Water Loading and Restriction in Essential Hypertension

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SUMMARY Blood pressure, plasma arginine vasopressin (AVP), and renal excretory responses to short-term water loading (oral load of 20 ml/kg body weight over 30–45 minutes) were compared in 10 normotensive and 13 mild to moderately essential hypertensive subjects. In addition, we examined the renal concentrating ability of an additional group of 10 normotensive subjects and 12 hypertensive subjects in response to a 24-hour water restriction and intranasal administration of 10 μg of [1-deamino,8-D-arginine]vasopressin. The hypertensive subjects exhibited both an exaggerated diuresis and natriuresis to the water load. At 20- and 60-minutes after water loading, hypertensive subjects had excreted 34 and 55% of the load, respectively, compared with 15 and 35% in normotensive subjects. Mean blood pressure rose significantly in both groups and hypertensive subjects exhibited a greater rise of systolic blood pressure (16 mm Hg) than normotensive subjects (8 mm Hg) 20 minutes after water loading. The maximum diuresis and natriuresis corresponded to the period in which the rise of blood pressure was greatest. The hypertensive subjects diluted and concentrated their urine as well as normotensive subjects did, indicating normal renal responsiveness to AVP. Plasma Na, osmolality, and AVP decreased similarly in both groups after water loading and rose similarly in the two groups after water restriction. This finding suggests that osmotic responsiveness of AVP is not altered in hypertensive subjects. In conclusion, the data suggest that the exaggerated renal response to water loading could be explained by the greater rise of blood pressure in hypertensive subjects rather than by altered AVP responses. (Hypertension 9: 407-414, 1987)

KEY WORDS • water loading • water restriction • renal excretion • exaggerated diuresis • exaggerated natriuresis • vasopressin • osmolality • plasma renin activity • blood pressure

THERE is abundant evidence that patients with essential hypertension generally have abnormalities in fluid and electrolyte regulation.1-10 Some studies have related the abnormalities to altered responsiveness of the renin-angiotensin-aldosterone system,1-6 whereas others have shown alterations in the renal handling of sodium and water.7-10 An exaggerated increase in sodium excretion is known to occur after short-term saline loading in patients with essential hypertension.6-21 Enhanced natriuresis in hypertension has also been observed after volume expansion with mannitol22 or glucose.23 Responses of hypertensive subjects to an oral water load, however, have not been systematically studied.

Recent studies in our laboratory have indicated that elevations of plasma arginine vasopressin (AVP) are often present in even mildly hypertensive subjects.15,34 There is little information about the ability of hypertensive subjects to excrete a short-term water load since, in the past, most of the attention has been focused on the exaggerated reaction to saline loading. It is unknown whether subjects with hypertension can suppress plasma AVP as well as can normal subjects with a water load. It is also unclear whether hypertensive subjects can excrete a water load as effectively and if they do so by the same mechanisms as normotensive subjects.
The present studies were therefore designed to compare the renal excretory responses to short-term water loading in normal and mild to moderately essential hypertensive subjects. The experiments also were designed to determine whether arterial pressure responses and two major endocrine controllers of renal excretion (renin and vasopressin) differed between the two groups. Studies were also performed to determine the renal concentrating ability of hypertensive subjects.

Subjects and Methods
Two groups of subjects were used in the present study, one for evaluation of water overhydration (Group 1) and the other for evaluation of water restriction (Group 2). Group 1 was composed of 23 subjects, 10 normotensive subjects and 13 hypertensive subjects. Normotensive subjects ranged from 21 to 48 years of age (mean, 35 ± 3 years), had a mean body weight of 82 ± 5 kg, and included five men, five women, seven whites, and three blacks. The 13 hypertensive subjects ranged in age from 24 to 66 years (mean, 43 ± 4 years), had a mean body weight of 89 ± 6 kg, and included seven men, six women, three whites, and 10 blacks.

Group 2 was composed of 10 normotensive subjects ranging in age from 23 to 54 years (mean, 35 ± 3 years); they had a mean body weight of 78 ± 4 kg and included four men, six women, four whites, and six blacks. Twelve hypertensive subjects were studied; they ranged in age from 24 to 55 years (mean, 40 ± 3 years), had a mean body weight of 85 ± 6 kg, and included nine men, three women, three whites, and nine blacks.

