

*For Debate . . .***Does sodium restriction lower blood pressure?**

D E GROBBEE, A HOFMAN

Abstract

Data from 13 randomised trials on the effect of sodium restriction on blood pressure were analysed. The hypotensive effect of sodium restriction was found to be small and restricted largely to systolic blood pressure, which fell by an average of 3.6 mm Hg (range 0.5-10.0 mm Hg). The reduction increased with age and in those with higher blood pressure.

Sodium restriction therefore seems to be of limited use in those who are most eligible for non-pharmacological treatment of high blood pressure—namely, young patients with mild hypertension.

Introduction

The merits of sodium restriction in primary hypertension are currently the subject of debate. We reviewed 13 randomised trials of the effect of sodium restriction on blood pressure, considering especially which variables were the best predictors of the effect of sodium restriction.

Methods

Data from 12 studies, comprising 13 randomised trials, were used.¹⁻¹² From these studies eight characteristics were recorded (see table).

(1) The design of the trial—that is, whether it was an open or blind trial and whether a parallel group or crossover design was used.

(2) The number of participants from whom complete sets of data were obtained, the mean age of the groups studied, and the duration of the intervention period.

(3) The initial systolic and diastolic blood pressures recorded. Readings taken when patients were in the supine position were used when provided. When the trial included a lead in period the blood pressure measured at the start of the intervention period was used.

(4) Daily sodium and potassium intake, based on the 24 hour urinary electrolyte excretion. When no data on urinary sodium excretion were included the intake was based on an estimate of the sodium content of the diet.¹⁰ Some reports did not provide data on potassium intake or excretion.^{1,2,9}

(5) The maximum reduction in sodium intake achieved and the change in potassium intake during intervention.

(6) The change in systolic and diastolic blood pressures during intervention. The method used depended on the design of the trial. In crossover trials the difference in blood pressure between the intervention and control periods was used,^{1,3,4,6,8,10-12} and in trials with a parallel group design the difference in the change in blood pressure from the baseline value between the intervention and the control groups was used.^{2,5,7,9}

(7) The significance of the results. In most trials a *t* test for unpaired or paired observations was performed. Results were considered to be significant when a two sided *p* value was <0.05.

(8) The year the study was published. Although trials on sodium restriction have been conducted since the beginning of this century, trials before 1970 often were very small and did not match current criteria for design and data analysis.¹³ Thus only studies published from 1970 to 1985 were included. From one study unpublished data were used.¹²

Although there were substantial differences between the trials, each trial was given equal weight. The data were analysed in two ways. Firstly, variables that predicted the fall in blood pressure during sodium restriction were studied by simple linear and multiple linear regression analysis, in which the fall in blood pressure was the dependent variable and its potential predictors were the determinants in the model. Secondly, trials were grouped by their design and the significance of the results, and differences between the groups were tested with a *t* test for unpaired observations. The results of statistical tests are expressed as two sided *p* values.

Results

The table summarises the features of the trials included in this analysis. All of them showed an average fall of 3.6 mm Hg (range 0.5-10.0 mm Hg) in systolic blood pressure during sodium restriction, though the fall was significant in only three trials. Diastolic blood pressure showed an average decrease of 2.0 mm Hg (range 3.0-7.0 mm Hg), though in three trials it rose (range 1.2-3.2 mm Hg). Five trials were double blind; all of these had been performed in the past three years. The intervention period was four weeks or shorter in six trials, five to 12 weeks in three, and a year or more in two.

A total of 584 subjects participated in the trials; their mean age was 38.5 years, the average age in each trial ranging from 16 to 60. Five trials were conducted in adolescents or young adults. The average sodium intake in the trials overall was 157 mmol(mEq)/24 h and the average potassium intake 64 mmol(mEq)/24 h. No significant association between initial blood pressure and sodium or potassium intake was found. Initial sodium intake tended to be lower in the studies published more recently; this association, which remained after adjustment for age (coefficient of linear regression (*b*) = -5.1 (SE 2.4) mmol/year, *p*=0.05), may indicate an overall downward trend in sodium consumption in the West. The mean reduction in sodium intake was 78 mmol/24 h (range 26-170 mmol/24 h).

