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Effect of salt intake on blood pressure and cardiovascular outcome:

critical evaluation of reported trials and meta-analyses

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A clinical trial is a study in which you investigate the effect of an intervention (usually a medication or a non-pharmacological intervention, for instance a sodium reduced diet) in a group of study participants by measuring predefined variables (for instance blood pressure) before and after the intervention period. However, the possible change observed may be due to other overlooked factors (confounders) than the intervention itself. Consequently it could be a mistake to ascribe the observed change to the intervention. To minimize this risk, a control group should be included consisting of comparable participants, who receive a non-intervention ("placebo", for instance a non-reduced sodium diet) and who are also measured before and after the non-intervention. The change in this placebo group is subtracted from the change in the intervention group, and the difference between these two groups is the net-effect that can be ascribed to the intervention. To ensure that the two groups are comparable, study participants are placed in the groups by means of drawing lots ("randomisation") giving rise to a randomised placebo controlled study.

The purpose of a review article is to give an overview of a scientific topic, for instance all clinical trials that have investigated a specific intervention. Before the invention of meta-analyses, the conclusion of a review was often based on summaries of unsystematically selected studies. A meta-analysis is a more sophisticated review article that integrates statistically well-defined effect sizes from clinical trials selected on the basis of methodological criteria. Only randomised placebo-controlled clinical trials should be included into meta-analyses.

Blood pressure (BP) is measured as mm of mercury (mm Hg) during cardiac contraction (systolic blood pressure, SBP) and cardiac relaxation (diastolic blood pressure, DBP) and is usually shown as SBP/DBP.

For a century there has been a controversy between scientists, who believe that there is convincing proof that reduced dietary sodium intake (sodium reduction) reduces blood pressure and blood pressure related diseases ("supporters"), and scientists who do not ("sceptics"). The first randomised placebo controlled study of the effect of sodium reduction on BP was published in 1973 [1]. In 1986 the first meta-analysis [2] showed an effect of sodium reduction on BP of -3.6/-2.0 mm Hg in 13 studies. In 1991, a meta-analysis of 28 study populations showed an effect of for hypertensive persons and -1.0/-0.2 mm Hg for normotensive persons [3]. In 1996 a meta-analysis of 53 articles showed an effect of -3.7/-0.9 mm Hg in hypertensive persons and vin normotensive persons [4]. In 1998 the first meta-analysis to include other variables than blood pressure was published by the present author [5]. In 58 trials of hypertensive persons, the effect of sodium reduction was -3.9/-1.9 mm Hg. In 56 trials of normotensive persons, the effect was . In plasma there was a 3-4 times increase in the sodium regulating hormones, renin and aldosterone, which was proportional to the degree of sodium reduction. There was a significant decrease in body weight and an increase in noradrenalin, cholesterol and LDL cholesterol. This meta-analysis was the first also to be published as a Cochrane review [6]. In this revised version, studies on blacks and whites were separated. In trials of whites with normal blood pressure (57 trials), low sodium intake reduced BP by about and in trials of whites with elevated BP (58 trials), low sodium intake reduced BP by about -4.2/-2.0 mm Hg. In 8 trials of blacks with normal or elevated BP, low sodium intake reduced BP by about -6.4 /-2.0 mm Hg.

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He and MacGregor claimed that the low BP effects found in our analyses were due to the inclusion of short-term studies. However, in their own analysis in which they eliminated short-term studies [7], they found almost similar results in persons with normal BP (-2/-1 mm Hg) and in persons with elevated BP (-5.1/-2.7 mmHg).

The fact is that today supporters of sodium reduction and sceptics do not disagree about the effect size. Furthermore, they agree that sodium reduction can be useful in individuals with elevated BP. The controversial question is: Does an effect of 1-2 mm Hg in normotensive persons justify a general recommendation of sodium reduction in the whole population? The sceptics think not. The supporters think that any small decrease in BP will result in an improved survival and less morbidity. However a recent meta-analysis of the effect of anti-hypertensive beta-blockers indicates that this is not necessarily the case [8]. Beta-blockers were compared to placebo (4 trials with 23,613 participants). The risk of all-cause mortality was not different between beta-blockers and placebo. Consequently it cannot be assumed that a blood pressure decrease of 1-2 mm Hg, which is smaller than that obtained by a beta-blocker, is resulting in a reduced morbidity and mortality. You must have proof and this does not exist, as also shown in a recent review of epidemiological studies [9], which like the clinical trials could not relate dietary sodium to cardiovascular disease and death.

References

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