructed to relax his or her arm during a BP determination and to provide diary information for each hour the monitor was worn. The subject was then instructed to resume his or her normal daily activities and to return the following day for the removal of the recorder. The recorder was set to take a reading at 20-minute intervals between the hours of 6:00 AM and midnight and 60-minute intervals between the hours of midnight and 6:00 AM. A successful recording was one in which less than 25% of the readings during the recording were considered artifacts, and the subject’s recording had data for at least 20 hours of the day. Hourly averages were computed for each individual and coded according to whether the subject was awake or asleep during the hour. The average level of BP while awake and asleep was then determined for each subject.

Twenty-Four-Hour Urine Collection

The procedures for urine collections and analyses have been described in detail. In brief, urine containers with boric acid preservative were provided for the 24-hour urine specimens. Instructions (written and verbal) on proper 24-hour urine collection were given to each subject and parent before the procedure. Subjects who had 24-hour urine volume greater than 500 ml and creatinine clearance greater than 75 ml/min/1.73 m² were considered to have an adequate urine collection and were included in the analyses.

Plasma Renin Activity

The procedures for the collection and measurement of PRA and creatinine in our laboratory have been described in detail. In brief, the subjects were seated for 30 minutes before blood collection; while the subject was in the seated position, plasma samples were drawn at 7:00 AM in tubes containing EDTA, which were then immediately placed on ice. The samples were centrifuged at 4°C and stored at -60°C until analyzed. PRA was measured in duplicate by methods described by Haber et al using radioimmunoassay kits (Baxter Healthcare Corp., Cambridge, Mass.).

Data Analyses

Comparisons of subject characteristics were performed by analysis of variance on a Macintosh SE/30 computer with SUPERANOVA (Abacus Concepts Inc., Berkeley, Calif.). Overall analyses were performed by analysis of covariance using the SUPERANOVA program, using Type III sums of squares to test for main effects and interactions. The general form of the models included three factors: 1) race, 2) UNaV as a continuous variable, and 3) the interaction between race and UNaV to test if the slopes relating UNaV to BP in both black and white subjects were similar. (Note: when one of the independent variables is continuous and the other binary, the interaction term represents a test of the equality of the slopes between the two groups.) BSA was also included as a covariate in the models. The dependent variables included: 1) casual systolic BP (SBP), diastolic BP (DBP), and HR; 2) SBP, DBP, and HR while the subjects were awake; and 3) SBP, DBP, and HR while the subjects were asleep. Planned comparisons examining the slopes between UNaV and each dependent variable for both races were performed. A value of p<0.01 was considered significant. In addition, analyses were performed to test the relation between UNaV and both UNaV and PRA. Finally, separate models were run substituting UrV for UNaV in the general model to examine the relation between UrV and ambulatory BP patterns.

Results

Race, Age, Gender, Body Surface Area, and Sodium Excretion

The black subjects were older than the white subjects, with greater BSA (Table 1). The correlation between age and BSA was significant (r=0.60; p<0.01). There was a higher percentage of girls among the black subjects and a higher percentage of boys among the white subjects. UNaV was similar for black and white subjects (Table 1).

Race, Sodium Excretion, and Casual Blood Pressure

The effects of both race (p<0.01) and UNaV (p<0.001) on casual SBP were significant. In addition, the race by UNaV interaction was significant (p<0.001), indicating that the slopes between UNaV and SBP were different for black and white subjects. The slope was positive and significant for black subjects (p<0.001); the slope was not significant for white subjects (Figure 1). Further analyses were performed to test the relation between UNaV and both UUrV and PRA. Finally, separate models were run substituting UUrV for UNaV in the general model to examine the relation between UUrV and ambulatory BP patterns.
performed with the inclusion of gender in the model to control for group differences on this variable. The race by $U_{NaV}$ interaction remained significant ($p<0.01$). Although the effect of gender was significant ($p<0.01$), the interaction among race, $U_{NaV}$, and gender was not significant. Significant effects were not found for either DBP or HR.

Race, Sodium Excretion, and Ambulatory Blood Pressure While Awake

The effects of race, $U_{NaV}$, and the interaction between race and $U_{NaV}$ were not significant for SBP while the subjects were awake. However, further analysis indicated that the slope relating $U_{NaV}$ to awake SBP was positive and significant for the black subjects (Figure 2). Similar results were obtained after the inclusion of gender ($p=NS$) in the model. Significant effects were not found for either DBP or HR.

