Clinical Interaction of Salt and Weight Change on Blood Pressure Level

R.J. Prineas

Studies that examine the effect of altered body weight or dietary sodium on blood pressure level are reviewed. Emphasis is placed on studies that compare the effects of weight reduction or sodium restriction in separate comparison groups or analyze the independent effect of the two intervention modalities in multiple regression analysis. Additional analyses of the Hypertension Prevention Trial data are presented. Most studies, where comparison can be made, suggest a greater effect for weight reduction than for the achieved, moderate, or short-term reduction in sodium intake on subsequent lowering of blood pressure; the lowering effect on blood pressure of weight reduction is independent of the effect of dietary sodium restriction. However, long-term (over a year) substantial reductions (up to 70 meq/day) of dietary sodium have not been achieved in comparative trials, nor are the effects of combined weight and sodium reduction in the prevention and treatment of hypertension quantified. Future studies and potential problems are discussed. (Hypertension 1991;17[suppl I]:I-143–I-149)

The question of how much the lowering of blood pressure can be achieved by the effects of weight reduction and reduction of excess dietary salt has been around for most of this century. Although Rose1 in 1922 is credited with the first demonstration of obesity reduction effect on lowering blood pressure in hypertensive patients, George Norris, in his 1914 book2 Blood Pressure: Its Clinical Applications, cites a 1904 publication by Dunin3: “If hypertension is associated with adiposity, a reduction of weight produces a fall of pressure.” It was in the same year that Ambard and Beaujard4 published their discussion on the value of dietary sodium reduction in the treatment of hypertension.

Since that time, a vast and fundamental unraveling of the mechanisms of the effect of obesity and dietary sodium on blood pressure regulation and the effect on treatment of hypertension has been made. The latter notwithstanding, no definitive study at the level of long-term controlled intervention has been made that establishes the relative, independent, and interactive effects of the treatment or prevention of hypertension in diverse ethnic, sex, and age groups of obesity and dietary sodium reductions. This list might include too many factors to manage in one definitive trial. However, no published studies have been done (at the time of this symposium) to answer the questions about whether weight reduction or reduction of excess dietary salt have much different effects on long-term blood pressure lowering or whether the separate or combined application of one of these intervention modalities is more effective.

Although the question of the value of dietary sodium on lowering blood pressure in hypertensive persons has been around for at least 85 years, testing with clinical trials to examine this effect is less than 20 years old, and the attempted comparison of the combined effects of obesity and sodium reduction on blood pressure lowering are more recent. A review of all clinical trials on the effect of obesity reduction alone or salt reduction alone on blood pressure lowering is not attempted here because they do not address the interactional effect of sodium and obesity reduction on subsequent blood pressure change, nor do they compare the relative efficacy of one intervention with the other. Nevertheless, it is noteworthy that many such trials have shown that either weight reduction or dietary sodium restriction separately will effect the lowering of blood pressure.

A major problem of nutritional/behavioral intervention studies involves blood pressure measurement in unblinded studies. If technicians of blood pressure measurement are aware of the intervention group to which a participant is assigned, the subsequent blood pressure measurement levels that reflect the expected direction of blood pressure change can be biased. The suggestions for measurement in Table 1 are intended to obviate this bias. Masked studies of weight reduction alone are not possible. Blinded studies (for salt reduction) can be ethically con-
The mean change in urine sodium during the crossover period that preceded an 8-week crossover period averaged 67 mmol/day regardless of order. Multiple trained blood pressure technicians should be used at each center.

Participants
Participants in each treatment group should have blood pressures measured equally often. Participants in each treatment group should be equally familiar (or unfamiliar) with the blood pressure technician and location of blood pressure measurement.

Location/time
Intervention and blood pressure measurement should occur at separate locations. There should be no systematic differences between groups in participant attendance at the measuring location by time of the day (AM/PM), day of the week, or season of the year.

Sphygmomanometer
Ambulatory
Automatic
Random zero

Measurements
At least two blood pressure measurements should be made on each occasion, and special attention should be given to appropriate bladder cuff width/arm circumference ratio in obesity reduction trials.

