Reducing Dietary Sodium: The Case for Caution

Michael H. Alderman

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Michael H. Alderman, MD

AUTHORITATIVE RECOMMENDATIONS, SOMETIMES SANCtioned by government, routinely call for reduced dietary sodium. However, when the strength of evidence is made explicit, it is generally acknowledged to be opinion or common "practice."[1] Advocates contend that the recommendation is justified because sodium restriction has been convincingly proven to lower blood pressure and that this will surely prevent stroke and myocardial infarction. Skeptics argue that modification of this single surrogate end point does not guarantee a health benefit as measured by morbidity or mortality. Instead, they note that salt restriction capable of reducing blood pressure also unfavorably affects other cardiovascular disease surrogates.

Diet is a complicated factor involving a multitude of interrelating nutrients. Genetic, behavioral, and environmental factors determine wide interindividual variation in sodium intake compatible with good health. Thus, skeptics of the benefits of limiting dietary sodium argue that a recommendation to reduce sodium intake should be based on solid direct evidence that universal salt reduction will lower morbidity and mortality, be safe, and prevent otherwise dire consequences. The purpose of this Commentary is to discuss the available evidence most relevant to a recommendation for universal reduction of dietary sodium.

Surrogate End Points

Surrogate markers, such as blood pressure, are not clinical events, but usually are associated with the incidence of subsequent stroke, myocardial infarction, kidney dysfunction, or heart failure. Multiple randomized clinical trials (RCTs) have established that reduction of sodium intake sufficient to lower blood pressure also increases sympathetic nerve activity, decreases insulin sensitivity, activates the renin angiotensin system, and stimulates aldosterone secretion.[2,3] The health effects of sodium reduction will be the net of these conflicting effects.

Randomized Clinical Trials

RCTs with morbidity and mortality end points are the standard with which health and medical interventions are tested. The only such RCTs that have compared different sodium intakes involve patients with heart failure.[4] Randomization to a more restricted sodium intake (1840 mg/d; to convert from mg to mmol, divide by 23) significantly increased mortality and hospitalization compared with those randomized to sodium intake of 2760 mg/d (US mean, 2921 mg/d[5]). These results are consistent with the view that overzealous restriction of sodium may be harmful for patients with heart failure.[6] These trials, although applicable to heart failure patients, lack public health relevance. However, those studies add to the 3-year experience of Trials of Hypertension Prevention (TOHP) in which several thousand participants achieved long-term adherence to a reduced sodium regimen, and thus increase confidence in the feasibility of an RCT evaluating sodium restriction in persons at appropriate cardiovascular disease (CVD) risk.[7]

Observational Studies

Rarely, smoking excepted, do observational studies by repeated, robust, and consistently positive findings justify a public health recommendation. In fact, interventions based on observational data are often flawed. The 1980 National Dietary Guidelines recommended population-wide reduction of total fat intake. In response to an unanticipated epidemic of obesity and diabetes, to which the authors concluded the 1980 recommendations might have contributed, the 2000 committee withdrew its earlier recommendation.[8] Trans-fat consumption and postmenopausal hormone therapy are other examples of how well-meaning interventions, based on insufficient science, can have hazardous consequences.

At least 13 observational cohort studies have examined the relationship between sodium consumption and clinical outcomes, and these studies include more than 100 000 participants and more than 800 morbid and mortal events. The results have been conflicting[3,5,7,9] (BOX). In 2 studies with high mean daily sodium consumption (Finland, 4600 mg/d; Japan, 5428 mg/d), the association between salt and CVD events was positive.[3] In 11 studies with mean sodium intakes between 2070 mg/d and 3680 mg/d, 2 detected a positive association between salt and CVD events, and each was a post hoc subgroup analysis with findings not entirely consistent with the overall study results. For instance, in the NHANES I, the association between salt intake and CVD was positive in the obese subset of study participants but was inverse in the entire sample. Likewise in the morbidity follow-up of a subset of participants in TOHP I and II, the association between salt and CVD was positive, whereas in the mortality follow-up of the entire population, the association also was positive, but not statistically significant.

In 5 of these 11 studies, there was no association between salt intake and clinical outcome. One of these 5 studies involving follow-up of 2275 TOHP controls had the unique advantage of estimating usual sodium intake (3634 mg/d) by collecting 4 to 5 urine samples over 24 hours dur-

Author Affiliations: Albert Einstein College of Medicine, Department of Epidemiology and Population Health, Bronx, New York.
Corresponding Author: Michael H. Alderman, MD, Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Room 1315 Belfer Bldg, 1300 Morris Park Ave, Bronx, NY 10461 (michael.alderman@einstein.yu.edu).

ing the initial 3-year period.[9] In 4 studies, sodium intake was inversely associated with CVD events. Thus, higher salt intake was adversely associated with CVD risk in societies with high salt intake, whereas lower salt intake was associated with worse outcomes in some societies with moderate salt intake. A J-shaped curve, in which the most favorable dietary sodium range surrounds 3450 mg/d—with possible risk above and below this level—is a hypothesis that may best accommodate the available data.[3]

In a recent meta-analysis including many of the same observational studies,[10] but without stratification to account for the sharp differences in ambient sodium intakes, the authors detected a significant positive association of sodium intake with stroke. This finding was driven by studies involving populations with high salt intake. However, there was no association between salt intake and CVD events, and total mortality was not reported.

Not surprisingly, given different populations, different diets and sodium intakes, different methods and conflicting results, more than 1 explanatory hypothesis has emerged. Neither more observational studies nor further debate over the available studies is likely to resolve this public health controversy.

The key point, however, is not which hypothesis best fits the observed data. The real issue relates to the inherent limitations of observational studies. These investigations describe the course persons who follow a chosen diet might have but provide no information about what might happen if that diet were altered. That requires a randomized clinical trial.

Conclusions

There are at least 2 paths forward. The rash route is through universal sodium reduction. For countries like the United States, this means changing the diet of all its residents by reducing the sodium content of prepared foods. Despite the heterogeneity of blood pressure response to sodium reduction, advocates of this strategy are confident that known beneficial effects will outweigh known negative effects and that there will be no serious unintended consequences. An alternate, more cautious approach, calls for rigorous, large-scale, population-based randomized clinical trials. These trials will likely demand a commitment by thousands of individuals for several years but will result in greater precision and scientific credibility to help answer the question—and vastly smaller risk of human and material resources. In the absence of definitive evidence, both the rash and cautious paths are experimental. Based on what is known, the prudent course of action may well be caution.

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Box. Observational Studies Linking Dietary Sodium to Cardiovascular Disease Outcomes[a]

Lower Salt Intake Associated With Cardiovascular Events

Worksite Hypertension Study, 1995
National Health and Nutrition Examination Survey
- I, 1998
- II, 2006
- III, 2008[5]

Salt Intake Had No Association With Cardiovascular Events

Honolulu Heart Study, 1997
Scottish Heart Health Study, 1997
Health Professional Study follow-up, 1997
Multiple Risk Factor Intervention Trial, 2000
Trials of Hypertension Prevention[7]
- 1 and 2 follow-up mortality, 2007
- Controls, 2009[9]

Increased Salt Intake Associated With Cardiovascular Events

National Health and Nutrition Examination Survey, involving obese patients, 2000
Finnish Heart Study, 2001
Takayama, 2005
Trials of Hypertension Prevention 1 and 2, follow-up morbidity, 2007[7]

[a]Unless otherwise indicated, all studies listed herein are referenced in Alderman.[3]

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