Variables that predicted a fall in blood pressure—During sodium restriction systolic blood pressure fell by a greater amount in the patients with higher initial blood pressure (fig 1), but for diastolic blood pressure this association did not reach significance. The falls in systolic and diastolic blood pressures also increased with age. This finding was more obvious for diastolic pressure (fig 2), but after adjustment of initial blood pressure for age and vice versa neither of the associations reached significance. We did not observe any apparent relation between the fall in blood pressure and initial sodium or potassium intake or the fall in blood pressure and reduction in sodium intake. There was also no association between the duration of the trial and the number of subjects included.

Open and blind studies—Blood pressure is susceptible to a variety of factors other than a reduction in sodium intake. Uncontrolled and open studies may therefore show a fall in blood pressure greater than that caused solely by sodium restriction. The five blind trials were generally of shorter duration than the eight open trials. In open trials the baseline sodium intake was higher (mean 168 (SE 13) mmol/24 h) than that in blind trials (139 (6) mmol/24 h) (*p*=0.07). The fall in systolic and diastolic blood pressures observed in open trials tended to be greater: the average fall in systolic blood pressure was 4.3 (0.9) mm Hg in open trials compared with 2.6 (1.8) mm Hg

Department of Epidemiology, Erasmus University Medical School, Rotterdam, The Netherlands

D E GROBBEE, MD,
A HOFMAN, MD, PHD,

Correspondence to: Dr D E Grobbee, Department of Epidemiology, Erasmus University Medical School, PO Box 1738, 3000 DR Rotterdam, The Netherlands.

Compilation of data from trials included in analysis

Trial No	Type of trial	Design	Duration of sodium restriction (days)	No of participants	Mean age (years)	Initial mean blood pressure (mm Hg)		Sodium intake (mmol/24 h)		Potassium intake (mmol/24 h)		Change in blood pressure (mm Hg) during intervention			Year of publication
						Systolic	Diastolic	Baseline or during control period	Change during intervention	Baseline or during control period	Change during intervention	Systolic	Diastolic	Significance	
1	Open	Crossover	28	22	41	175	112	191	-98			-6.7	+3.2	p<0.05	1973
2	Open	Parallel group	730	62	60	163	97	191	-38			-2.0	-7.0	p<0.05	1978
3	Open	Crossover	14	20	23	125	73	210	-170	71	-6	-2.7	-3.0	NS	1981
4	Double blind	Crossover	28	19	49	154	97	162	-76	65	-6	-10.0	-5.0	p<0.05	1982
5	Open	Parallel group	84	90	49	141	87	150	-113	77	+3	-5.2	-3.4	NS	1982
6	Double blind	Crossover	28	18	52	137	83	143	-56	54	+3	-0.5	-0.3	NS	1983
7	Open	Parallel group	365	28	55	163	99	149	-21	60	+5	-8.7	-6.3	NS	1983
8	Open	Crossover	35	12	40	150	92	210	-100	55	+8	-5.2	-1.8	NS	1984
9	Open	Parallel group	28	94	46	157	101	130	-58			-3.0	-2.5	NS	1984
10	Open	Crossover	24	113	16	103	61	113	-70	49	+16	-0.6	-1.4	NS	1984
11	Double blind	Crossover	28	31	23	111	64	128	-60	64	-1	-0.5	+1.4	NS	1985
12	Double blind	Crossover	28	35	22	114	63	131	-74	61	-6	-1.4	+1.2	NS	1985
13	Double blind	Crossover	42	40	24	137	73	129	-72	77	-3	-0.8	-0.8	NS	

Conversion: SI to traditional units—Sodium and potassium: 1 mmol/l=1 mEq/l.

