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RANDOMISED CONTROLLED TRIAL OF A NO-ADDED-SODIUM DIET FOR MILD HYPERTENSION

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Summary 90 patients on medication for mild hypertension were randomly allocated to diet and control groups and kept under surveillance by their own doctors every 2 weeks for 12 weeks to test the short-term effectiveness of a diet free from sodium additives as an alternative to medication. Mean urinary sodium excretion was reduced to 37·0 mmol/24 h in the diet group and 161·0 mmol/24 h in the control group, with average K/Na ratios of 3·9 and 0·50. Both groups had a fall in mean systolic and diastolic blood pressure, but the diet group finished on half of the initial amount of medication, with 1 patient in 3 off medication and 4 out of 5 having either stopped or reduced the dose. The control group remained on almost the full amount of medication, with 2 patients out of 3 having made no reduction. The diet group had a mean weight loss of 2·1 kg, a rise in serum potassium, and a fall in serum bicarbonate. There was no increase in overall frequency of muscle cramp, and the diet group reported feeling happier, less depressed, and less dependent on analgesics. Two-thirds of the diet group intend to continue to diet indefinitely. Reduction of sodium intake permitted drug treatment to be substantially reduced without side-effects or loss of blood-pressure control.

Introduction

NO single advance in community health would improve the quality of life more than the control of hypertension.[1] Drug treatment has been recommended even for mild hypertension,[2-4] but implementing this recommendation would mean that up to one-fifth of the entire adult population of a country like Australia would require medication for life,[5] with substantial problems of cost and compliance and with no effect on primary prevention.

An alternative to medication is to avoid excess dietary sodium. The treatment effect of such a diet has been known for nearly 80 years[6-9] but regarded as inconvenient and unpalatable, especially since the advent of diuretics that remove excess sodium.[10] Evidence that a feasible and palatable diet could still be effective[11-13] is supported by the findings of a randomised double-blind controlled trial with placebo.[14]

The real need is the primary prevention of hypertension, and the unique claim made for adding less sodium to food is that it might prevent new cases.[15-17] Intakes below 100 mmol/24 h would be expected to control the epidemic[12] and intakes below 35 mmol/24 h to eliminate it.[16] To test the second claim a generation of children would need to grow up without sodium additives. This might be feasible (1) if food could be made palatable to the whole family without adding sodium and (2) if hypertensive parents obtained enough treatment effect from such a diet to recruit whole family groups willing to follow it indefinitely. The purpose of this trial was to ascertain the practicability of these two conditions in a Western community, by finding out whether a no-added-sodium diet would permit treated hypertensives to finish with similar blood pressures to a control group but with substantially less medication, and whether a substantial proportion of such patients would be willing to continue the diet indefinitely.

Methods

A randomised controlled trial was undertaken to determine the short-term effect of a no-added-sodium diet on blood-pressure. Patients aged 25–69 years, who were receiving antihypertensive medication and who had a premedication diastolic blood pressure (DBP) of 95–109 mm Hg and systolic blood pressure (SBP) under 200 mm Hg, were referred by 34 local general practitioners. Pregnant women and those taking an oral contraceptive were excluded, and both sexes were excluded for severe intercurrent illness, serum creatinine >0·20 mmol/l, or history of antihypertensive medication for less than 3 months. After small-group discussion and informed consent, a total of 113 entered the trial, in three intakes of 30–40, at 6-week intervals. Their own doctors countersigned the consent forms, accepting clinical responsibility during and after the trial. Patients received verbal and written instructions about accurate collection of 24 h urine specimens and completed a pretested questionnaire on personal health and life style. Height and weight were recorded, and a casual sitting blood pressure (mean of two readings) was taken to the nearest 2 mm Hg with the Hawksley random-zero machine, using a 13 cm × 35 cm bag and the 5th-phase DBP. All readings were taken by one of two nurses whose results had shown good agreement and internal consistency in practice sessions. Blood for analysis was taken by a technician on a separate occasion. For each intake patients were allocated randomly to the diet or control group.

We urged the control group in small-group discussion, with a written briefing, to maintain their usual sodium intake until it was their turn to try the diet. We gave the diet group a shopping guide and address list for obtaining unsalted foods, including unsalted wholemeal bread and cakes made with potassium baking-powder, and unsalted restaurant meals. For 4 weeks they attended weekly 2 h

small-group discussions at which slides were shown, recipes exchanged, and urine results discussed under code numbers. One of us (W.R.G.) also gave individual nutritional counselling to every family. The natural sodium content of a balanced diet was described as rather generous but safe. Milk (Na 21–28 mmol/l) was rationed and edible seaweed (kelp) prohibited. Patients received the Australian dietary guidelines[18] to eat less fat and sugar, more cereals and breads (preferably wholemeal), and more fruits and vegetables but were asked not to diet for weight reduction during the trial period.