The normal subjects were healthy volunteers with a blood pressure consistently below 140/90 mm Hg and no history of hypertension. The hypertensive subjects were diagnosed to have mild to moderate essential hypertension with untreated diastolic pressures ranging between 95 and 114 mm Hg and grade 0 to 1 ocular fundi on ophthalmoscopic examination. Secondary hypertension was excluded by history, physical examination and blood chemistry values, urinalysis and, when warranted, radiographic evaluations and measurements of urinary catecholamines or vanillylmandelic acid. None of the patients had a history or findings of malignant hypertension, stroke, heart disease, liver disease, gout, or renal disease. Their serum creatinine level was 0.7 to 1.4 mg/dl. All antihypertensive medications were discontinued at least 2 weeks before entry into the study.

The study was approved by the Institutions Review Committee of the Medical College of Wisconsin, and informed consent was obtained from all subjects. On entering the study, the subjects were instructed to follow a 3-day diet containing sodium, 100 mEq/day, and potassium 75 mEq/day. On the third day they were admitted to the Clinical Research Center and kept on a similar sodium and potassium diet. All subjects abstained from smoking and drinking coffee or tea for at least 12 hours before the test. They were studied the next morning after an overnight fast; body weight and vital signs were recorded on admission.

Group 1: Water Overhydration
The response to an oral water load was studied in normal and hypertensive subjects of Group 1. At the beginning of the test, a 1-hour urine sample was collected and body weight recorded after the subject had voided. An indwelling catheter for blood sampling was inserted into an antecubital vein of the left arm and kept open with a microdrip infusion of 5% dextrose in water. After the subject had rested supine for 60 minutes, pulse rate was counted and blood pressures taken in the opposite arm with a standard mercury sphygmomanometer using the cuff method. The first and fifth phases of Korotkoff sounds were recorded as systolic and diastolic blood pressure, respectively. Blood and urine samples were collected immediately after three sets of heart rate and pressure measurements were obtained. Following control measurements and collections, the subjects were given an oral water load of 20 ml/kg body weight over a 30- to 45-minute period. Measurements and collections were repeated 20, 60, 100, and 120 minutes after completion of the water load. Subjects remained supine during the entire test period and stood only to void. The study was terminated if the subject experienced nausea or any acute discomfort. None of the subjects vomited following the water load.

Group 2: Water Restriction
The renal concentrating ability was assessed in normal and hypertensive subjects of Group 2. Following an overnight fast, subjects were asked to void before recording body weight, and a 1-hour control urine collection was then started. An indwelling catheter was inserted into an antecubital vein of the left arm for blood sampling. After the subject had rested supine for 60 minutes, pulse rate was counted and blood pressure taken in the opposite arm with a standard mercury sphygmomanometer using the cuff method. Blood and urine samples were collected immediately after three sets of heart rate and blood pressure measurements were obtained. Following control measurements, a light breakfast containing 97 g of water was served. Water was then restricted for 24 hours by withholding all fluids and hydrated foods except those provided at lunch (186 g water content) and dinner (335 g water content). Urine was collected over the 24-hour period of water restriction, and blood pressure and heart rate were determined at the end of the 24 hours just before withdrawal of the second blood sample. At this time, a similar light breakfast was provided, and 10 µg of [1-deamino,8-D-arginine]vasopressin (dDAVP; Desmopressin; Parke-Davis, East Lansing, MI, USA) was given intranasally. A timed urine collection was started and continued for 4 hours. At the end of this period, blood pressure and heart rate were again determined, a blood sample was drawn for analysis, and urine was collected. Subjects were then given lunch and discharged from the Clinical Research Center.
Chemical Analysis

Blood samples for measurement of plasma AVP levels, plasma renin activity (PRA), electrolyte levels (NA and K), and plasma and urine osmolality and creatinine were collected during the control period and 20, 60, 100, and 120 minutes after water loading.

Plasma AVP levels were determined with a radioimmunoassay procedure developed in our laboratory and described previously. Plasma samples were collected in chilled glass tubes containing EDTA and were processed within 1 hour of collection. Plasma was extracted within 60 days of collection. The mid-range of the assay averaged 4.8 pg/ml, with a sensitivity of 0.3 pg/ml. The intraassay coefficient of variation averaged less than 5%, and interassay variation averaged less than 10%. Plasma blanks were determined on each subject and subtracted from the binding obtained. Final concentrations were corrected for losses during extraction (23%).

