Importance of Dietary Salt in the Hemodynamic Adjustment to Weight Reduction in Obese Hypertensive Men

OVE K. ANDERSSON, BJÖRN FAGERBERG, AND THOMAS HEDNER

SUMMARY Twenty-three moderately obese middle-aged men with previously untreated hypertension (World Health Organization classification 1-2) were evaluated to assess the effects on blood pressure (BP) of a diet restricted in energy (fats and carbohydrates) but unrestricted in sodium (Group 1) compared to a diet restricted in energy and sodium (Group 2). The patients were randomly allocated to either of the two groups and were comparable in age, sex, weight, and BP. The same energy- and sodium-restricted diet was given to both groups, but the intake of Group 1 (n = 13) was supplemented with dietary sodium. The average urinary sodium output for Group 1 was 192 ± 39 mmol/24 hr at baseline and 200 ± 56 mmol/24 hr during the diet. For Group 2 (n = 10), which remained on the initial diet, urinary sodium excretion changed from 188 ± 53 mmol/24 hr at baseline to 97 ± 32 mmol/24 hr (p < 0.001). Intraarterial BP, cardiac output (CO), plasma volume, circulating norepinephrine (NE), and urinary NE were measured at baseline and at the end of the dieting periods. Before the dietary sodium supplement while on the initial diet, the patients in Group 2 showed a reduction in body weight from 97.3 ± 10.5 kg to 88.6 ± 9.9 kg (p < 0.001). Heart rate (HR) and urinary NE output were significantly reduced in comparison with baseline, but intraarterial BP was unchanged. No change in cardiopulmonary blood volume, CO, or stroke volume (SV) was observed. Total blood volume was unchanged, but it was relatively increased when corrected for body surface area (BSA) or body weight. Group 2 had a significant reduction in body weight of from 98.2 ± 9.6 kg to 89.5 ± 9.3 kg (p < 0.001). Significant reductions were also observed in intraarterial BP, HR, CO, circulating NE, and urinary NE compared with baseline. In comparison to Group 1, Group 2 also had a mean arterial pressure that was significantly reduced (p < 0.05). Total blood volume was unchanged during restriction of dietary sodium and energy. In conclusion, we found that hemodynamic adjustment and BP reduction were associated with weight reduction only when the dietary sodium was also restricted. The results indicate a reduction of sympathetic nervous tone in both groups, probably as a consequence of energy restriction. How normal sodium intake offsets the hypotensive response to weight reduction is not known. (Hypertension 6: 814-819, 1984)

KEY WORDS • hypertension • obesity • weight reduction • sodium • norepinephrine • hemodynamics • blood volume

WEIGHT reduction generally causes a fall in blood pressure (BP) in hypertensive patients with moderate as well as morbid obesity. Hypertensive as well as normotensive obese patients show BP reduction, in some studies associated with reduced levels of plasma norepinephrine (NE) and of urinary NE excretion. Starvation and reduced energy intake clearly impair sympathetic nervous system activity in animal experiments as well as in humans. Other mechanisms, such as reductions in plasma renin activity (PRA) and aldosterone, may also be involved in modifying BP following weight reduction. Restriction of dietary salt has been proposed as an important influence, and energy reduction without salt restriction has also been proposed as an effective BP control in moderately obese hypertensive patients.

The present study is a repeated hemodynamic investigation of two groups of obese men with mild to moderate hypertension who reduced their body weight with and without dietary sodium restriction. The objectives were to study hemodynamic and fluid volume changes and the adaptation of the sympathetic nervous system, to better understand the mechanisms behind the altered BP regulation after weight reduction.
Methods

Patients
We studied 23 men with a mean age of 51 years (range, 41-59 years) who had recently been diagnosed as having hypertension (WHO Stage 1-2) but who were untreated. All patients were 20% to 40% overweight and had diastolic BPs of 95 to 105 mm Hg after 10 minutes of supine rest on at least two occasions. The cuff used measured 16 x 36 cm. Secondary forms of hypertension were excluded according to usual routines.

Protocol
The study protocol was approved by the Ethics Committee of the Sahlgrenska University Hospital, and all patients were given detailed information about it and gave their consent. Before inclusion in the study, the patients were randomly allocated to either of two groups. During a basal diet period of 4 to 6 weeks, four 24-hour urinary sodium samples were collected, which started at 0700. Determination of urine sodium, potassium, creatinine, and urine volume was done. The creatinine content of each portion of the samples was used as an index of completeness of collection, and a 24-hour collection was not accepted if the urinary creatinine content was less than 8.8 mmol (1 g). The last 24-hour urine collections during baseline and dieting were delivered on the morning of the hemodynamic investigations. All patients were also interviewed by a dietitian, and their diet habits were recorded for 4 days. Initially, Groups 1 and 2 were put on a diet restricted in energy and sodium, but the patients in Group 1 had individually adjusted energy-reduced diets with sodium chloride supplementation. The diet periods lasted for 9 to 11 weeks.