All doctors used mercury sphygmomanometers, cleaned, recalibrated, and fitted with new cuffs with 13 cm×35 cm rubber bags. All recorded the DBP to the nearest 2 mm Hg at the 5th phase (obtainable in all patients). They reduced or stopped medication if the DPB (mean of two readings) was <90 mm Hg at two consecutive consultations and continued or increased it if the mean DBP was ⩾90 mm Hg at two consecutive consultations. They withdrew diuretics from all patients with urinary Na<50 mmol/24 h, control of blood pressure being maintained in these cases with other medication where necessary. Doctors reported mean blood pressures and management decisions at every consultation on a special form, which revealed any departure from the protocol.

Patients were asked to collect a baseline 24 h urine specimen and four others at the weekends of weeks 2, 4, 6, and 11. Volume and sodium, potassium, and creatinine levels were recorded. Patients answered a final questionnaire on health and lifestyle, and the diet group reported compliance and future intentions. Weight, random-zero blood pressure (measured by a nurse), and blood-analysis results were repeated. Constituents of urine and serum were measured with an 'AutoAnalyzer'.

Ethical approval was given by the clinical research committee, John Curtin School of Medical Research, Australian National University.

TABLE I—MEDICATION CHANGES IN DIET AND CONTROL GROUPS

Type of medication	No. of tablets per day*			
	Start		Finish	
	Diet	Control	Diet	Control
Diuretics, K-sparing	6	5	0	2
Diuretics, other	26	27	1	25
K supplements	4	3	0	3
Beta-blockers	80	70	53	62
Other antihypertensives	47	41	21	48
Total	163	146	75	140
Average per patient	3·6	3·2	1·7	3·1

*To nearest whole number.

TABLE II—SUMMARY OF MAIN CHANGES OBSERVED IN THE TRIAL

—	Diet	Significance	Control
Subjects:			
Randomly allocated	56		57
Removed (Na<60 mmol/24 h in baseline urine)	4		6
Dropped out	7		6
Remained in trial	45		45
Stopped medication	14 *(31%)*	p<0·001	4 *(9%)*
Reduced dose	23 *(51%)*		11 *(24%)*
Failed to stop or reduce dose	8 *(18%)*		30 *(67%)*
Urinary excretion, electrolytes (mmol/24 h):			
Sodium (and SD)			
Start (n=83: diet 43, control 40)	150·1 (±65·1)	NS	174·7 (±90·1)
Finish	37·0 (±22·3)	p<0·001	161·0 (±61·7)
	p<0·001		NS
Potassium			
Start	76·6 (±22·7)	NS	71·0 (±22·5)
Finish	79·9 (±22·5)	p<0·05	70·5 (±21·2)
	NS		NS
Average K/Na ratio, molar			
Start	0·61 (± 0·32)	NS	0·50 (± 0·30)
Finish	3·92 (± 3·25)	p<0·001	0·53 (± 0·21)
	p<0·001		NS
Mean blood pressure (mm Hg):			
Systolic—start	142·3 (±13·9)	NS	138·9 (±18·6)
finish	131·0 (±17·6)	NS	132·8 (±15·4)
	p<0·001		p<0·01
Diastolic—start	88·3 (±10·2)	NS	86·2 (±11·2)
finish	82·0 (± 8·7)	NS	83·3 (± 9·4)
	p<0·001		NS
Mean body-weight (kg):			
Start	79·98 (±13·99)	NS	77·81 (±12·88)
Finish	77·87 (±14·11)	NS	78·09 (±13·29)
	p<0·001		NS
Serum electrolytes (mmol/l):			
Potassium—start	4·10 (± 0·52)	NS	4·00 (± 0·49)
finish	4.33 (± 0·42)	p<0·001	4·01 (± 0·48)
	p<0·025		NS
Bicarbonate—start	29·18 (± 2·31)	NS	28·96 (± 2·85)
finish	27·76 (± 1·90)	NS	28·39 (± 3·09)
	p<0·01		NS

Statistical significance of a difference between groups is shown between columns, and significance of a change within a group is shown below the finishing figure. Standard deviations are shown in brackets. NS=not significant at p<0·05.