... study. In a subsequent study among nine hypertensive, diabetic patients, Dodson et al7 showed significantly lower systolic blood pressure during the moderate compared with high sodium-intake phase in a 2-month blinded crossover study. Two other blinded studies of the effect of sodium on blood pressure did not show a significant effect of sodium intake change on blood pressure level. However, both of these studies by Watt et al8 and Grobee et al9 had very poor power to show an effect because of small sample sizes. In a more recent small but longer term double-blind study of the effect of sodium intake change on blood pressure level, MacGregor et al10 showed a substantial effect. Among 20 patients with mild hypertension untreated, there was a three-phase crossover study with 1 month in each of the three phases of sodium intake (average sodium excretion in each phase was 49 mmol/day, 108 mmol/day, and 190 mmol/day). The average systolic/diastolic blood pressures at the end of the two lower-intake phases, 147/91 and 154/95 mm Hg, were significantly lower than the average blood pressure of 163/100 mm Hg at the end of the high-sodium-intake group. In a more recent study reported by Masciioli et al11 in this supplement, a double-blind study of sodium supplementation was made among 46 men and women (aged 30–59 years) with high-normal blood pressure (diastolic blood pressure of 80–90 mm Hg and systolic blood pressure less than 150 mm Hg) that compared blood pressures at the end of two 4-week periods on 100 meq Na+/day or placebo, with a 2-week intervening washout period. Before and during the study, all patients in each group received counseling for a low sodium diet. Overnight urinary sodium excretion was 51 meq/8 hr after the sodium supplementation and 19 meq/8 hr after placebo. The supplementation of 100 meq/day sodium resulted in an average increase of 3.6 mm Hg systolic blood pressure and 2.3 mm Hg diastolic blood pressure. This blood pressure effect for dietary sodium change is similar to that found among the studies of mildly hypertensive patients described above.

Many unblinded studies have shown the efficacy of both obesity reduction and sodium reduction separately and have been reviewed many times (Maxwell and Waks12 and Grimm and Prineas13); results of other studies presented at this meeting also show the blood pressure–lowering effects of weight or sodium reduction separately.

Combined Effects of Salt and Weight Reduction
To separate the effects of obesity reduction from those of sodium restriction on blood pressure lowering, it is necessary to examine evidence from studies in intervention trials that test the concomitant effects of both modalities (sodium and weight). The aforementioned single-modality change trials cannot test this interaction. The following studies have examined the interaction; therefore, because few such studies are available in the literature, both uncontrolled and...
controlled studies are examined in a review of the literature, together with previously unpublished data. Dahl postulated that the association of obesity with hypertension is caused by a parallel increase in sodium intake and that with weight reduction the hypophagia is accompanied by a reduction in ingested sodium, which in turn causes the blood pressure lowering that accompanies the weight loss. Many population studies have shown that obese adults have a reduced calorie intake compared with the nonobese; it is also possible to alter the diet to reduce sodium intake without altering calories and yet maintain nutrient balance. In other words, obese populations can maintain high blood pressure without a high calorie diet, and sodium intake is not necessarily directly related to calorie intake.

Furthermore, in separate studies by Reisin, Tuck, and Gillum and their colleagues, independent effects for blood pressure lowering have been shown for weight reduction and reduction of excess dietary salt when these interventions were combined. Tuck et al have shown among very obese (averaging 70% overweight) hypertensive individuals given severe caloric restriction (320 kcal/day), which resulted in a 20-kg weight loss, that blood pressure lowering of similar magnitude was achieved whether the patients were given diets of 40 or 210 meq/day sodium.

Studies of Reisin et al have shown that marked short-term blood pressure reduction could be achieved in obese hypertensive patients adhering to a low calorie diet while instructed to eat a high salt diet. The urinary sodium excretion at the end of a 2-month period was high, and the reduction in blood pressure correlated with a change in body weight. However, there was no baseline measurement of sodium excretion, and actual sodium intake and serial blood pressure measurements were not made throughout the study. After further experience during the years since this study was reported, the difficulty of maintaining substantial long-term dietary salt reduction in many subsequent studies demonstrates the apposite nature of Reisin's findings.

In sequential, short-term studies of weight reduction alone, dietary sodium reduction alone, or combined weight reduction and salt reduction, Gillum et al obtained changes in blood pressure among middle-aged white men with moderate obesity and mild, established, elevated blood pressure (Table 2), such that additive effects of weight reduction and sodium reduction on the subsequent fall in blood pressure seemed to occur. Those studies did not incorporate an untreated group, and the relative separate effects of sodium restriction and weight and salt reduction cannot be quantified.

Studies by Fagerberg et al and Andersson also achieved short-term blood pressure reduction in obese hypertensive persons when sodium was also restricted but not when weight reduction alone was applied. The differences in these studies from those of Reisin et al are not readily explained, although Fagerberg's studies are flawed because of the low number of subjects and single-clinic visits before and after intervention to judge blood pressure change. In addition, there was a relatively high alcohol intake reported by his study participants, and no untreated control group was used.

Longer-term studies of the effects of salt and weight reductions on the degree of blood pressure lowering are few; none quantify the separate and interactive effects of weight and sodium reductions in different age–race–sex groups for different levels of obesity and blood pressure, different initial levels of dietary salt ingestion, and different achieved goals of weight and dietary salt reductions (urinary sodium excretion). The predicted fall in blood pressure for a given change in weight varies greatly and is difficult to compare between studies, given the varying time of follow-up, sample size, and structure of the aforementioned variables.