Diet
The diet was balanced (15%—20% of energy taken as protein, 25%—30% as fat, and 50%—60% as carbohydrates) with a low sodium content and was aimed at a weight reduction of 1 kg per week. Group 1 patients received added table salt in preweighed packages and sodium tablets (Natriumklorid, 0.5 g, ACO, Solnd, Sweden); the amount was estimated from the four previous 24-hour urinary sodium outputs. All patients were interviewed by the dietitian every 2 to 3 weeks, and body weight as well as urinary sodium output was determined. Adherence to the diet was checked by interview and by 4-day dietary records. The hemodynamic and intravascular fluid variables were reexamined after a body weight reduction of 5% or more.

Patient Compliance
During baseline and dieting programs, the patients had been instructed not to change exercise, smoking, or drinking habits. Questionnaires were used for between-group and within-group comparisons and revealed no differences before or during dieting. As judged from diet histories, Group 1 patients on energy restriction while on sodium supplement consumed 1270 ± 190 kcal/day (5.1 megaJoule [MJ]), which consisted of 26% ± 4.1% fat with a polyunsaturated/saturated fat ratio of 0.24 ± 0.05. The energy intake of Group 2 patients was 1200 ± 140 kcal/day (5.1 MJ) and consisted of 25.1% ± 5.6% of energy taken as fat, with a polyunsaturated/saturated ratio of 0.23 ± 0.06. The amount of sodium excreted during baseline and dietary periods are shown in Table 1.

Central Hemodynamics, Plasma Volume, and Catecholamines
Hemodynamic studies, including plasma volume estimations and sampling for plasma catecholamines, were performed in the morning. The patients arrived at 0800 after a standardized breakfast at home (tea and toast). The same methods were used in the reinvestigation, and they were performed by the same staff and technicians. Polyethylene catheters were inserted percutaneously into the left brachial artery and into a cubital vein (Seldinger technique). The venous catheter was advanced to the right atrium or superior caval vein and the arterial catheter to the ramifications of the subclavian artery from the aortic arc. Positions of the catheters were checked by x-ray.

At 30 minutes after placement of the catheters, with the patient resting supine, Evans blue dye was injected for plasma volume determination. Blood samples were drawn from the central circulation at 5, 10, 15, and 20 minutes after the injection. The hypothetical plasma concentration of the dye at zero time was calculated from a plot of log concentration against time. From that concentration and the amount of dye injected, the plasma volume was calculated. Total blood volume was calculated from the plasma volume and the hematocrit with correction for the difference between total body and large vessel hematocrit. Samples for circulating catecholamines were drawn intravenously immediately prior to the infusion of Evans blue dye. The plasma was immediately separated, and the samples were frozen at 70°C. Plasma NE was assayed by high pressure liquid chromatography; the normal range for plasma NE in our laboratory is 1.18 to 2.37 nmol/liter. In this reference group of patients with essential hypertension, plasma NE after supine rest for 45 minutes was 2.19 ± 0.12 nmol/liter (n = 61). For two of the 24-hour urinary collections, the NE excretion was determined by a modified method of von Euler and Lishajko. The coefficient of variation was 11% for urinary NE at a known concentration of 199 nmol/liter. The normal range in our laboratory is 70 to 420 nmol/24 hr.

Before determination of cardiac output (CO), simultaneous indirect and intraarterial BP measurements were done by the same nurse who made all auscultatory BP measurements in the study. Intraarterial BP was recorded with a pressure transducer (EMT 34, Siemens Elema, Solna, Sweden). Intraarterial mean pressure (MAP) was obtained from electrically damped curves and recorded immediately prior to each CO determination. The CO was determined by dye dilution (Indocyanamin green) with a cuvette and densitometer (Cardiognost, Atlas, Bremen, West Ger-
many). The blood was reinfused after each determination, and at both examinations the mean of at least five separate determinations, which had been taken at 5-minute intervals, was used. Cardiopulmonary blood volume was calculated as the product of the mean transit time and blood flow per second at the tip of the catheters. This value provided an estimate of the distribution of the total blood volume with regard to central (cardiopulmonary) circulation. Stroke volume (SV) was calculated from the CO and from the heart rate (HR), measured by electrocardiogram (ECG), and total peripheral resistance (TPR) was calculated from the MAP and CO. The CO, TPR, and SV were corrected for body surface area (BSA), and the indices for these values (CI, TPRI, and SVI) were derived.

Statistical Methods

Standard methods were used for calculation of means, standard deviation (SD), and correlation coefficients (r). Differences in means within and between groups were tested with Student’s t-test; only two-tailed tests were used.