The PRA was determined by the radioimmunoassay procedure of Sealey and Laragh. Angiotensin I antibodies were kindly provided by Dr. Jean E. Sealey. Plasma and urine creatinine levels were determined by autoanalyzer (Technicon, Tarrytown, NY, USA).

Urine and plasma electrolyte concentrations were determined by flame photometry (Model 443; Instrumentation Laboratory, Lexington, MA, USA). Plasma and urine osmolality were determined in triplicate within 10 days of collection using a vapor pressure osmometer (Model 5100C; Wescor, Logan, UT, USA). The coefficient of variation of multiple determinations was 0.4 to 0.8%.

Statistical Analysis

Data are presented as means ± SEM. Measurements obtained during the experimental periods were compared with baseline (control) values using a two-way analysis of variance followed by a Dunnett's t comparison. Between-group comparisons of the different variables were made using a t test for unpaired data. Results were considered significant if the p value was less than 0.05.

Results

Group 1: Overhydration

Table 1 summarizes the average values of the various measurements obtained in the two groups of subjects during the control period. Note that blood pressure and heart rate were significantly higher in hypertensive subjects than in normal subjects (p < 0.05), whereas serum creatinine level, 24-hour creatinine clearance, plasma sodium and potassium, plasma osmolality, and urine sodium and osmolality were not significantly different between groups.

Plasma AVP averaged 4.0 ± 0.8 pg/ml in normotensive subjects (range, 0.7–7.8 pg/ml) and 2.4 ± 0.4 pg/ml in hypertensive subjects (range, 0.8–6.1 pg/ml), although the difference between groups was not statistically significant. Mean PRA values tended to be lower in the hypertensive subjects but did not differ significantly from those of normal subjects.

Diuretic Response to Short-term Water Loading

Figure 1 compares the diuretic response of the two groups of subjects. Mean urine flow rate, sodium excretion, and free water clearance increased significantly in both groups of subjects; however, the magnitude
of the response differed significantly between the two groups. In normotensive subjects, urine flow increased from 0.6 ± 0.1 to 12.1 ± 3.0 ml/min compared with the increase from 1.1 ± 0.2 to 29.0 ± 6.0 ml/min (p < 0.05) in hypertensive subjects during the 20-minute period after the water load. Similarly, an increase was observed at 20 minutes in sodium excretion, which rose to significantly greater levels in hypertensive subjects (from 160 ± 30 to 1070 ± 170 mEq/min) as compared with normal subjects (from 80 ± 20 to 490 ± 100 mEq/min). By 60 minutes after the water load, however, urine flow and sodium excretion in both groups had declined toward control rates, so that group differences no longer existed. The response of free water clearance was different in that it appeared to be more prompt in hypertensive subjects, as seen by the increase at 20 minutes that was significantly greater in hypertensive subjects (p < 0.05).

Figure 2 compares the volume of urine (expressed as percentage of total water load) excreted during the 2-hour period after the water load in the two groups of subjects. Note that 20 minutes after water loading, hypertensive subjects had excreted 34% of the water load compared with only 15% in normal subjects (p < 0.05). By the end of 60 minutes, hypertensive subjects had eliminated over half of the volume load (55%) whereas normotensive subjects had eliminated only 35% (p < 0.05). The total amount of urine excreted over the 2-hour period averaged 1437 ml, or 82%, in hypertensive subjects and 1198 ml, or 74%, in normotensive subjects, but this final difference did not reach statistical significance.

Changes in Plasma and Urine Sodium and Osmolality and Plasma Arginine Vasopressin

Plasma sodium, plasma osmolality, and urine osmolality decreased significantly in both groups of subjects after the water load (Figure 3). Plasma sodium decreased to a minimum of 3.1 mEq/L below control in normal subjects and 2.1 mEq/L in hypertensive subjects, 20 to 60 minutes after water loading. Plasma osmolality followed a similar pattern of decrease, to levels of 6.7 and 5.6 mosm/kg below control in normal and hypertensive subjects, respectively. Urine osmolality decreased progressively in both groups and reached a minimum level of 70 ± 9 mosm/kg at 100 minutes in normotensive subjects and 84 ± 10 mosm/kg at 60 minutes in hypertensive subjects. Decreases in plasma sodium, plasma osmolality, and urine osmolality did not differ significantly between groups.