Race, Sodium Excretion, and Ambulatory Blood Pressure While Asleep

The effect of $U_{NaV}$ on SBP while the subjects were asleep was significant ($p<0.01$). In addition, the race by $U_{NaV}$ interaction was significant ($p<0.03$), indicating that the slopes between $U_{NaV}$ and SBP were different for both black and white subjects. The slope was positive and significant for black subjects ($p<0.01$); the slope was not significant for white subjects (Figure 3). The race by $U_{NaV}$ interaction remained significant ($p<0.03$) after the inclusion of gender ($p=NS$) in the model. Significant effects were not found for either DBP or HR.

Race, Sodium Excretion, and Plasma Renin Activity

Both black and white subjects had similar levels of PRA (Table 1). The slope relating PRA to $U_{NaV}$ was negative for the white subjects and approached statistical significance ($r=-0.22; p<0.06$). PRA and $U_{NaV}$ were not related for black subjects ($r=0.07$).

Race, Sodium Excretion, Potassium Excretion, and Blood Pressure

Black subjects had significantly lower levels of $U_{K^{+}}$ than white subjects (Table 1). The slopes relating $U_{NaV}$ to $U_{K^{+}}$ were similar for black subjects ($\beta=1.360; p<0.001$) and for white subjects ($\beta=1.662; p<0.001$), with a higher intercept for the black subjects (97.21 meq/24 hr) than for white subjects (58.8 meq/24 hr). In addition, $U_{K^{+}}$ was not related to any measure of BP (casual, awake, or asleep) for either group.

Discussion

The increased prevalence of essential hypertension among black adults is well documented. Previously, we demonstrated that healthy normotensive black adolescents have higher levels of BP than white individuals at night, despite similar levels of BP during the day. Furthermore, we and others demonstrated that healthy, normotensive black adults have a smaller nocturnal decline in BP than previously observed in white adults. Based on these observations, we hypothesized that the additional "cardiovascular strain" resulting from the blunted nocturnal decline in BP among black individuals may be a contributing factor to the racial difference in the prevalence of hypertension.
The present study suggests that Na⁺ handling and regulation contribute to the racial differences in ambulatory BP patterns. The slopes relating UₙaV to SBP were different for both black and white subjects. Specifically, UₙaV was related to casual SBP in black subjects, with higher levels of Na⁺ intake (as determined by UₙaV) associated with higher levels of SBP. Similar relations were found between UₙaV and SBP while awake and UₙaV and SBP while asleep. In contrast, UₙaV was not related to SBP for white subjects under any condition.

These findings are consistent with the only study to our knowledge to examine the influence of Na⁺ intake on 24-hour BP. In that study, 20 healthy subjects had 24-hour recordings performed before and after Na⁺ restriction (107 versus 11 meq/24 hr). The mesor (a “running mean”) for SBP was significantly lower after the reduction in Na⁺ intake (115 versus 104 mm Hg). As in the present study, DBP was not affected. It should be noted that the previous study was performed under hospital conditions and required the subjects to remain in a reclining position throughout the recording.

These findings are also consistent with research indicating that Na⁺ handling contributes to racial differences in the prevalence of essential hypertension. The studies of Luft and his colleagues demonstrated that black subjects as a group were more salt-sensitive (SS) than white subjects as a group. The black subjects excreted significantly less Na⁺ than white subjects the first 10 hours and 24 hours after Na⁺ loading. The delayed excretion of the Na⁺ load of the black subjects was associated with a greater increase in BP. In addition, they demonstrated that a diet of 800 meq of Na⁺ was needed to raise BP for black subjects compared with a diet of 1,200 meq Na⁺ for white subjects, with a correlation between UₙaV and BP of 0.73 for black subjects and only 0.48 for white subjects. Sullivan examined the responses of normotensive and borderline hypertensive subjects in response to a sodium-restricted diet and during the return to their ad libitum diet. He found that 27% of the black and 15% of the white normotensive subjects, as well as 50% of the black and 24% of the white borderline hypertensive subjects were SS, defined as a 5% or greater change in mean BP from the sodium-restricted diet to their ad libitum diet. During Na⁺ depletion, BP was significantly lower in the SS than in the salt-resistant (SR) normotensive subjects. The changes observed in mean BP were paralleled by changes in forearm vascular resistance, which was significantly higher during Na⁺ repletion in the SS subjects. BP was significantly higher in the borderline hypertensive subjects. In contrast, forearm vascular resistance was not significantly different between the normotensive and borderline hypertensive groups, but was significantly higher in the SS subjects. Venous capacitance was significantly lower in the SS hypertensive than in SR hypertensive subjects. Although a similar trend was seen in normotensive subjects, the differences were not significant, and changes in capacitance did not accompany changes of Na⁺ intake. During Na⁺ depletion, PRA was significantly lower in SS than in SR subsets of subjects and remained significantly lower even with the added stimulus of upright posture. Plasma aldosterone concentration was also significantly lower in the SS subjects during Na⁺ depletion with a significant negative correlation between the change in BP with Na⁺ repletion and either PRA during Na⁺ restriction or the increment in PRA during Na⁺ depletion. Sowers and his colleagues examined changes in BP from a normal Na⁺ diet to a low Na⁺ diet in two groups of black subjects: 11 hypertensive black subjects and 14 normotensive black subjects with a strong family history of hypertension. All of the subjects had 5–10 mm Hg decreases in mean BP with similar decreases for both normotensive and hypertensive subjects. Dustan and Kirk reported racial differences in BP changes in response to 3 days each of Na⁺ loading and depletion with greater changes for black subjects than white subjects. In a study of 38 white and 83 black subjects, Falkner and Kushner found that 37.3% of the black subjects compared with 18.4% of the white subjects were SS.