In 1985, Rissanen et al reported from Finland on the effects of a 12-month intervention follow-up among 64 obese hypertensive patients (more than 75% of whom were taking antihypertensive medication). They reported similar significant improvement in hypertension control among each of two groups that achieved weight reduction alone and combined weight and sodium reductions, although the latter only achieved reduction to approximately 150 meq sodium excretion/day from over 200 meq sodium excretion/day, illustrating the difficulties of achieving salt reduction in the face of few locally available low salt foods. The group with sodium reduction alone did not achieve significant blood pressure or medication control. However, in addition to the poor sodium restriction achieved, there were differences in baseline weight, sex, and blood pressure levels among the three intervention groups. Even in nonobese hypertensive persons, weight loss without change in urinary sodium excretion leads to a fall in blood pressure.
with a concomitant fall in antihypertensive medication as reported by Imai et al.28

In the Dietary Intervention Study in Hypertension (DISH), Langford et al29 studied 325 obese people (mostly black women) with established hypertension after cessation of antihypertensive drug treatment. There were three groups assigned to weight reduction alone, reduced dietary sodium alone, or no dietary intervention. Compared with the no-change group, both treated groups achieved better antihypertensive drug-free blood pressure control (without reinstatement of antihypertensive medication), with the best effect gained for the weight reduction group after a mean of 56 weeks of intervention. The weight reduction averaged 4.5 kg, and the sodium reduction resulted in an average decrease of 50 meq/day. In two groups of nonobese hypertensive subjects in the same study, salt reduction alone (with an average of 44 meq/day) also increased blood pressure control during the study.

More recently, a multi-intervention strategy of the combined nutritional intervention of salt, weight, and alcohol intake reductions by Stamler et al,30 which was conducted over a 5-year period among men and women with high-normal blood pressure (in a randomized, controlled, intervention study), showed independent effects of weight reduction and salt restriction on blood pressure lowering. In multiple regression analysis, an average 4.5-kg weight loss was associated with a difference of 2.1 mm Hg systolic and 1.5 mm Hg diastolic blood pressure fall. The change in blood pressure associated with sodium and alcohol reductions was not independently significant. The net sodium urinary excretion was modest, from 3,980 mg/day to 3,039 mg/day.

In another controlled but unblinded clinical trial begun in 1984, The Hypertension Prevention Trial (HPT),31 a partial factorial design for intervention among 841 men and women with high-normal blood pressure, was conducted, and participants were followed over a 3-year period. Participants were randomly assigned to a control treatment group (no dietary counseling) or one of four dietary counseling treatment groups: reduced calories, reduced sodium, reduced sodium and calories, or reduced sodium and increased potassium. Participants were observed for a 3-year period to assess the effect of their dietary changes on blood pressure.

Changes achieved after 6 months included a net (over control) average overnight urinary sodium reduction of 3.3 mmol/8 hr (13%, p=0.0002), a potassium increase of 1 mmol/8 hr (8%, p=0.102), and a decrease in average mean body weight of 5.8 kg (7%, p=0.001). At 3 years, the sodium and weight reductions were 5 mmol/8 hr (p=0.053) and 3.5 kg (p=0.001), respectively. There was no potassium change. All net changes were adjusted for covariates, which included age, race, sex, social class, body mass index, tobacco and alcohol use, and baseline levels of the intervention variables.

All four treatment groups had lower blood pressures than those observed for the control group.

The largest net reductions occurred in the calorie counseling treatment group (6 months: diastolic blood pressure, 2.8 mm Hg and systolic blood pressure, 5.1 mm Hg; 3 years: diastolic blood pressure, 1.8 mm Hg and systolic blood pressure, 2.4 mm Hg; and p values: 0.010, 0.001, 0.045, and 0.031, respectively). Participants in all four treatment groups also had fewer hypertensive events (systolic blood pressure 140 mm Hg or more or diastolic blood pressure 90 mm Hg or more or a prescription of antihypertensive medication) than those assigned to the control group. Results of the trial suggested a modest, separate, beneficial effect for reductions in both weight and sodium intake in relation to the prevention of hypertension.
TABLE 4. Possible Future Studies

| Intervention | 1) Factorial experiments of weight reduction, salt reduction, and weight and salt reduction |
| Duration     | 2) 2 Years (to estimate recidivism) |
| Participants | 3) Blacks, whites, children, adults, aged, and on/off medication |
| Blood pressure severity | 4) Normotensive, High-normal blood pressure, Hypertensive (mild/moderate/severe) |
| Obesity      | 5) General, Central |
| Level of intervention | 6) Weight loss for those ≥110% of ideal weight to 10% weight loss or less than 110% ideal weight (whichever is greater loss) |
|              | Weight loss for those at <110% of ideal weight to 10% lower weight to maximum loss to 90% of ideal weight |
|              | Sodium intake restriction for those with sodium intake ≤150 to ≤70 or ≤100 meq/day |
|              | Sodium intake restriction for those with sodium intake greater than 150 meq/day to 50% of current intake |
| End points   | 7) Blood pressure measured on multiple occasions, Left ventricular mass measured on echocardiogram |
| End point measurement | 8) Central, blinded echocardiogram measurements, Automatic sphygmomanometer (ambulatory?) |

*Achievable sodium intake reduction will depend on current optimal behavioral intervention and the local availability of low salt foods (prepared and unprepared).