Results

Comparability of Groups

Of 113 patients accepted, 56 were originally randomised to the diet group and 57 to the control group. 6 of the control group and 4 of the diet group were excluded because of low baseline sodium excretion (<60 mmol/24 h). 13 more (7 from the diet group and 6 from the control group) dropped out (10 in the first week), mainly for social reasons. 45 remained in each group.

All were white and of similar socioeconomic status, and 7 in each group were born outside Australia. The male/female ratio was 27/18 in the diet group and 24/21 in the control group, and the mean ages were 48·4 and 49·6 years. At the start there was no significant difference in age distribution, body weight, body mass index (mean and distribution) serum Na, K, Cl, HCO_3, blood-urea nitrogen, serum creatinine, calcium, urate, or postprandial glucose. 4 in each group entered with a raised serum gamma-glutamyltransferase (γ-GT) level. Data processing of the questionnaires showed no significant differences in reported alcohol consumption, tobacco consumption, drug compliance, consumption of meat, fat, bread, tea, or coffee, doctors' estimates of compliance, previous stability and quality of blood-pressure control (DBP>95 mm Hg), types of medication (table I), or life-event scores.[19] Mean duration of previous drug treatment was 37·8 months in the diet group and 51 months in the control group. This was not significant at $p<0·05$, because of high variance. 83 of the 90 patients produced baseline 24 h specimens, all judged to be complete, and none over-collected. Group differences in baseline excretion rates (table II) were again not significant, because of high variance. 1 control-group patient, after eating take-away food exclusively for 2 days, passed 578 mmol sodium/24 h.

Sodium Excretion during the Trial

In the first routine specimen 24 members of the diet group passed <50 mmol sodium/24 h, and the 14 taking a diuretic discontinued it. Mean sodium excretion in the other three urine collections was 37·0 mmol/24 h in the diet group and 161·0 mmol/24 h in the control group, with average K/Na ratios of 3·9 and 0·50 (table II).

Blood Pressure and Drug Management

Both groups had a fall in mean SBP and DBP, but the diet group showed greater falls after halving its total medication, whereas the control group made very little net reduction in medication (table I). 4 out of every 5 patients in the diet group stopped medication or reduced the dose, whereas two-thirds of the control group failed to do so ($p<0·001$) (table II).

Changes permitting a reduction of medication began in 3–6 weeks, but some patients on high doses were still reducing after 12 weeks, and the trial was too short to measure the full effect in all cases. 2 patients in the diet group stopped only a single tablet of a diuretic daily, but the other 12 stopped a total of 45 tablets daily without rebound hypertension, including one who had started on 6 tablets of clonidine daily. 8 of the 14 who stopped all medication in the diet group had a lower SBP and DBP after stopping 1–4 tablets (diuretics, beta-blockers, and/or other agents) than at entry.

On the other hand, 8 patients failed to respond to the diet, including 2 who had to continue their single tablet of a beta-blocker despite excellent compliance, as shown by sodium excretion rates in one case of 10, 25, and 11 mmol/24 h and mean K/Na ratio of 6·0.

Departures from the Protocol

Contrary to the protocol for drug management, the practitioners allowed 2 members of the diet group to remain on reduced medication despite DBP>90 mm Hg at two consecutive consultations. Conversely, 3 in the control group who should have reduced medication according to their DBP did not. 5 other reported departures from the protocol had no effect on the patients' categories in table II (for example, a further reduction omitted in a patient who qualified for it). 1 patient in the control group was said to be under too much stress to reduce medication, and medication was continued in the other 2 because of a relatively high SBP. The diet-group patients had a low SBP and infringed the protocol for DBP by only 1–2 mm Hg in the mean reading. Infringements did not affect the numbers stopping medication. If the practitioners had applied the protocol strictly to their reported data, the two groups in table II would still have shown a difference at $p<0·001$.

Other Outcomes

The only reported changes in general health significant at $p<0·01$ (Wilcoxon's test) occurred in the diet group, who felt happier, had less depression (both mild and severe), and used fewer analgesics. Both diet and control groups reported a slight improvement (not significant, $p<0·01$) in both mild and severe muscle cramp. Serum potassium and bicarbonate changed to more normal values in the diet group. The diet group lost an average of 2·1 kg ($p<0·001$) and the control group gained 0·28 kg (not significant), but no statistical association (χ^2) was seen between weight change and outcome. Some patients with significant weight change failed to stop or reduce medication, and some who stopped medication gained weight.