Plasma AVP levels decreased consistently in all subjects following water load. In normotensive subjects levels fell from 4.0 ± 0.8 pg/ml to a minimum value of 2.68 ± 0.8 pg/ml (−33%) at 60 minutes. In hypertensive subjects levels fell from 2.35 ± 0.4 pg/ml to a minimum of 1.56 ± 0.3 pg/ml (−34%) at 60 minutes. The average fall in plasma AVP (expressed as a percentage of change from control) did not differ significantly between groups at any of the collection periods (see Figure 3).
Blood Pressure, Heart Rate, and PRA Responses

Mean arterial pressure rose significantly in both groups after the short-term water load, 7 mm Hg in normal and 10 mm Hg in hypertensive subjects (Figure 4). In normotensive subjects, 20 minutes after the water load, systolic pressure was increased 5.8 mm Hg (+5%; p < 0.05) and diastolic pressure was increased 7.3 mm Hg (+10%; p < 0.01). Pressures subsequently declined toward baseline over the 100 minutes following water loading. Twenty minutes after the water load, hypertensive subjects exhibited a significantly greater rise of systolic pressure as compared with normotensive subjects that averaged 15.9 mm Hg (+11%). Diastolic pressure, which rose 7.9 mm Hg (+6%), was not significantly greater than in normotensive subjects. A significant difference between the normal and hypertensive group was present only at 20 minutes after the water load. As seen in Figures 1 and 4, this exaggerated rise of pressure corresponded to the period in which there was a statistically greater excretion of both sodium and water in hypertensive subjects. This relationship is seen clearly in Figure 5, which compares the sequential changes of pressure and urine flow rate in normal and hypertensive subjects. Hypertensive subjects exhibited nearly a 60% greater rise of mean arterial pressure than did normotensive subjects 20 minutes after the water load. This rise was associated with a twofold greater increase in urine flow rates. As seen in Figure 5, this exaggerated pressure response was a result of a significantly greater rise of systolic pressure in hypertensive subjects.

As seen in Figure 4, mean heart rate did not change significantly in the two groups after water loading. PRA tended to decrease after the water load in normal subjects, but the fall was not statistically significant; no measurable changes was seen in hypertensive subjects.

Group 2: Water Restriction

Table 2 summarizes the average values of measurements made in both normotensive and hypertensive subjects during a control period, after 24 hours of water restriction, and 4 hours after administration of dDAVP. Plasma AVP increased similarly in both normal and hypertensive subjects with 24 hours of water restriction. Plasma osmolality increased 5 to 6 mosm/kg in both groups, as reflected by a rise of plasma sodium. This increase was associated with a significant rise in urine osmolality of nearly equal amounts in both groups. The maximum urine concentrating ability after intranasal administration of dDAVP was also similar in both groups, with urine osmolality averaging 1105 ± 37 mosm/kg in normotensive subjects and 1059 ± 13 mosm/kg in hypertensive subjects. Urine volume was also comparably reduced in both groups with 24 hours of water restriction and with administration of dDAVP. Systolic pressure and heart rate were unchanged throughout the study in normal subjects, while diastolic pressure fell slightly after 24 hours of water restriction. Hypertensive sub-
TABLE 2. Comparison of 10 Normotensive and 12 Hypertensive Subjects After 24 Hours of Water Restriction and 4 Hours After Administration of dDAVP