Results

Body Weight and Sodium Excretion

Patients on caloric restriction and unchanged sodium intake (Group 1) had a reduced body weight of from 97.3 ± 10.5 to 86.6 ± 9.9 kg (ABW 8.7 ± 2.5 kg; p < 0.001). The urinary excretions of sodium were unchanged from baseline. The diet histories showed a highly significant reduction of energy intake (Table 1).

The patients on energy- and sodium-restricted diets (Group 2) had significant weight reduction of from 98.2 ± 9.6 to 89.5 ± 9.3 kg (ABW 8.7 ± 3.0 kg; p < 0.001). They showed a considerable, highly significant reduction in sodium excretion.

Hemodynamics

The patients in Group 1 showed a significant reduction in heart rate but not in BP during energy restriction but unchanged sodium intake (Table 2). The other hemodynamic variables (cardiopulmonary blood volume, CO, SV, TPR) were unchanged.

The patients in Group 2 showed a significant reduction of systolic and diastolic BP and consequently MAP (Table 2), which was associated with a significant reduction in HR and CO; SV was unchanged. When corrections were made for BSA, there was also a significant reduction (14%). No changes were noted in cardiopulmonary blood volume, in the ratio of cardiopulmonary-to-total blood volume, or in TPR (Table 2).

Blood Volume

There was no change in total blood volume in Group 1 (Table 1). When blood volume was corrected for weight and BSA, a significant increase was observed.

The patients in Group 2 had unchanged blood volume and blood volume indices (ErSr).

Norepinephrine

In Group 1, there was a significant reduction in the urinary output of NE of from 374 ± 96 nmol/liter/24 hr to 296 ± 89 nmol/liter/24 hr (p < 0.01). However, there was no significant reduction in plasma NE: 1.56 ± 0.47 nmol/liter/24 hr compared to 1.24 ± 0.30 nmol/liter/24 hr (NS).

In Group 2, the urinary output of NE was significantly reduced from 363 ± 88 nmol/liter/24 hr to 313 ± 79 nmol/liter/24 hr (p < 0.01). In the reexamination after the same dietary period, plasma NE was reduced from 1.42 ± 0.36 to 0.95 ± 0.36 nmol/liter/hr (p < 0.01).

Correlations

In Group 2, there were positive correlations between AMAP and Abody weight (r = 0.61; p < 0.05) and between AMAP and AU NE/24 hr (r = 0.13; p < 0.01). There were no significant correlations observed between AMAP and changes in hemodynamic variables or intravascular blood volume. No significant correlations were noted between blood volume and CO or SV. No correlations were observed between HR and plasma NE or urinary NE excretion.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1 (n = 13)</th>
<th>Group 2 (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Diet</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>50.9±5.2</td>
<td>50.7±3.6</td>
</tr>
<tr>
<td>LV hypertrophy (x-ray)</td>
<td>3/13</td>
<td>3/10</td>
</tr>
<tr>
<td>Eye-ground changes (I/II)</td>
<td>6/13</td>
<td>5/10</td>
</tr>
<tr>
<td>WHO Stage (1/2)</td>
<td>6/7</td>
<td>5/5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>177.3±5.0</td>
<td>180.4±4.4</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>97.3±10.5</td>
<td>88.6±9.9*</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>2.14±0.13</td>
<td>2.06±0.12*</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>2300±400</td>
<td>1200±140*</td>
</tr>
<tr>
<td>Sodium excretion (mmol/24 hr)</td>
<td>192±39</td>
<td>200±56</td>
</tr>
</tbody>
</table>

Values are means ± SD. LV = left ventricle; BSA = body surface area.

*p < 0.001 in comparison to the predicting level.
Our results demonstrate that weight loss lowers the BP only when the diet is restricted in both calories and sodium; only a relatively modest restriction of sodium intake is necessary. This observation supports the results of Dahl and of Raison and co-workers, but is contrary to the results of other investigators. One of these latter studies was uncontrolled with regard to predicting sodium excretion, however, and makes us question its conclusion that BP reduction was caused by energy restriction only. Yet, several studies of severe energy restriction have indicated that BP reduction is independent of sodium intake.