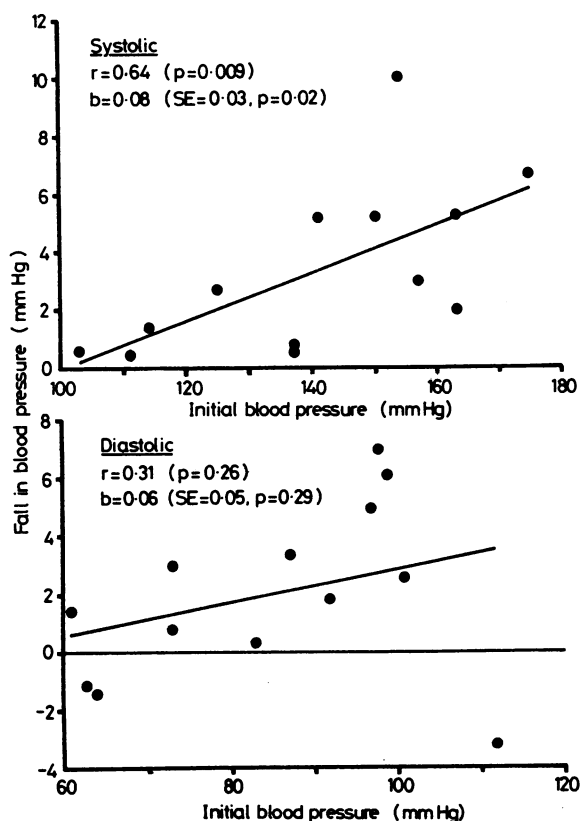


FIG 1—Fall in systolic and diastolic blood pressures during sodium restriction plotted against initial blood pressure.

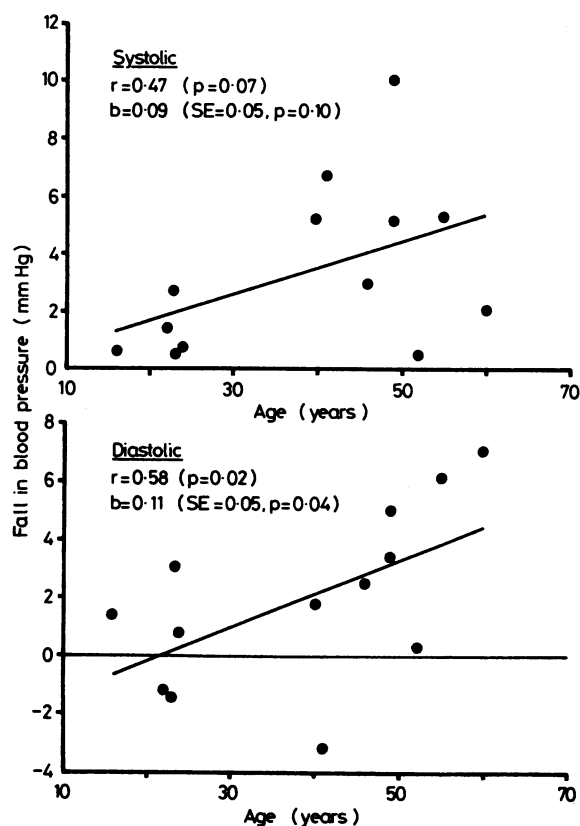


FIG 2—Fall in systolic and diastolic blood pressure during sodium restriction plotted against age.

in blind trials, and for diastolic blood pressure these figures were 2.8 (1.1) mm Hg and 0.7 (1.2) mm Hg respectively. These differences did not reach significance.

Positive and negative results—Only three trials reported a significant positive result. Positive trials were more often open and tended to include fewer women, and the subjects were older. Baseline sodium intake was higher in positive trials (181 (10) mmol/24 h) than in negative trials (150 (11) mmol/24 h) (p=0.06), but the average reduction in sodium intake was similar (71 (18) mmol/24 h in positive trials and 80 (13) mmol/24 h in negative trials).

Discussion

The results of this analysis of 13 trials of the effect of sodium restriction on blood pressure support the general hypothesis that a reduction in sodium intake may lower blood pressure. This fall in blood pressure seems to increase with age and in those with a higher initial blood pressure. It is impossible to say from our results whether age or degree of hypertension is a better predictor of the effect of sodium restriction.

To appreciate these observations some points need to be discussed. Only three studies showed a significant fall in blood pressure during sodium restriction. Moreover, as the present analysis was necessarily based on a small sample some predictors of lesser magnitude might not have been detected because of the limited statistical power. This suggests that any generalisations from other reports might be hazardous. A separate analysis, however, which included three trials that did not have a control group, supported our findings in almost every respect.¹⁴⁻¹⁶ In all studies that included a lead in period blood pressure tended to fall in this period without any planned intervention. Accordingly, blood pressure at the first screening was higher than that at the start of the intervention, which was the reading used in this analysis. In comparison with the reading taken at the first screening our interpretation of "initial" blood pressure may overestimate the association between initial blood pressure and the fall in blood pressure during sodium restriction.