Although the greatest blood pressure fall occurred in the group counseled for reduced calories alone, the next greatest drop in blood pressure occurred in the group counseled for calorie and dietary sodium restrictions. However, the average weight loss in the latter group was less than that in the former (calorie reduction alone), which was 4.1 versus 5.8 kg at 6 months and 2.0 versus 3.5 kg at 3 years, whereas the sodium excretion in the combined sodium and caloric reduction group was greater (though modest) compared with the sodium reduction alone group. The interaction of calories x sodium was not statistically significant at 6 months or 3 years for diastolic blood pressure lowering and only for systolic blood pressure at 6 months. This interactive effect showed a net gain in systolic blood pressure at 6 months, unlike the fall in systolic blood pressure for the independent effects of weight loss or sodium restriction. Such a finding has not been reported in any other study and may be partially explicable due to a lower weight loss in the combined intervention group. However these results are interpreted, the weight loss effect on lowering blood pressure clearly does not depend on a concomitant reduction of dietary sodium, which is reflected in a decrease of urinary sodium. Also noteworthy is a sodium effect on systolic blood pressure that can be detected after 3 years, even though the net change is less than 20 mmol reduction in sodium excretion extrapolated to 24 hours.

Further supplemental analysis of the HPT data set was done that combined treatment and control groups to examine, with multiple linear regression analysis, the independent effects of weight and sodium reductions on blood pressure level in four separate sex-weight groups (adjusted for baseline covariables) with complete data sets. Blood pressures for individuals placed on antihypertensive medications during follow-up were imputed: diastolic blood pressure as the greater of the measured diastolic blood pressure at the visit before starting antihypertensive medication or a level equal to 95 mm Hg, and systolic blood pressure as the greater of the measured systolic blood pressure at the visit before starting antihypertensive medication or a level equal to 140 mm Hg. Table 3 shows the results of these analyses for change in diastolic blood pressure and systolic blood pressure, respectively, from baseline to 6 months and baseline to 3 years separately. A change in systolic blood pressure level was significantly related to the changes in diastolic and systolic blood pressures at 3 years for overweight groups of men and women. This relation was also apparent at 6 months for all except the high weight group of women for diastolic blood pressure. A change in urinary sodium excretion was not independently related to changes in diastolic and systolic blood pressures at 3 years for overweight groups of men and women. This relation was also apparent at 6 months for all except the high weight group of women for diastolic blood pressure. A change in urinary sodium excretion was not independently related to diastolic blood pressure change for any of the four sex-weight groups. However, a change in urinary sodium excretion was significantly and independently related to a change in systolic blood pressure for women of normal weight at 6 months and for high weight men and women at 3 years. The systolic/diastolic differences may be due to the larger absolute change in systolic compared with diastolic blood pressure.

Future Studies

Future studies of the separate and combined effects of lessening excess dietary salt and weight reduction, if they are deemed necessary to quantify the effects on the treatment and prevention of hypertension, will need to address the points of design given in Table 4. In particular, studies of normotensive persons and those with high-normal blood pressure...
are needed to establish the effectiveness of primary prevention. The association of increased risk with increased levels of blood pressure is continuous.32 Small changes in an individual’s blood pressure level translate to substantial population benefits of blood pressure lowering. For example, a 2 mm Hg shift to lower blood pressure levels in the distribution of diastolic blood pressure in the general population has the potential for reducing stroke mortality by 13%, and a 6 mm Hg shift could lower it by 43%.32 Long-term studies in severely hypertensive patients are ethically only in the context of nutritional intervention that supplements effective drug therapy; control groups can be treated with test drugs without the added nutritional intervention. Blinded trials are not possible in the latter context, and trial end points should include objective evidence of end-organ damage.

The differential effects on blood pressure lowering of obesity reduction among those with central obesity versus those with lower body obesity also needs to be examined, given the specific, demonstrated, independent relation between central obesity and hypertension.33–36 On balance, data appear to support the concept of combining weight reduction and reduction of excess dietary salt for the treatment of hypertensive individuals (whether or not combined with active antihypertensive drugs) and prevention for those at risk, whatever their blood pressure level.

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R J Prineas

_Hypertension_. 1991;17:I143
doi: 10.1161/01.HYP.17.1_Suppl.I143

_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1991 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

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