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Editorial

Population Data on Blood Pressure and Dietary Sodium and Potassium Do Not Support Public Health Strategy to Reduce Salt Intake in Canadians

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See article by Mente et al., pages 319-326 of this issue.

The health consequences of the vital regulators of intracellular and extracellular fluid, potassium and sodium, have been deemed differently. Potassium is generally recognized as a "friend," whereas sodium by many public health programs is considered to be a "foe" because of an idea that sodium causes hypertension. These health programs generally recommend lowering sodium intake to < 2000-2400 mg, which is very radical, because this upper limit implies that 95% of all individuals eat too much salt. The hypothesis that a reduced sodium intake will reduce blood pressure (BP) and subsequently reduce morbidity and mortality was first suggested in 1904,[1] and the discussion developed into an ideological conflict between advocates and opponents long before modern standard scientific studies were performed in humans.[2] Specifically, the first randomized controlled trial (RCT) on the effect of sodium reduction (from 10 to 5 g/d) on BP was performed in 1973,[3] and the first prospective observational study directly linking individual sodium intake with mortality was performed in 1985.[4] Paradoxically, many subsequent RCTs and observational studies have failed to solve the controversy but have rather served to refine the stakeholders' strategies aimed to refute the results from their counterparts in the debate. For instance, the results of several observational studies on mortality have been refuted because of issues regarding the quality of the individual measurements of sodium intake used.[5] In their study on sodium intake in the Canadian population published in this issue of the *Canadian Journal of Cardiology*,[6] Mente et al. have obviated this concern by being very careful in the standardization of the individual measurements of sodium intake and potassium intake by using 24-hour urinary excretion, which is the reference standard.

Mente et al. show that Canadian sodium and potassium intake is within a range comparable to those of other Western countries. Because of the general agreement on the health consequences of potassium, this editorial will focus mainly on the sodium findings. The study by Mente et al. contributes to the emerging evidence that sodium intake is very similar all over the world.[7] The finding of very similar sodium intakes in very different cultures may seem surprising, but the explanation is probably simple. Sodium, like water, is an essential nutrient without which life is not possible, and sodium metabolism is therefore very tightly regulated by an interplay between neurons and peripheral hormones.[8,9] In general, Africans have the lowest sodium intake (1.5-2.5 g), whereas central Asian countries including China and Japan have high sodium intake of up to 6 g.[10] Countries in Europe, North America, Australia, India, North Africa, and South America typically have sodium intake between 2.5 g and 5 g.[10] Consequently, sodium intake does not seem to follow the developmental level of a region but rather the geographic and ethnic status. In this context, it is not surprising that the pattern in Canada follows that of Europe and North America. It is possible to survive on a very low sodium intake, <1000 mg, as exemplified by the Yanomami Indians in the Brazilian jungle, who compensate for a very low sodium intake by means of extreme production of the sodium-conserving hormones renin and aldosterone.[11] Whether this is healthy is an open question. It is often pointed out that the low BP observed in this population is a direct consequence of the low sodium intake, but this population has a mean survival age of about 40 years, so it is difficult to directly compare Yanomami Indians with Western populations.

Despite the equivocal effects of sodium reduction and the lack of specific evidence for an upper limit of sodium intake, many governmental institutions recommend a sodium intake < 2300 mg. The growing number of observational population studies indicating an association between a sodium intake < 2300 mg and increased mortality have pushed the American Heart Association (AHA) to defend the 2300 mg upper level of sodium intake and motivated the US Centers for Disease Control (CDC) to initiate an Institute of Medicine (IOM) investigation.[12,13] However, the conclusion of this IOM investigation did not unambiguously support the 2300 mg level. Subsequently, the CDC distanced itself in part from the

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report.[14] A publication from the AHA stated that the different measurements of sodium intake are imprecise and that population studies are therefore not trustworthy, especially when linking individual measurements of sodium intake to outcome.[5] However, imprecise measurement of the causal exposure in population studies is a general problem. For instance there is significant individual BP variation (single measurement or 24-hour measurement) and a significant variation between the measurements of BP by different methods (mercury manometers, aneroid manometers, digital manometers, and intra-arterial pressure transducers). Nevertheless, spot measurements of individual BP values are used in long-term prospective observational studies to associate BP with mortality. The outcomes of these studies contribute to the conceptual foundation on which the sodium reduction policy builds: a low sodium intake reduces BP and reduced BP reduces mortality. In that context, the qualitative distinction between observational studies linking BP with mortality on the one side and observational studies linking sodium intake with mortality on the other side does not seem logical. Furthermore, it should be emphasized that the reason that prospective observational studies are accepted to produce valid evidence is not the precision of the individual measurements but rather the statistical power of the number of measurements. The Canadian study is laudable,[6] not only because the researchers behind the study have been very careful in the standardization of individual measurements but also because the study is part of the world's largest population study to link sodium intake with mortality, ensuring impressive statistical power.[15,16]

