EDITORIAL

Dietary Sodium- and Potassium-Enriched Salt Substitutes—The Tipping Point?

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In 2000, Malcolm Gladwell articulated the concept of the tipping point.[1] He explained that many things happen building toward a change without change occurring, until suddenly, some new information takes the idea to the threshold—and the change occurs suddenly. Two studies published in this issue of *JAMA Cardiology* add in substantial ways to the growing and compelling evidence for the benefit of a lower sodium intake in the general population and in patients with or at high risk for vascular disease (in this study, stroke). A tipping point?

Related articles

The Association of Salt Legislation with urinary sodium and blood pressure in the Health and Aging in Africa: Longitudinal Studies in South Africa (HAALSI) cohort study offers observational evidence related to primary prevention of hypertension and thus, primordial (population) prevention of cardiovascular disease.[2] This study presents evidence that lower intake of dietary sodium and lower mean BP levels in middle-aged and older adults 4 and 7 years after legislation required lower sodium content in some processed foods. South Africa is among dozens of countries taking action to reduce dietary sodium intake in the general population. It is among a minority of those nations to effect this through legislation or regulation requiring those changes as opposed to voluntary limits. This study demonstrates that government action with accountability is able to impact not only sodium intake but blood pressure levels as well.

The impact of a potassium-enriched salt substitute on secondary stroke prevention was reported in the Effect of Salt Substitution in People with a History of Stroke on Recurrence and Death study.[3] This predetermined secondary analysis of the Salt Substitute and Stroke Study (SSaSS) demonstrated evidence at the other end of the prevention/disease spectrum—secondary prevention. This analysis demonstrated significant reductions in recurrent stroke and all-cause mortality in patients with a history of stroke using the potassium-based salt substitute.

Two issues frequently raised about the SSaSS study[4] are safety concerns regarding hyperkalemia and whether the stroke prevention is from decreased sodium or increased potassium. The SSaSS study did not measure serum potassium but evaluated the presence of hyperkalemia through common clinical manifestations including death and hospitalizations related to arrhythmias. Neither were increased in the group using the potassium-based salt substitute. Some programs promoting the use of potassium-based salt substitutes raise caution about using them in older patients, patients with diabetes, and in combination with angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists. Of note, potassium intake is often below the World Health Organization–recommended level of at least 3510 mg daily. Even with potassium-based salt substitutes, potassium intake remained below recommended levels.[5] However, the only cautions based on strong evidence are patients with stage 3 or 4 chronic kidney disease or patients taking a potassium-sparing diuretic. The debate about the importance of increased potassium or reduced sodium as the primary driver of the benefit of the potassium-based salt substitute will continue but should not delay use of this strategy as it is proven to be effective and safe for most people.[4]

In general, nutrition research is more challenging to perform than medication treatment trials and is often criticized by the inherent limitations of study design and concerns about generalizability. For example, the predominant source of sodium intake, whether discretionary or nondiscretionary, will inform interventions to reduce sodium consumption. The HAALSI cohort study[2] was performed in a setting where much of the dietary sodium is derived from purchased processed foods, ie, mainly nondiscretionary. In contrast, the SSaSS study[3] was performed in rural areas of northeast China where most of the dietary sodium is derived from meals prepared at home, ie, predominantly discretionary. Viewed in the context of other evidence, this advances the idea of the use of potassium-based salt substitutes to not only lower dietary sodium intake and lower blood pressure but to reduce the risk of vascular events and death, particularly in settings where discretionary sodium intake is high. The HAALSI study adds credibility to moving beyond voluntary efforts by governments and food industries to legislation or regulations with real accountability, especially in settings where nondiscretionary sodium intake is high.