The specific objectives of the studies included in the analysis varied. This is reflected in the criteria used to select participants. In some studies subjects were selected from a general population,¹² whereas in others only patients attending a hypertension clinic⁴ or sharing a genetic predisposition to high blood pressure¹¹ were eligible. Moreover, in most studies, because of the nature of the intervention, several people invited to participate refused to be included. This implies that the general applicability of the results may be limited.^{17,18}

Obviously no conclusions can be drawn from this analysis regarding an additive effect of sodium restriction on antihypertensive drugs. Moreover, the type of studies discussed here give information primarily on the hypotensive potential of sodium restriction, not on the role of dietary sodium in the aetiology of high blood pressure. It remains doubtful whether further trials will give more positive information. We observed a negative association between the year of study after 1980 and a net fall in systolic and diastolic blood pressure on sodium restriction (systolic: $b = -1.2$ (SE 0.8) mm Hg/year, $p = 0.08$; diastolic: $b = -1.2$ (0.4) mm Hg/year, $p = 0.02$). This finding may, of course, have resulted from different methods of selecting cases in more recent trials, but it may also be associated with the observed downward trend in sodium intake in the past decade.

A question not yet answered is whether there is a subgroup in which sodium restriction may be most effective. The findings of the present analysis suggest that sodium restriction may be most effective in older patients with relatively high blood pressure. Genetic factors have also been implicated in the response of blood pressure to sodium restriction. In a recent report by Watt *et al* a family history of hypertension did not seem to be related to susceptibility to sodium,¹¹ but the findings in an open study by Skrabal *et al* suggested the opposite.³ Initial plasma concentrations of catecholamines, in particular dopamine, may be associated with the fall in systolic blood pressure with sodium restriction.¹² The role

of plasma renin, prostaglandins, cellular electrolytes, and circulating natriuretic factors in discriminating between hypertensive patients who are and are not sensitive to sodium needs further consideration. The smaller net changes in blood pressure observed in blind trials compared with open trials once again suggest that blind trials are a necessity in research into blood pressure.

This analysis suggests that sodium restriction may reduce blood pressure but that the effect is small and restricted largely to systolic blood pressure. The fall in blood pressure seems to increase with age and in those with higher initial blood pressure. This implies that sodium restriction may, unfortunately, be of limited use in those who seem to be most eligible for non-pharmacological treatment—namely, young patients with mild hypertension.^{19,20}

This work was supported by a grant from The Netherlands Heart Foundation.

