EDITORIAL

Low Sodium Intake — Cardiovascular Health Benefit or Risk?

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Hypertension is the most common modifiable risk factor for cardiovascular disease and death. Worldwide, it is estimated that more than 1 billion adults have hypertension, that this figure is projected to climb to 1.5 billion by the year 2025, and that hypertension accounts for more than 9 million deaths annually.[1,2] Because of its high prevalence and related morbidity and mortality, population-wide approaches to reducing blood pressure, and therefore the burden of cardiovascular disease, have been recommended. Among these strategies, reducing dietary sodium and, to a lesser extent, increasing dietary potassium have been included in many guidelines for the treatment of hypertension and prevention of cardiovascular disease. However, recent studies have raised questions about potential adverse effects associated with low sodium intake on important health outcomes, including cardiovascular disease and death.[3]

In response to controversy about the health effects of low sodium intake, the Institute of Medicine convened an expert committee to evaluate the evidence for a relation between sodium and health outcomes.[4,5] The committee concluded that most evidence supports a positive relation between high sodium intake and risk of cardiovascular disease but that results from studies with health outcomes were insufficient to conclude whether low sodium intake (<2.3 g per day or <1.5 g per day, as recommended in current dietary guidelines[6,7]) is associated with an increased or reduced risk of cardiovascular disease in the general population. The committee found limited evidence that low salt intake may be associated with adverse health effects in some subgroups, including some patients with heart failure or other forms of cardiovascular disease, diabetes, or chronic kidney disease.

Results from three studies, reported in this issue of the *Journal*, bear on this matter. The Prospective Urban Rural Epidemiology (PURE) study provides new evidence about the association between sodium and potassium intake, estimated from morning urine specimens, and blood pressure, death, and major cardiovascular events.[8,9] The procedure for estimating electrolyte excretion was validated elsewhere.[10] The PURE study included more than 100,000 adults sampled from the general population of 17 countries that varied in their economic development and acculturation to an urban lifestyle. Approximately 90% of the participants had either a high (>5.99 g per day) or moderate (3.00 to 5.99 g per day) level of sodium excretion; approximately 10% excreted less than 3.00 g per day, and only 4% had sodium excretion in the range associated with current U.S. guidelines for sodium intake (2.3 or 1.5 g per day).

Across this broad range of populations, the relation between sodium excretion and blood pressure was positive but nonuniform: it was strong in participants with high sodium excretion, modest in those in the moderate range, and nonsignificant in those with low sodium excretion. The authors concluded from the findings that a very small proportion of the worldwide population consumes a low-sodium diet and that sodium intake is not related to blood pressure in these persons, calling into question the feasibility and usefulness of reducing dietary sodium as a population-based strategy for reducing blood pressure. There was also an interaction between sodium excretion and potassium excretion: high sodium excretion was more strongly associated with in-

creased blood pressure in persons with lower potassium excretion. The authors suggested that the alternative approach of recommending high-quality diets rich in potassium might achieve greater health benefits, including blood-pressure reduction, than aggressive sodium reduction alone. After a mean of 3.7 years of follow-up, the composite outcome of death and cardiovascular events occurred in 3317 participants (3.3%). As compared with those who had a moderate level of sodium excretion, those with a higher or lower level of sodium excretion had an increased risk of cardiovascular-disease outcomes.

The authors attempted to rule out residual confounding or reverse causation as explanations for their findings by showing that participants with a low level of sodium excretion had a similar mean INTERHEART Modifiable Risk Score and higher intake of fruit and vegetables, as compared with those with a moderate level of sodium excretion, and that more than 90% of the cohort was free of antecedent cardiovascular disease. The findings were not altered by the exclusion of participants with prior cardiovascular disease, cancer, or use of blood-pressure medication, by the exclusion of outcome events occurring in the first 2 years of observation, or by adjustment for all identifiable confounders.

The major weaknesses of the PURE study, inherent in its study design and scope, include the absence of direct measurement of 24-hour urinary excretion on multiple occasions, which is the accepted model for assessing electrolyte intake, and the lack of an intervention component to assess the direct effects of altering sodium and potassium intake on blood pressure and cardiovascular-disease outcomes, thus making it impossible to establish causality. Nevertheless, this large study does provide evidence that both high and low levels of sodium excretion may be associated with an increased risk of death and cardiovascular-disease outcomes and that increasing the urinary potassium excretion counterbalances the adverse effect of high sodium excretion. These provocative findings beg for a randomized, controlled outcome trial to compare reduced sodium intake with usual diet. In the absence of such a trial, the results argue against reduction of dietary sodium as an isolated public health recommendation.

The authors of the third article, from the Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCode),[11] used modeling techniques to estimate global sodium consumption and its effect on cardiovascular mortality.[12] The investigators quantified global sodium intake on the basis of published surveys from 66 countries and used a hierarchical Bayesian model to estimate global sodium consumption. They then estimated the effects of sodium on blood pressure in a meta-analysis of 107 published trials and estimated the effects of systolic blood pressure on cardiovascular mortality by combining the results of two large international pooling projects that included individual-level data. They found a strong linear relationship between sodium intake and cardiovascular events and estimated that 1.65 million cardiovascular deaths in 2010 were attributable to excess sodium consumption. The NutriCode investigators should be applauded for a herculean effort in synthesizing a large body of data regarding the potential harm of excess salt consumption. However, given the numerous assumptions necessitated by the lack of high-quality data, caution should be taken in interpreting the findings of the study. Taken together, these three articles highlight the need to collect high-quality evidence on both the risks and benefits of low-sodium diets.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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