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group</th>
<th>Control</th>
<th>24-hour water restriction</th>
<th>4-hours post-dDAVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (mm Hg)</td>
<td>NT</td>
<td>119±2*</td>
<td>119±1*</td>
<td>118±3*</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>79±1*</td>
<td>75±2*†</td>
<td>77±1*</td>
</tr>
<tr>
<td>Systolic</td>
<td>NT</td>
<td>142±4</td>
<td>135±3†</td>
<td>135±6</td>
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<tr>
<td></td>
<td>HT</td>
<td>99±2</td>
<td>95±1†</td>
<td>97±1</td>
</tr>
<tr>
<td>Diastolic</td>
<td>NT</td>
<td>63±2</td>
<td>65±2</td>
<td>65±2</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>68±2</td>
<td>68±3</td>
<td>67±3</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>NT</td>
<td>2.4±0.4</td>
<td>5.0±0.7†</td>
<td>4.0±0.6†</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>3.4±0.6</td>
<td>6.1±0.9†</td>
<td>4.0±0.8</td>
</tr>
<tr>
<td>Plasma AVP (pg/ml)</td>
<td>NT</td>
<td>1.9±0.3</td>
<td>2.6±0.6</td>
<td>2.4±0.8</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>2.0±0.8</td>
<td>2.8±0.9</td>
<td>3.4±0.9</td>
</tr>
<tr>
<td>PRA (ng ANG I/ml/hr)</td>
<td>NT</td>
<td>137.8±0.8*</td>
<td>140.7±0.9</td>
<td>142.0±1.8†</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>140.5±1.0</td>
<td>142.2±1.4</td>
<td>141.2±0.7</td>
</tr>
<tr>
<td>Plasma Na (mEq/L)</td>
<td>NT</td>
<td>4.12±0.2</td>
<td>4.3±0.2</td>
<td>4.16±0.1</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>4.26±0.11</td>
<td>4.26±0.11</td>
<td>4.14±0.15</td>
</tr>
<tr>
<td>Plasma K (mEq/L)</td>
<td>NT</td>
<td>283±1</td>
<td>288±2†</td>
<td>286±2</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>284±1</td>
<td>290±2†</td>
<td>286±1</td>
</tr>
<tr>
<td>Plasma osmolality (mosm/kg)</td>
<td>NT</td>
<td>70.3±14</td>
<td>25.3±2.3*†</td>
<td>30.5±2†</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>63.8</td>
<td>36.5±4.0†</td>
<td>29±4†</td>
</tr>
<tr>
<td>Urine flow (ml/hr)</td>
<td>NT</td>
<td>796±73</td>
<td>1082±49†</td>
<td>1105±37†</td>
</tr>
<tr>
<td></td>
<td>HT</td>
<td>760±59</td>
<td>1038±10†</td>
<td>1059±13†</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
dDAVP = [1-deamino,8-arginine]vasopressin; NT = normotensive; HT = hypertensive; ANG I = angiotensin I.
*p < 0.05, compared with values in hypertensive subjects.
†p < 0.05 (within-group comparison), compared with control value.

Subjects exhibited a small but significant decrease in systolic (7 mm Hg) and diastolic (4 mm Hg) pressure after 24 hours of water restriction.

Discussion

The present study revealed clear differences in the response to a short-term water load in normotensive subjects and subjects with mild to moderate essential hypertension. Specifically, hypertensive subjects responded by excreting the water load more rapidly than did the normotensive subjects. They also exhibited exaggerated increases in sodium excretion and free water clearance during the diuresis. Both groups had nearly identical control levels of plasma sodium, plasma potassium, plasma osmolality, as well as urinary sodium and osmolality, so it appears that the differences between them could not be explained by differences in their state of hydration.

Furthermore, hypertensive subjects appeared to be as capable as normal subjects of suppressing plasma AVP in response to the water load. In all subjects water loading produced significant decreases in plasma osmolality followed by a sustained decrease in plasma AVP levels and consequent dilution of urine. Both the fall in plasma osmolality and the magnitude of AVP suppression were similar in both normal and hypertensive subjects. These data indicate that osmotic regulation of AVP within the narrow range studied was not altered in subjects with mild hypertension and that renal responsiveness to AVP was not impaired. Hypertensive subjects were able to dilute their urine to a level (80 mosm/kg) as low as that achieved by the normotensive subjects. Moreover, they were able to dilute their urine more rapidly, as indicated by the earlier achievement of a positive free water clearance at 20 minutes compared with 60 to 100 minutes in normotensive subjects. Hypertensive subjects were also able to increase their plasma AVP and to concentrate their urine to a level as high as that in normotensive subjects in response to water restriction and stimulation by dDAVP.

Other investigators have examined the osmotic responsiveness of plasma AVP in patients with uncomplicated essential hypertension using hypertonic saline infusion to stimulate AVP.11,13 Ganguly and Robertson11 showed that the slope of linear regression relating plasma AVP and plasma osmolality observed after osmotic loading was not different in normotensive and hypertensive subjects and suggested that osmoregulation of AVP was normal in chronic essential hypertension. In contrast, Thibonnier et al.13 observed with hypertonic infusions that plasma AVP responses to the osmotic load were blunted in hypertensive patients.
However, the responses of urine osmolality were similar in both groups.