References

- 1 Parijs J, Joossens JV, Van der Linden L, Verstreken G, Amery AKPC. Moderate sodium restriction and diuretics in the treatment of hypertension. *Am Heart J* 1973;85:22-34.
- 2 Morgan T, Adam W, Gillies A, Wilson M, Morgan G, Carney S. Hypertension treated by salt restriction. *Lancet* 1978;ii:227-30.
- 3 Skrabal F, Aubock J, Hortnagel H. Low sodium/high potassium diet for prevention of hypertension: probable mechanisms for action. *Lancet* 1981;ii:895-900.
- 4 MacGregor GA, Markandu ND, Best FE, *et al*. Double-blind randomised crossover trial of moderate sodium restriction in essential hypertension. *Lancet* 1982;ii:352-4.
- 5 Beard TC, Cooke HM, Gray WR, Barge R. Randomised controlled trial of a no-added-sodium diet for mild hypertension. *Lancet* 1982;ii:455-8.
- 6 Watt GCM, Edwards C, Hart JT, Hart M, Walton P, Foy CJW. Dietary sodium restriction for mild hypertension in general practice. *Br Med J* 1983;286:432-6.
- 7 Silman AJ, Locke C, Mitchell P, Humpherson P. Evaluation of the effectiveness of a low sodium diet in the treatment of mild to moderate hypertension. *Lancet* 1983;ii:1179-82.
- 8 Richards AM, Nicholls MG, Espiner EA, *et al*. Blood-pressure response to moderate sodium restriction and to potassium supplementation in mild essential hypertension. *Lancet* 1984;ii:757-60.
- 9 Erwtaman TM, Nagelkerke N, Lubsen J, Koster M, Dunning AJ. β Blockade, diuretics, and salt restriction for the management of mild hypertension: a randomised double blind trial. *Br Med J* 1984;289:406-9.
- 10 Cooper R, Van Horn L, Liu K, *et al*. A randomized trial on the effect of decreased dietary sodium intake on blood pressure in adolescents. *Journal of Hypertension* 1984;2:361-6.
- 11 Watt GCM, Foy CJW, Hart JT, *et al*. Dietary sodium and arterial blood pressure: evidence against genetic susceptibility. *Br Med J* 1985;291:1525-8.
- 12 Grobbee DE, Hofman A, Roelandt JTRC, Boomsma F, Schalekamp MADH, Valkenburg HA. Sodium restriction and potassium supplementation in young people with mild hypertension (submitted to *Journal of Hypertension*).
- 13 Gibson CB, Chapman TB. The diet and hypertension. *Medicine* 1950;29:29-69.
- 14 Longworth DL, Drayer JIM, Weber MA, Laragh JH. Divergent blood pressure responses during short-term sodium restriction in hypertension. *Clin Pharmacol Ther* 1980;27:544-6.
- 15 Parfrey PS, Markandu ND, Roulston JE, Jones BE, Jones JC, MacGregor GA. Relation between arterial pressure, dietary sodium intake, and renin system in essential hypertension. *Br Med J* 1981;283:94-6.
- 16 Miller JZ, Daugherty SA, Weinberger MH, Grim CE, Christian JC, Lang CL. Blood pressure response to dietary sodium restriction in normotensive adults. *Hypertension* 1983;5:790-5.
- 17 Schwartz D, Lellouch J. Explanatory and pragmatic attitudes in therapeutic trials. *J Chronic Dis* 1967;20:637-48.
- 18 Pocock SJ. *Clinical trials*. Chichester: John Wiley and Sons, 1983.
- 19 Ilsley CD, Millar JA. Hypertension in children. *Br Med J* 1985;290:1451-2.
- 20 Anonymous. Treatment of hypertension: the 1985 results [Editorial]. *Lancet* 1985;ii:645-7.

(Accepted 18 March 1986)

MATERIA NON MEDICA

Cuba libre

The Old Man and the Sea was a schoolboy blurr. We were forty five miles east of Havana towards that "other" resort of Varadero (popular with non-communists). My holidaying companions were a mixed bunch of East Germans and Russians, save for two rather obvious Americans. The Irish were here also, but at a "special camp."

You could choose a plantation with horse riding and the inevitable tree climbing native. My new wife left me for this. The adolescent machismo of the alternative appealed.

After minimal haggling the price was set: thirty US dollars (half price). No name was apparent on the boat as far as I could see, but a proud flag was unfurled on our immediate departure. First stop America.

I tried daiquiri, Hemingwayesque. The language barrier was complete. I was the only passenger ("Should take four," according to our humourless guide). Hot sun, dry and wrinkled Cubans, and the ubiquitous stale

sandwich were my travelling companions. The first hour was sloth. I sat mesmerised. The right line tugged and wailed but no one seemed excited. Five minutes later it was all over. Barracuda. Ugly fish. Clubbed into oblivion with a baseball bat. (Is this a capitalist influence?) I was pleased, and my reward was a toothless grin from behind a stale, authentic Havana cigar. This tall, gangly Cuban was a contented soul. Suddenly, "Marlin, marlin, blue marlin!" "Where?" I took my place on the chair, strapped in, feet against the railings. The line extended outwards, on and on, taking with it the tip of a finger. I took hold of the rod and the engine roared on. Immediately, starboard, the waves spread apart and the fish rose. It climbed upwards, bright blue and shining, only to land with a thunderous splash. Again and again, with almost angelic fortitude, it struggled. Four hundred pounds, I later found out.

Minutes later the hook slipped out. My despair was complete. I now know that fish was immortal. I now know how Hemingway must have felt.—DAVID KERR, Nottingham.