In our present study, the patients on combined energy- and-sodium restriction showed significant reduction in BP, HR, and CO, but unchanged TPR. In a recent study by Reisin and co-workers, obese hypertensive men showed a considerable weight reduction associated with significant BP reduction. Hemodynamic and plasma volume studies were performed during ad libitum sodium intake; the loss in body weight and the reduction in BP, HR, and CO were similar to those in our study. They observed an unchanged TPR in relation to a reduced CO, as in our study. In the study by Raison and co-workers, nine obese patients with mild hypertension reduced their weight during dietary energy restriction with moderately reduced sodium intake (90 mmol/day). That study was uncontrolled, but showed a significant BP reduction as well as HR and CO reduction; the TPR did not increase. When we compare our study with the two referred to, we note remarkably consistent changes in hemodynamic parameters following dietary energy restriction with weight reduction. Furthermore, our observations of a reduction in circulating NE and/or urinary NE output are similar. Inconsistencies do exist, however,
regarding blood volume observations and the interpretation of cardiovascular adaptation to weight reduction.

In our study, neither caloric restriction alone nor concomitant moderate energy-and-sodium restriction resulted in reduced blood volume or changes in cardiopulmonary blood volume. Furthermore, when we corrected for body weight or BSA, we found that blood volume was increased in patients with unchanged sodium intake during energy restriction. This fact may partly explain the unchanged SV, CO, and BP that we noted following mode-rate weight reduction in these patients. The discrepancy between our data for blood volume and those from other groups is probably explained by variations in study design, diet composition, and patient compliance. In the study by Raison and co-workers, energy as well as sodium was more severely restricted and resulted in "only minimal changes in plasma volume." Their patients lost more weight than ours, and hence a small but statistically significant reduction of blood volume was possible.

Our observation after correction for body weight that blood volume was unchanged or even increased is similar to that of most investigators studying patients during weight reduction and reflects, simply, the smaller fluid volume per unit weight of adipose tissue as compared to lean body mass. In our opinion, an overall reduction in sympathetic tone may well result in unchanged intravascular volume or even in blood volume expansion, as is shown with drugs that inhibit sympathetic function. Furthermore, plasma and blood volume are negatively correlated with MAP and the elevated transcapillary escape rate of albumin and fluid in hypertension could theoretically be reversed when systemic BP is reduced. Such a reversal could result in preservation or even expansion of intravascular fluid volume.

The repeated finding in our study was the reduction in urinary NE and in HR in both groups of patients during a moderate reduction in energy intake with and without sodium restriction, an observation previously well documented after caloric restriction. Circulating NE, too, was reduced in patients on energy and sodium restriction. These findings suggest reduced activity of the sympathetic nervous system and could well explain the hemodynamic changes in patients on energy and sodium restriction, especially since a redistribution of the blood volume from the cardiopulmonary to the peripheral circulation cannot explain the CO reduction. Reduced sympathetic activity should alter CO directly by decreasing the myocardial contractility as well as HR. Reduced vasoconstrictor activity should affect arteriolar tone and offset an increase in TPR that would otherwise be caused by the lowered CO output.

On the basis of NE levels in the venous plasma, it has been suggested that increased sympathetic activity may contribute to the increased BP in obese patients. Conversely, weight reduction during caloric restriction results in a progressive decrease in the abnormal plasma NE levels so that a normal range is reached in normotensive obese subjects as well as in borderline hypertensive obese patients. The reduction of plasma NE occurs irrespective of dietary sodium intake. Our hypertensive patients had levels of plasma NE that did not exceed the normal range, but on the other hand, we have no reference for normal values in obese patients under similar circumstances. It must be assumed that plasma NE levels reflect the degree of relaxation the patients are allowed, and we believe our patients were very calm and relaxed, since many of them fell asleep. Another sign of rather basal sympathetic activity during supine rest in our laboratory is a low HR (Table 2). After caloric restriction, our obese patients showed reduced urinary NE output regardless of restricted or normal dietary sodium, which suggests the same response from the sympathetic nervous system as has been shown by other investigators. There was a discrepancy in the plasma NE levels noted in Groups 1 and 2 after weight reduction; only patients on concomitant caloric and sodium restriction had significantly lowered circulating NE. Whether this was due to different adrenergic responses to caloric restriction with or without normal sodium intake is hard to understand, especially since the HR and urinary NE decreased in both groups. A less pronounced reduction in vasoconstrictor tone, however, might be one explanation for the fact that BP did not normalize in patients on unrestricted sodium intake.

In the present investigation, maintenance of baseline sodium intake offset the hypotensive effect of energy restriction; no hemodynamic alterations except a reduction in HR were noted. From our data, we can only conjecture that an increased vascular sensitivity from chronically reduced sympathetic activity during unchanged sodium intake could probably maintain a constant BP in spite of reduced vasoconstrictor tone.

In summary, we have evidence that patients on reduced caloric intake resulting in moderate weight loss have decreased sympathetic nerve outflow and neuronal release of NE. When dietary sodium is also restricted, the BP, HR, and CO are reduced. If the sodium intake is not reduced, the BP and CO values remain unchanged despite the reduction in dietary energy. Alterations in blood volume or its distributions following the dietary intervention were not necessary for the normalization of BP.

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References

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