The exaggerated diuresis and natriuresis seen in hypertensive subjects after water loading could be related to the greater rise of arterial pressure seen in these subjects. The rise in pressure occurred almost immediately after the water load and was closely correlated in time to the ensuing diuresis. A significant pressure difference between groups was seen only 20 minutes after water loading, which was also the only period in which hypertensive subjects exhibited a significantly greater diuresis and natriuresis.

The exaggerated diuresis in hypertensive subjects also could have been related to the lower levels of plasma AVP reached in these subjects. We do not believe this explanation can account for the differences between the groups, however, for several reasons. First, plasma AVP decreased proportionately in both groups and remained suppressed throughout the entire 100-minute period, whereas the exaggerated diuresis-natriuresis was seen only during the first 20 minutes after water loading. Second, plasma AVP levels were not statistically different between the groups either in the control period or after water loading. Although the present group of hypertensive subjects tended to have plasma AVP levels lower than those in the normotensive groups, this difference was probably due to the small number of subjects studied, since we have previously found in a larger population study (n = 120) that plasma AVP tends to be elevated in moderate essential hypertension.

It is also possible that the kidneys of hypertensive subjects could have responded differently to water loading due to basic differences in medullary solute concentration gradients. Although the water restriction studies were performed in different groups of subjects, we could find no evidence of impairment of renal concentrating ability in this similar group of moderate hypertensive subjects. All of our patients had normal serum creatinine levels and creatinine clearances (see Table 1), indicating an absence of major defects in renal function.

Since PRA was not significantly altered in either normotensive or hypertensive subjects, this factor also did not appear to contribute to the observed differences in diuresis or natriuresis. Atrial natriuretic peptide was not measured in these studies, although it is possible that hypertensive subjects released excess amounts of atrial natriuretic peptide in response to the volume load that contributed to exaggerated renal responses. Further research is warranted to examine this point.

The increase in blood pressure after water loading probably is related to the short-term volume overload. The abrupt onset and short duration of the pressure response could well reflect the rapidity with which the water load was administered and the extravascularization of the water. It is interesting that, in hypertensive subjects, systolic pressure rose more than diastolic pressure following the water load. This disproportionate rise in systolic pressure may be a reflection of decreased arterial compliance, which is characteristic of established hypertension. Patients with essential hypertension are also reported to have reduced venous distensibility. Therefore, volume expansion in hypertensive subjects could result in a greater increase in venous return because of decreased venous capacity, with the resultant greater increase in stroke volume and, hence, systolic blood pressure.

In the absence of any difference in the response of plasma AVP, renin, heart rate, or maximum renal concentrating or diluting ability, it is reasonable to propose that the greater increase of blood pressure in hypertensive subjects is at least partly responsible for the exaggerated diuresis and natriuresis seen in the present study. It is also possible that other yet unidentified mechanisms responding to volume expansion, such as atrial natriuretic peptide release, could also have contributed to these responses.

The intrarenal mechanism of the exaggerated diuresis and natriuresis after water loading in hypertensive subjects was not explored in the present study. Bucklew et al. has shown that, during hypotonic saline loading in maximally hydrated subjects, changes in free water clearance were less in hypertensive subjects than in normal controls and that this response coincided with the development of the exaggerated natriuresis. They attributed this abnormal response of hypertensive subjects to a defect in sodium reabsorption in the loop of Henle. They also noted that the absolute increase in urine volume per milliliter of glomerular filtrate was greater in hypertensive subjects than in normal controls and further suggested that proximal tubular sodium reabsorption was also decreased during volume expansion. Lowenstein et al. has demonstrated that exaggerated diuresis in hypertensive subjects during saline infusion was associated with a greater increase in wedge renal venous pressure and suggested that the increased systemic arterial pressure in hypertension is transmitted beyond the renal arteriole and results in increased intrarenal pressure, causing a pressure natriuresis. Such a mechanism may account for the enhanced diuresis and natriuresis observed in our study during water loading.

Finally, even though hypertensive subjects exhibited a greater increase in urine flow during early diuresis as compared with normotensive subjects, in time they excreted nearly the same volume as the normotensive subjects. Thus, hypertensive subjects approached a state of water balance more rapidly than normotensive subjects. The present study suggests that the greater rise of arterial pressure in hypertensive subjects in response to a water load could account in part for both the exaggerated diuretic and natriuretic responses. The study also provides evidence that mildly hypertensive subjects suppress AVP as well as do normal subjects in response to a water load.

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