Reported alcohol consumption was stable in both groups. The raised serum γ-GT changed only in the diet group, where 2 patients reverted to normal and 1 patient, normal at entry, had a raised γ-GT at the end of the trial. No other significant changes in life style, including exercise, were reported by either group. Admitted dietary infringements occurred almost exclusively for social reasons rather than taste, and 30 of the 45 patients (67%) intend to stay off added sodium indefinitely.

Discussion

The important finding was that, after coming close to a mean sodium excretion rate of 35 mmol/24 h, the diet group finished with a lower mean SBP and DBP than the control group, on about half the medication (table I). Drugs were either stopped or reduced in 4 out of 5 in the diet group, compared with 1 in 3 of the control group (table II). These proportions are not affected by the known departures from the protocol.

Observer bias could affect blood-pressure measurements made without automated equipment, placebo control, or "blind" conditions. Steady improvement can occur on a placebo through familiarisation,[4] but special attention has an additional effect, as seen in a placebo-controlled trial of very moderate sodium restriction by Silman et al.,[20] where the control group improved as much as the diet group. Our own control group received equal attention from their doctors, but less attention from the research team. Also our patients were

rather fully medicated, leaving room for adjustment of dosage. Finnerty[21] found the majority of his patients with a stable DBP<90 mm Hg could reduce their medication without relapse even after 18 months' further observation. He reduced it without dietary or other intervention, merely on the assumption that they were slightly overmedicated.

Practitioners could have been tempted to give the diet group preferential treatment in having their medication reduced, and known departures from the protocol affecting outcome were in this direction. But this does not alter the fact that the two groups finished on very different therapeutic regimens, with blood pressures taken by independent nurse observers on random-zero equipment showing no advantage over the more heavily medicated control group.

Other extraneous factors probably had little influence. Patients had been under routine medical care for long enough to reduce the effects of familiarisation and regression towards the mean. Questionnaires revealed no differences significant at $p<0\cdot01$ in consumption of alcohol, fat, fibre, coffee, or meat, or in habitual exercise. There was no difference in stress according to the life event score.[19] The benefit of a reducing diet is largely attributable to the fact that less food provides less sodium.[22] An independent effect of weight reduction, with sodium intake held constant, has been reported,[23,24] but there was no statistical association (χ^2) in this trial between weight change and outcome. The mean weight loss of 2·1 kg in the diet group probably represents unavoidable water loss on the lower sodium intake.

Despite the acknowledged advantages of automated blood-pressure measurement, a casual sitting blood pressure measured with an ordinary sphygmomamometer has predictive value.[25] Our patients were examined by their own doctors under standardised and familiar conditions, end-points were based on a trend confirmed at two consecutive consultations, and the findings are consistent with those of other controlled studies.[11,12,26,27] They also resemble those of an uncontrolled trial with a similar protocol by Dodson and Humphreys,[13] in which remissions occurred in similar proportions and were stable during long-term follow-up. We propose to extend the present study to include a 2-year follow-up.

Considering the comparability of their final blood pressures, with differences in favour of the diet group, the two groups finished with a striking differences in the amounts of active medication. It is clear from other work[14] that some of this effect must be attributed to the different sodium intake, or to the different K/Na ratio, of the diet group.

Some patients in the diet group complained of tiredness at first but, even in the Australian summer, hypotension was not reported and there was no net increase in muscle cramp. On the other hand significantly less reliance on analgesics, and especially the improvement of serum potassium and bicarbonate, should improve prognosis.[28–30] This occurred only in patients who stopped a diuretic and was probably a reversal of drug-induced hypokalaemic alkalosis. Elevation of mood contrasted with the conventional image of "the misery of lifelong salt restriction".[31]

The sodium-hypertension hypothesis can never be proved, only disproved,[32,33] and we need more critical intervention studies designed to disprove it. The purpose of the present trial was to ascertain the feasibility and outcome of culinary reform in a sample of the Australian population to the level suggested by Freis.[16] It has been found feasible and has had an outcome consistent with the findings of others. A drop-out rate of 1 in 8 seems acceptable among patients complying with the inconvenience of the research protocol in addition to overcoming the present cultural barriers to reduction of sodium intake by a factor of 4–10. With cooperation from the food industry the way may be open for trials in primary prevention at this level of intake.

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