In addition to their critique of the measurement methods for sodium intake, the authors of the AHA publication argue that the association of low sodium intake with increased mortality observed in observational studies may reflect the fact that sick individuals have low sodium intake (they suggest reverse causality and argue that sick persons with high mortality might have a low sodium intake, rather than the low sodium intake somehow increasing mortality).[5] Although this question is not addressed in the Canadian study, it is explored in the Prospective Urban Rural Epidemiology (PURE) study.[15,16] This evaluation involving more than 100,000 individuals shows that the elimination of sick individuals from the total population consolidates the statistical association between low sodium intake and increased mortality. A similar finding was obtained in a meta-analysis including almost 400,000 individuals.[17] Thus, a low sodium intake does not seem to be a confounder but rather an independent risk factor for increased mortality. These findings were opposed by those of the Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NUTRICODE) analysis.[18] In this study, the authors adopted sodium reduction and BP data mainly from a Cochrane review,[19] and used these data to analyze a dose-response relationship between sodium intake and BP. With the use of data from observational studies linking BP to mortality, the sodium-BP dose-response relationship was then applied to translate sodium reduction into projected reductions in mortality. The model estimated that 1.65 million deaths from cardiovascular causes worldwide in 2010 were attributable to sodium consumption greater than a reference level of 2.0 g/d. However, about 80% of the studies in the dose-response analysis included participants with a high baseline BP, for which the analysis was not adjusted, thus exaggerating the dose-response relationship. Furthermore, the authors chose not to include data on hormones and lipids in the model, although these data were published in the same Cochrane review from which the BP data were adopted.[19] These considerations could explain why the modelled outcome of the NUTRICODE study (the saving of 1.65 million lives) was not in accordance with the outcomes of studies based on real data, which suggest a mortality *increased* by about 10%-27% in individuals with a sodium intake $<$ 2-3 g.[15-18]

The study by Mente et al.[6] is especially interesting because it not only shows what the sodium intake in the population is but also relates the sodium intake to BP. The lack of significant association between sodium intake and BP in this study is in accordance with the INTERSALT study, which found a significant relation between sodium intake and BP in only 8 of 52 study populations.[20] This lack of significance may result in part from lack of power, because when all 52 INTERSALT study populations were pooled (N = 10,079), there was a significant relation between sodium intake and systolic BP, but it was small (1.0 mm Hg/2300 mg sodium). Furthermore, there was no significant effect on diastolic BP (0.03 mm Hg/2300 mg sodium). The associations between sodium intake and BP in the PURE study[15,16] were higher. However, the baseline BP in the PURE study (131.7/82.2 mm Hg) was higher than in the Canadian study (127.5/78.4 mm Hg) and also higher than in the INTERSALT study, in which 50 of the 52 study populations had a mean BP $<$ 125/80 mm Hg. Therefore, the associations between sodium intake and BP in the different population studies are consistent,[6,16,20] and collectively they show a statistically significant but quantitatively weak association between sodium intake and systolic BP, and no association between sodium intake and diastolic BP, in populations with normal BP. In hypertensive study populations, there is a moderate and measurable effect of about 5/2.5 mm Hg/2300 mg sodium.[15,16] These findings are in accordance with the BP effects detected in RCTs.[19]

Mente et al.'s study confirms that the association between sodium intake and BP is weak, especially in individuals with normal or low BP. Combined with the findings from population studies that a low sodium intake is associated with increased mortality, and the findings from RCTs that a low sodium intake is associated with several potential side effects, Mente et al.'s conclusion that their data do not support the public health strategy to reduce sodium intake to $<$ 2400 mg seems quite reasonable. Furthermore, the relatively neutral association of sodium as well as potassium with BP in this study is in accordance with the notion that the intuitively paradoxical distinction between the "friend" potassium and the "foe" sodium might merely be the result of a historical coincidence. Although radical sodium reduction has become a mantra for many public health programs, this approach would seem to merit serious reconsideration.

Disclosures

The author has no conflicts of interest to disclose.

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