The development of scientific evidence is often considered a linear process. In the sodium and cardiovascular risk relationship, the evidence was first documented with the association with blood pressure in population studies. Next, many short-term clinical trials demonstrated a cause-and-effect relationship. Further, long-term studies showed that same lowering of blood pressure with a reduction in sodium intake. Nonetheless, many in the scientific/public health communities felt the then-current evidence that decreased dietary sodium reduced blood pressure and cardiovascular disease risk was scientifically insufficient for implementation of salt reduction strategies—including the use of government regulation to limit sodium intake.[6]

When asked what would be required to move a government agency from recommending a reduction in sodium con-

tent in processed foods to requiring a reduction, the often-heard response is "a clinical trial demonstrating that a reduction in dietary sodium caused a reduction in cardiovascular events." The SSaSS study including this secondary analysis provides that. It also provides credibility for use of similar interventions for primary and primordial prevention.

These 2 studies on dietary sodium[2,3] bring to mind the development of science in the area of lipids and cardiovascular disease. The observational relationship led to clinical trials of drugs that lower low-density lipoprotein cholesterol. The earliest clinical trials were performed in persons with cardiovascular disease (CVD) and demonstrated a reduction in recurrence of vascular events. These early studies combined with the observational evidence led to further clinical trials eventually leading to the current situation: government agency-required food content changes for primordial prevention, use of diet and government agency–approved drugs for primary prevention of CVD in high-risk individuals, and implementation of those strategies for secondary prevention.[7]

To their credit, government agencies around the world have responded to existing sodium evidence with programs to encourage lower dietary sodium intake. However, most governments have only advised and encouraged sodium reduction, which have limited effectiveness.[8] In recent years, more governments, including South Africa, have moved to requirements of the food industry for sodium reduction in processed foods, which are more effective than voluntary approaches.[9]

Government agencies and policymakers are appropriately concerned about the issues of personal choice and are reluctant to impose dietary limitations on the public or on the food industry. This an important factor for some countries that have not yet moved to a system of requirements with accountability. But, sometimes, a tipping point drives a decision to move away from voluntary change to mandated change for the good of the public. The automotive industry provides a good example. As evidence of harm from air pollution from gasoline-based internal combustion engines of cars, companies were advised to manufacture smaller vehicles with better gas mileage that produce less pollution. In the 1970s, feeble attempts were made by the industry, but little change occurred. As the evidence mounted, government agencies moved to mandated regulations regarding both gas mileage and carbon emissions. Dramatic improvements occurred including a meaningful development of electric-powered vehicles. Evidence drove change including government agency regulations.

Not surprisingly, many public health government agencies desire evidence from studies conducted in their own countries before imposing regulations in their country. The concern about generalizability of clinical trials and observational evidence is often raised.[10] The HAALSI observational study[2] from South Africa could be repeated in many countries that already have longitudinal observational CVD studies in place. The SSaSS study from China,[3] on the other hand, will not be easy to replicate in most countries. The logistics of performing similar research projects are daunting. The number needed to recruit, the almost certain need for cluster randomization, the challenges of group informed consent, and the expense are obstacles that will be challenging to manage in most locations. This reality leads to an important question. Are there conditions that call on researchers and policymakers to acknowledge and accept the evidence that exists, even if not seemingly ideal? A 2020 article by leading CVD researchers examined the specific issue of the feasibility of a randomized clinical trial of sodium reduction with hard CVD end points in the US.[9] The conclusion was that it was not feasible. One of the authors of this editorial attempted such a study and came to the same conclusion.[11]

Regulatory agencies including the US Food and Drug Administration should work in collaboration with consumers, scientists, and the food industry to reexamine the level of existing evidence to consider implementation of mandatory sodium limits in processed foods. If the conclusion of those discussions is that more evidence is necessary before taking steps toward mandatory limits, strong consideration should be given to examining existing observational evidence using evolving contemporary rigorous statistical approaches to offer the necessary confidence for decisions. Delaying the crucial step of limiting dietary sodium in the American diet is predicted to cost hundreds of thousands of quality-adjusted life-years.[12]

These 2 articles[2,3] provide evidence at the bookends of dietary sodium reduction and cardiovascular disease—primordial and secondary prevention. Both provide evidence of benefit and safety. This, along with evidence from years of sodium research, should convince clinicians to increase attention to a low-sodium diet including the use of a potassium-based salt substitute in most patients. Perhaps these studies can be the tipping point for more public health leaders, government agencies, and patient advocacy organizations to move toward mandatory policies regarding sodium content of foods.[13]

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