In this issue of *Hypertension*, Suckling et al make an important new contribution toward understanding the potential clinical benefit of reducing dietary salt intake in patients with type 2 diabetes mellitus. A significant amount of data suggests that dietary salt restriction is an important clinical step toward blood pressure control in both normotensive and hypertensive populations, and especially in African Americans where the prevalence of salt-sensitive hypertension is high. Nevertheless, whether it is appropriate to use population-wide strategies to reduce salt intake has remained a subject of debate over the past several decades. Adding to the debate, a recent meta-analysis of 269 reports set out to assess whether dietary salt reduction lowered all-cause mortality and risk for cerebro-cardiovascular disease. Although 55% of those studies supported the concept of salt reduction to reduce mortality and cerebro-cardiovascular risk, 46% either contradicted the idea or were not conclusive. Moreover, the analysis showed that studies were significantly more likely to only cite papers that were in agreement with the results of the study, suggesting that sweeping conclusions about population-wide salt restrictions still need to be made with caution.

From the continued discussion surrounding population-wide salt restriction, the importance of dietary salt restriction to provide health benefits beyond cardiovascular risk is also becoming evident. For example, the potential exists for the impact of dietary salt on the gut microbiota and its implications for metabolic disease and obesity also represents a new potential area of investigation. Still, although investigators delve into the complex interaction of salt with immune system function and other areas of physiology and pathophysiology, much remains to be learned about the impact of dietary salt in common diseases, such as type 2 diabetes mellitus.

The risk of developing cardiovascular disease, and mortality resulting from cardiovascular disease, is markedly increased in patients with type 2 diabetes mellitus. Factors that contribute to the increased cardiovascular risk in these patients include obesity, hyperglycemia, dyslipidemia, and hypertension. Although several studies have examined the impact of dietary salt restriction in patient populations with type 2 diabetes mellitus, the impact of salt remains unclear. For example, high salt intake has been reported to promote renal injury in type 2 diabetics, and Suckling et al conducted a meta-analysis concluding that dietary salt restriction attenuated diabetic kidney disease (both type 1 and type 2). However, others reported that when dietary sodium was below 8 g/d, the odds ratio of developing albuminuria was increased and that a reduction in urinary sodium excretion was associated with increased cardiovascular risk and all-cause mortality in type 2 diabetics. The conflicting reports may result from the observational nature of some of the studies, but still leaves a significant gap in knowledge about the role of dietary sodium in cardiovascular risk in type 2 diabetics that could be addressed in a well-controlled clinical study.

In the study by Suckling et al, the authors examine whether modest, relatively short-term, modification of dietary salt intake can reduce blood pressure, urinary albumin excretion, arterial stiffness, and markers of endothelial function in patients with type 2 diabetes mellitus. A randomized double-blinded crossover design was used in 51 obese individuals (average body mass index =34) ranging in age from 30 to 80 years who either have impaired glucose tolerance or type 2 diabetes mellitus (46 completed the study). The participants were acclimatized for 4 weeks at which time they were trained to reduce their daily salt intake to 5 g/d. After 2 weeks on this diet, the participants began the randomized double-blind crossover trial where they were given either slow sodium or placebo tablets for a period of 6 weeks before switching to the opposite tablet for another 6 weeks. Slow sodium is slow release tablet of sodium chloride that is often used clinically to counter sodium depletion. In this study, it is used as a controlled source of dietary salt. At the conclusion of each 6-week period, a number of measurements were made to assess cardiovascular, renal, and hormonal status of the patients, including 24-hour ambulatory blood pressure, carotid–femoral pulse wave velocity for arterial stiffness, endothelial independent vasodilation via digital volume pulse analysis, and 24-hour urine collections for assessment of sodium, potassium, calcium, creatinine, and albumin.
Using this experimental design, a significant reduction in sodium intake was achieved between the slow sodium (9.5 g/d) and placebo (6.8 g/d) as assessed by 24-hour urinary sodium. A major finding of this study was that this relatively modest reduction in salt intake only over a period of 6 weeks was sufficient to reduce systolic pressure by 4.2 mm Hg and diastolic pressure by 1.7 mm Hg. Coincident with the reduction in blood pressure, the lower dietary salt intake was associated with lower albumin to creatinine ratio, raising the possibility that the low salt provides protection against pressure-mediated glomerular injury. An increase in albumin excretion increases the risk for cardiovascular disease. Importantly, these cardiovascular and renal improvements occurred without changes in notable metabolic parameters, such as insulin or cholesterol. Finally, the authors provide data suggesting that endothelial function may have been improved in individuals during the placebo arm of the study; however, this failed to reach significance, perhaps reflecting the rather modest difference in salt intake between placebo and slow sodium groups. Variability may have also been introduced as a result of the diverse participant age range (from 30 to 80 years), ethnicity, and the inclusion of both sexes.

As is common for clinical studies like this one, the rather small sample size limits the ability to fully apply these results to broader populations. However, the authors address this issue through discussion of larger scale studies related to dietary salt restriction and blood pressure. There are 2 major advantages of this study that have helped to provide a better understanding for the potential clinical benefit of salt restriction in type 2 diabetes. The first strength is the experimental design itself given that the randomized double-blind placebo-controlled study is often considered as the gold standard to determine whether an intervention is effective or not. A second major advantage of the study is the methodologies used to assess the desired end points. For example, blood pressure is not only assessed in the clinic, but also is assessed in 40 participants using 24-hour ambulatory blood pressure monitoring (which happens to have good agreement with the pressures measured in the clinic). Similarly, the urinary measurements are made from 24-hour collections rather than spot collections, providing greater confidence in the accuracy of the urinary protein, creatinine, and ultimately the assessment of sodium intake/excretion. Although it is difficult to draw definitive conclusions related to vascular changes that accompany the low salt diet, the utilization of state-of-the-art methods including pulse wave velocity and digital volume pulse analysis to assess arterial stiffness and endothelial function, respectively, are also strengths of the study.

Taken together, the current study by Suckling et al provides clear evidence, using a robust experimental design and methodologies, to demonstrate that salt restriction can significantly reduce blood pressure and albuminuria in patients with type 2 diabetes mellitus. This has important clinical implications as cardiovascular disease is a major contributor to mortality in type 2 diabetics and that there has been and continues to be a rise in the prevalence and incidence of diabetes mellitus in the United States.12

Disclosures

None.

References

"Slow"ing Cardiovascular Risk in Type 2 Diabetics by Restricting Dietary Salt Intake
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Hypertension. published online May 9, 2016;
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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/early/2016/05/09/HYPERTENSIONAHA.116.07224.citation

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