Several characteristics of SS subjects have been identified that may account for the observed differences in Na⁺ handling. Salt sensitivity has been associated with altered adrenergic regulation. Results of these studies suggest that SS individuals fail to adequately suppress the adrenergic system under conditions of high Na⁺ intake. Other studies, including those of Sullivan and Luft described above, suggest that SS individuals do not regulate the renin-angiotensin system appropriately in response to changes in Na⁺ intake. The correlation between UₙaV and PRA was negative and approached significance in white subjects, suggesting that PRA decreases in response to increases in Na⁺ intake. However, PRA was not associated with UₙaV in black subjects. The studies of Williams and Hollenberg indicate that a subset of SS subjects referred to as “non-modulators” do not alter the responsiveness of the renal vasculature and the adrenal gland to angiotensin II in response to changes in Na⁺ intake. Specifically, Na⁺ restriction did not enhance adrenal responsiveness to angiotensin II and Na⁺ loading did not increase baseline renal blood flow or renal vasculature responses to angiotensin II. In addition, these individuals showed delayed suppression of PRA after Na⁺ loading, coupled with a reduction in the ability to excrete the load. More recent studies have demonstrated the heritability of this response pattern and demonstrated that the majority of these abnormalities are corrected by angiotensin converting enzyme inhibition. Other investigators have shown that SS subjects have abnormal baroreceptor reflex function, and still others have found a relation between sodium sensitivity and erythrocyte sodium concentration.
The influence of Na\textsuperscript{+} on BP may be mediated by K\textsuperscript{+}. Morgan and his colleagues\textsuperscript{9,10} demonstrated that K\textsuperscript{+} supplementation prevents Na\textsuperscript{+}-induced rises in BP in people with SS hypertension. In addition, Svetkey et al\textsuperscript{11} showed that K\textsuperscript{+} supplementation was more effective in reducing BP in black than in white adults with mild hypertension. In the current study, black subjects were characterized by lower levels of U\textsubscript{NaV}. However, the slopes relating U\textsubscript{Kv} to U\textsubscript{NaV} were positive and similar for both black and white subjects, suggesting that the influence of K\textsuperscript{+} on Na\textsuperscript{+} handling was similar. In addition, U\textsubscript{Kv} was not related to casual, awake, or asleep BP in either black or white subjects after adjustment for body size.

In summary, the results of the current study suggest that Na\textsuperscript{+} handling is one factor responsible for racial differences in ambulatory BP patterns in children and adolescents. Within black subjects, the relation between U\textsubscript{NaV} and BP was positive and linear for casual SBP, awake SBP, and asleep SBP. In contrast, U\textsubscript{NaV} was not associated with SBP in white subjects under any condition. U\textsubscript{NaV} was not associated with DBP or HR in either group under any condition. Further analyses indicated these results were not due to racial differences in U\textsubscript{Kv} but were consistent with the hypothesis that black individuals do not adequately suppress PRA in response to increases in Na\textsuperscript{+} intake.

Interpretation of these results must take into account the cross-sectional design of the study. Further research is needed to determine if directly manipulating Na\textsuperscript{+} intake in black subjects will increase awake and asleep BP but will not change BP in white subjects. In addition, U\textsubscript{NaV} was collapsed across 24-hour periods, which did not allow us to examine directly the relation between U\textsubscript{NaV} and BP under each condition. Additional studies are needed to determine if U\textsubscript{NaV} while awake is directly related to BP while awake and if U\textsubscript{NaV} during sleep is directly related to BP during sleep. However, the results are consistent with the literature demonstrating the importance of Na\textsuperscript{+} on the regulation of BP for black individuals and extends these results to BP while awake and while asleep.

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