Salt Restriction in the Treatment of Isolated Systolic and Combined Hypertension
Is That Enough?

Myron H. Weinberger

The most recent recommendations of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VII) have emphasized dietary sodium (salt) restriction as a major lifestyle intervention with which to reduce blood pressure in those with “prehypertension” and as adjunctive therapy in combination with antihypertensive drugs in those with established hypertension. The benefit of a reduction in salt intake in lowering blood pressure in many, but not all hypertensive subjects, is well known and widely accepted on the basis of numerous trials. Nonetheless, debate continues regarding the extent of restriction required and whether all forms of hypertension benefit. He et al, in this issue of Hypertension, provide new insight into the impact of modest salt restriction on blood pressure in those with isolated systolic hypertension, as well as those with combined systolic–diastolic hypertension by reanalyzing data from 4 previous trials that they conducted. Among 24 subjects with isolated systolic hypertension and an average age of 63 years, a mean reduction of urinary sodium excretion from 175 to 87 mmol/d for 1 month resulted in an average decrease of 10/1 mm Hg (systolic/diastolic) (baseline 166/86; intervention 156/85) in blood pressure. These findings are similar to much larger drug intervention studies in such subjects demonstrating significant decreases in systolic pressure without appreciable changes in diastolic pressure. Among 88 younger (average age, 55 years) subjects with systolic/diastolic hypertension, a reduction from 175 to 98 mmol/d in average sodium excretion resulted in an average blood pressure decrease of 7/4 mm Hg. The smaller reduction in systolic blood pressure with salt restriction in this group may be, in part, attributable to their lower baseline systolic pressure that averaged 161 mm Hg in comparison with those with isolated systolic hypertension who averaged 165 mm Hg at baseline. Moreover, a greater number of black subjects, a group known to be more sensitive to manipulation of dietary salt intake, were included in the systolic/diastolic hypertension group, increasing the likelihood of a blood pressure response. Given the variability in urinary sodium reduction observed in the studies, it would have been interesting to determine whether a threshold for blood pressure reduction was seen in either group.

The authors correctly point out that blood pressure changes of these amounts are comparable to those demonstrated for approved antihypertensive drugs given as monotherapy. However, in neither group studied was the average blood pressure reduction <140/90, the conventional goal for such subjects. Thus, it is apparent that this nonpharmacological approach alone would not suffice to control blood pressure and would require the addition of drug therapy in most, if not all, subjects. In view of the JNC VII recommendations to begin 2 drugs when the initial blood pressure is >20 mm Hg above the systolic blood pressure goal, it would seem naive to believe that dietary sodium restriction alone would suffice.

The authors further provide estimates of the dramatic potential magnitude of reduction in cardiovascular events, specifically stroke, ischemic heart disease, and congestive heart failure, which could be anticipated with salt restriction alone based on the surrogate reduction of blood pressure observed. However, this striking potential reduction in such events, although highly desirable, must be regarded as theoretical until prospective outcome trials are performed to provide confirmation. Such efforts would require large numbers of study subjects, certainly much larger than the 24 and 88 subjects comprising He et al’s current analysis, and a sufficiently long duration of study to provide definitive results.

The modest salt restriction used by He et al in their studies was not associated with discernible changes in serum sodium, potassium, creatinine, or blood urea nitrogen concentrations, suggesting that month-long restriction of this degree does not produce adverse effects on serum electrolytes or renal function in a small group of individuals free from such abnormalities at the outset. Although reassuring, this does not provide such confidence in those with renal impairment, hyponatremia, or with longer periods or more severe levels of salt reduction. Thus, additional studies will be required to cover the broader hypertensive spectrum and to define the “dose–response” characteristics of reduction in dietary salt intake and blood pressure.

An important aspect of the blood pressure response to dietary sodium restriction was not addressed by the authors in their study, namely the mechanism(s) involved in the responses. The same authors have previously reported that black subjects, who demonstrated a greater blood pressure decline than whites to the same level of dietary sodium restriction, had significantly lower levels of plasma renin and
aldosterone in response to reduction in salt intake. We have similarly found that the decline in blood pressure in response to dietary salt restriction was inversely correlated with the vigor of the renin response to sodium and volume depletion observed 6 months earlier. Thus, these 2 observations suggest that an impaired renin response to salt intake and/or volume depletion exerts a permissive effect with respect to the magnitude of blood pressure decline seen with salt restriction and appears to provide an explanation for the heterogeneity in human blood pressure response to sodium and volume depletion repeatedly demonstrated in normotensive and hypertensive individuals. A variety of other potential candidates for mediation of the blood pressure responses to sodium and volume changes are also of interest. These include components of the eicosanoid system, the kallikrein–kinin system, nitric oxide, and a host of others for which the length restrictions of the present commentary do not permit elaboration. Perhaps future studies will identify these components and provide new information of both therapeutic and predictive benefit.

The authors suggest that dietary sodium restriction and the blood pressure reduction associated with it provides evidence for improvement in vascular compliance and elasticity. They cite a decrease in pulse pressure as the main evidence for this conclusion. However, any agent that lowers systolic pressure more than diastolic pressure, a rather ubiquitous group of blood pressure-lowering approaches and drugs, particularly in the elderly with a disproportionate elevation of systolic pressure, would lower pulse pressure. In addition to vascular compliance, stroke volume also contributes importantly to pulse pressure. Stroke volume typically decreases with extracellular fluid volume reduction, which could be expected to occur with dietary salt restriction. However, direct measurements of vascular compliance have not uniformly shown that the resistance in small vessels necessarily decreases with a reduction in pulse pressure. Thus, confirmation of the salutary (pun intended) effect of salt restriction on vascular structure and function is requisite.

He et al also remind us of the predominant impact of systolic blood pressure elevations in comparison to diastolic in contributing to cardiovascular events. The fact that systolic blood pressure increases with age and that this age-related change in blood pressure has been associated both epidemiologically and physiologically with sodium intake makes the present report more compelling. Once again, only the results of long-term intervention trials to determine: (1) if dietary salt restriction can prevent or delay the age-related increase in systolic pressure and (2) whether dietary salt restriction will reduce the occurrence of cardiovascular events in a susceptible population can provide the evidence on which to base broad societal recommendations. Given the length and tremendous costs of an adequately designed and powered study to accomplish these aims, it is unlikely that we will soon have a definitive answer.

References

Salt Restriction in the Treatment of Isolated Systolic and Combined Hypertension: Is That Enough?
Myron H. Weinberger

Hypertension. 2005;46:31-32; originally published online June 13, 2005;
doi: 10.1161/01.HYP.0000171473.34145.b3
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/46/1/31

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/