Population Dietary Salt Reduction and the Risk of Cardiovascular Disease

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Raised blood pressure (BP) is the first cause of death and disability in adults worldwide, mainly due to cardiovascular disease (CVD). The risk of CVD increases progressively with increasing BP. However, the majority of CVD death and morbidity attributable to BP occur at level around or below 130/80 mmHg, because there are so many individuals in the population with this BP. Clinical guidelines would not treat the majority of these individuals with drugs. Furthermore, there is a graded relationship between BP and CVD down to at least 115/75 mmHg. Therefore a population-approach through non-pharmacological measures (diet and life-style) is the most feasible option.

Dietary salt consumed at current levels is one of the major causes of chronic ill-health in the world. Extensive evidence from animal studies, human genetics, epidemiological and migration studies, natural experiments, population-based interventions and randomized controlled clinical trials demonstrates a close, direct and dose-response relationship between the levels of salt intake and the levels of BP. A 4.6g reduction in salt intake decreases BP by 5.0/2.7 mmHg in hypertensive individuals and by 2.0/1.0 mmHg in normotensives individuals.[1] The predicted effects on stroke and other cardiovascular outcomes were quantified in a recent meta-analysis of prospective population studies.[2] A 5g higher salt intake was associated with a 23% greater risk of stroke and 17% greater risk of CVD, supporting programs of population salt reduction to prevent cardiovascular disease worldwide.

A recent publication in the *Journal of the American Medical Association*[3] has reported that a low salt intake 'increases' the risk of CVD. The paper reports on two separate cohorts (FLEMENGHO and EPOGH) studied in different European countries using similar methodologies. It examined 24h urinary sodium excretion (as a marker of salt intake) in relation to BP, hypertension, and fatal and non-fatal outcomes. The authors concluded that low sodium intakes increased CVD and should not be recommended on a population basis.

As in a handful of other discrepant cohort studies there are concerns about the methods, and unaccounted confounding. Inaccuracy of exposure assessment is a major limitation of this study leading to misclassification and bias. People in the lowest sodium tertile tended to have higher cardiovascular risk factors. They had the lowest educational attainment, higher baseline systolic BP, smoking rates and serum total cholesterol. Sodium intake covaries with caloric intake and the physically active would tend to be in the high sodium intake group. The study did not correct for socio-economic status or physical activity. The lower sodium group (across genders and population samples) also had lower urinary creatinine, potassium and volume not explained by differences in body mass. A likely explanation is under collection, either due to non-adherence with the instructions or illness. Non-adherence is a substantive confounder. Non-adherence even to placebo is associated with high mortality rates. The finding of low urine potassium in those excreting low sodium is paradoxical as the major mechanism for marked reduction in sodium intake is by eating unprocessed

foods, which are high in potassium. The presence of low potassium excretion in the group with low sodium excretion strongly suggests substantive residual confounding variables such as low overall food intake and poverty. Moreover, the 'inverse' association between urinary sodium-to-potassium ratio and CVD outcomes is another unexplained paradox. The study lacks statistical power for reliable and robust conclusions as it is based on very few events. This is true particularly for stroke, the outcome most strongly associated with high salt intake and BP, as shown in a meta-analysis of 5,346 incident strokes[2]. When the results of the present study are added to the meta-analysis, the RR pooled estimate of effect becomes 1.20 [95% CI: 1.03 to 1.41], n=15; p=0.026 for stroke and 1.14 [0.99 to 1.33], n=13; p=0.07 for CVD. Participants in FLEMENGHO were in large part recruited through family members and it is not clear if also EPOGH had such a component. This does raise the question on how representative this population is of a general population and what degree of contamination their recruitment design introduces in such a study. The study reports a significant relationship between changes in sodium and changes in systolic BP, yet the latter do not translate into changes in CVD. It would be worrying if the change in BP, irrespective of sodium intake, did not predict an increase in stroke and CVD.

In conclusion, the methods and results of the present study are flawed and their interpretation is misleading. Our recommendation is that the present study does not detract from the evidence accumulated so far to inform a public health agenda. Rather than pursuing the objective of 'whether' salt intake should be reduced to prevent CVD, the health priority is and should remain 'how' to reduce population salt intake to save lives.

References:

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