Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride: a meta-analysis

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Authors' objectives
To estimate the effects of reduced sodium intake on systolic and diastolic blood-pressure (SBP and DBP, respectively), body weight, and plasma or serum levels of renin, aldosterone, catecholamines, cholesterols and triglyceride.

Searching
MEDLINE was searched from 1966 to 1997 using the search terms provided. The reference lists of the retrieved papers and four previous meta-analyses were also examined for relevant literature.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs). Double-blind, single-blind, or open studies with a parallel or crossover design were included.

Specific interventions included in the review
Low-sodium versus high-sodium diets. No definition of low- or high-sodium diet was provided. Sodium intake, however, had to be estimated by a 24-hour urinary sodium excretion, either on the basis of a 24-hour urine collection or from a sample of at least 8 hours.

Participants included in the review
Participants (either hypertensive or normotensive) randomised to high- or low-sodium diets. The mean age of the participants had to be over 15 years. Studies treating persons with a concomitant intervention, such as antihypertensive medication, potassium supplementation or weight reduction, were included only if the concomitant intervention was identical during the low- and high-sodium diets.

The median age of the patients in the hypertensive study samples was 49 years (range: 23 to 73), and the median study duration was 28 days (range: 4 to 365). Antihypertensive medication was received by patients in 13 of the 58 studies. The median age of the patients in the normotensive study samples was 27 years (range: 15 to 67), and the median study duration was 8 days (range: 4 to 1,100).

Outcomes assessed in the review
The studies had to evaluate at least one of the following effect parameters: SBP and DBP, body weight, and plasma or serum levels of renin, aldosterone, catecholamines, cholesterols and triglyceride.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The validity of the studies does not appear to have been formally assessed.

Data extraction
Two authors independently recorded the data from the included studies.

Methods of synthesis
How were the studies combined?
Two separate cumulative meta-analyses were conducted, one for hypertensive patients and one for normotensive patients. The effect size (ES), defined as the difference between the changes during a low- and a high-sodium diet, were calculated for SBP, DBP and body weight. For hormones and lipids, the ratio between the values obtained during the two diets was calculated. Unweighted and weighted methods were used to estimated the pooled ES, and a method of summarising t-values was used to combine probabilities.

How were differences between studies investigated?
The chi-squared test for homogeneity was used to assess whether the distribution of the ESs was compatible with the assumption that interstudy differences were attributable to random sampling alone.

**Results of the review**
Eighty-three references with 114 randomised study populations were included in the review: 58 hypertensive study samples (n=2161) and 56 normotensive study samples (n=2,581).

1. Difference between the low- and high-sodium diets in terms of the 24-hour sodium excretion, SBP and DBP.
   a) Hypertensive trials (58 studies; unweighted results):
      - the urinary sodium excretion was -129 mmol/24 hours (standard deviation, SD=57);
      - the mean change in SBP was 4.5 mmHg (SD=13.7; range: 4.3 to 5.4); and
      - the mean change in DBP was 2.3 mmHg (SD=9.7; range: 2.1 to 2.7).
      The final weighted effect of a reduced sodium intake, as measured by urinary excretion (weighted, 118 mmol/24 hours), on SBP was 3.9 mmHg (95% confidence interval, CI: 3.0, 4.8), and on DBP was 1.9 mmHg (95% CI: 1.3, 2.5).
   b) Normotensive trials (56 studies; unweighted results):
      - the urinary sodium excretion was -165 mmol/24 hours (SD=53);
      - the mean change in SBP was 1.6 mmHg (SD=11.2; range: 1.5 to 1.8); and
      - the mean change in DBP was 0.4 mmHg (SD=9.7; range: 0.33 to 0.47).
      The final weighted effect of a reduced sodium intake, as measured by urinary excretion (weighted, 160 mmol/24 hours), on SBP was 1.2 mmHg (95% CI: 0.6, 1.8), and on DBP was 0.26 mmHg (95% CI: -0.3, 0.9).

2. Effect on body weight (56 studies): the mean weight reduction during a low sodium intake was 0.961 kg (range: -0.4 to 3.0, P=0.01).

3. The effect of sodium reduction on hormones and lipids (hypertensive and normotensive studies combined) were as follows.
   For renin (53 studies), the mean sodium reduction was 182 (range: 50 to 341) and the ES was 3.63 (SD=2.57, P<0.001).
   For aldosterone (38 studies), the mean sodium reduction was 186 (range: 61 to 341) and the ES was 3.26 (SD=1.59, P<0.001).
   For noradrenaline (29 studies), the mean sodium reduction was 196 (range: 72 to 328) and the ES was 1.32 (SD=0.27, P<0.001).
   For adrenaline (10 studies), the mean sodium reduction was 126 (range: 72 to 178) and the ES was 1.19 (SD=0.18, P=0.02).
For cholesterol (19 studies), the mean sodium reduction was 179 (range: 56 to 280) and the ES was 1.04 (SD=0.04, \( P<0.001 \)).

For high-density lipoprotein (15 studies), the mean sodium reduction was 186 (range: 56 to 280) and the ES was 1.01 (SD=0.05, \( P=0.35 \)).

For low-density lipoprotein (13 studies), the mean sodium reduction was 203 (range: 56 to 280) and the ES was 1.05 (SD=0.04, \( P=0.003 \)).

For triglyceride (14 studies), the mean sodium reduction was 191 (range: 56 to 280) and the ES was 1.06 (SD=0.11, \( P=0.05 \)).

**Authors’ conclusions**
The effect of reduced sodium intake on blood-pressure was insufficient to justify a general recommendation for reducing the sodium intake, although reduced sodium may be used as a supplementary treatment in hypertension. The use of a long-lasting (greater than 4 weeks), moderate to high daily reduction (greater than 100 mmol/24 hours) has not yet been fully evaluated. High, short-term reduced sodium intake had small adverse effects on the lipid profile; whether this is of clinical significance, and whether the changes persist during long-term reduced sodium intake, remain to be proven in longer-term studies.

**CRD commentary**
This was a relatively well-conducted review with a clear aim, explicit inclusion criteria and appropriate statistical pooling. The literature search was limited to only one database; however, the use of four published meta-analyses in the area may have limited the potential for retrieval bias to some extent. Few details were provided on the primary studies, although this was not surprising considering the large number of studies included in the review. Although some design issues were considered, no formal validity assessment of the studies appears to have been conducted. In addition, it was unclear as to what extent study quality may influence the results of the meta-analyses. The authors’ conclusions concerning the use of sodium restriction appear to be fully justified, especially as only surrogate outcome measures could be used, and it was unclear to what extent these will translate into patient outcomes.

**Implications of the review for practice and research**
The authors suggest that the optimum solution to the controversy of the influence of sodium on blood-pressure are long-term trials with hard end points, such as stroke, myocardial infarction and survival.

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**Other publications of related interest**
This additional published commentary may also be of interest. Curzio J. Review: reduced sodium intake results in small reductions in blood pressure among people with hypertension. Evid Based Nurs 1999;2:46.
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