PAPERS AND SHORT REPORTS

Trial of relaxation in reducing coronary risk: four year follow up

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Abstract

On screening 192 men and women aged 35-64 were identified as having two or more of the following risk factors: blood pressure ≥140/90 mm Hg, plasma cholesterol concentration ≥6·3 mmol/l (243·6 mg/100 ml), and current smoking habit ≥10 cigarettes a day. They were randomly allocated to a group for modification of behaviour or to serve as controls. Both groups were given health education leaflets containing advice to stop smoking, to reduce animal fats in the diet, and on the importance of reducing blood pressure. In addition, the treatment group had group sessions of one hour a week for eight weeks in which they were taught breathing exercises, relaxation, and meditation and about managing stress. It had previously been found that after eight weeks and eight months there was a significantly greater reduction in both systolic and diastolic blood pressures in the group taught to relax compared with the control group. After four years of follow up these differences in blood pressure were maintained. Plasma cholesterol concentration and the number of cigarettes smoked were lower in the treatment group at eight weeks and eight months but not at the four year follow up. At four years more subjects in the control group reported having had angina and treatment for hypertension and its complications. Incidence of ischaemic heart disease, fatal myocardial infarction, or electrocardiographic evidence of ischaemia was significantly greater in the control group.

If the results of this study could be obtained in a larger study the financial and health care implications would be enormous.

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Introduction

The search for a non-pharmacological method of lowering blood pressure has led to an evaluation of behavioural techniques. Various modes of relaxation can significantly reduce blood pressure[1-15] and, possibly, other cardiac risk factors.[16-18] Many of these studies, however, included only highly motivated volunteers already receiving antihypertensive treatment, for whom follow up was short (at most 15 months) and treatment was given on a one to one basis, which is not suitable for general application.

We conducted a randomised controlled trial in subjects found at screening to have mild untreated hypertension or other cardiac risk factors. We showed that after eight weeks of training subjects taught relaxation had significantly lower blood pressures than controls, and these findings were still in evidence six months later.[19] After four years of follow up we now report changes in blood pressure, plasma cholesterol concentration, and smoking and morbidity from cardiovascular disease.

Subjects and methods

A group of 1268 men and women employed by one industry and aged 35-64 were invited for screening; 1132 attended. Blood pressure was measured by a trained nurse with a random zero sphygmomanometer after the subjects had been sitting quietly for five minutes. Diastolic blood pressure was measured at phase V (disappearance of Korotkoff sound). We recalled subjects with two or more of the following risk factors: an average of two measurements of blood pressure of ≥140/90 mm Hg and not taking antihypertensive drugs; non-fasting

plasma cholesterol concentration of ⩾6·3 mmol/l (244 mg/100 ml); and a current cigarette consumption of ⩾10 cigarettes a day.

Of the 312 subjects invited for re-examination, 289 attended. Each subject completed three self administered 24 hour dietary recall diaries. At this stage 59 subjects were excluded because they no longer had two or more risk factors as defined. Of the 230 subjects who qualified for the study, 204 agreed to participate. The subjects were then randomly allocated to a treatment or a control group.

TABLE I—*Details of subjects taught relaxation and controls at entry to study*

	Subjects taught to relax (n = 99)	Controls (n = 93)
No of men	60	58
No of subjects:		
Aged 35-44	22	18
Aged 45-54	41	39
Aged 55-64	36	36
Blood pressure:		
Mean systolic (SD)	145·2 (25·8)	144·2 (22·0)
Mean diastolic (SD)	87·4 (15·3)	87·9 (12·8)
No with systolic ⩾140 mm Hg	63	58
No with diastolic ⩾90 mm Hg	51	46
Mean systolic (SD) in group with high blood pressure*	163·6 (20·0)	160·3 (12·9)
Mean diastolic (SD) in group with high blood pressure*	100·1 (7·9)	98·7 (7·1)
Mean cholesterol concentration (mmol/l) (SD)	6·92 (0·97)	7·07 (1·03)
No with cholesterol concentration ⩾6·3 mmol/l	82	83
Mean cholesterol concentration (SD) in high cholesterol group†	7·22 (0·74)	7·27 (0·87)
No of smokers	81	64
Average No of cigarettes smoked/day	19	20

*High blood pressure defined as ⩾140 mm Hg systolic and ⩾90 mm Hg diastolic.
†High cholesterol defined as plasma cholesterol concentration ⩾6·3 mmol/l.
Conversion: SI to traditional units—Cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml.

terol concentrations, and electrocardiograms were recorded. Four measurements of blood pressure were taken on two separate days. Three 24 hour dietary recall diaries were completed at eight weeks and eight months. The questionnaire at four years also included a medical history and record of current treatment. Subjects who did not attend the four year follow up examination were asked to complete the questionnaire. For those who could not be traced death certificates were sought at the central registry of the National Health Service. Of the five subjects who had left the country, three were traced.

Results

Of the 107 subjects allocated to the group taught to relax, 99 completed the eight week programme, while of the 97 allocated to the control group, 93 completed the programme. The characteristics of the 14 people who dropped out of the study soon after randomisation were similar to those of the 192 subjects who completed the eight week follow up examination. Table I shows that the treatment and control groups were comparable at entry. Systolic blood pressure and current smoking habit were slightly higher in the treatment group; serum cholesterol concentrations were slightly higher in the control group.

Further analysis was restricted to those who were available at the four year follow up. Of the 99 subjects in the group taught to relax eight were lost to follow up and two had died; 89 filled in the questionnaire, of whom 86 were examined (91 accounted for). Of the 93 subjects in the control group, nine were lost to follow up and two had died; 82 filled in the questionnaire, of whom 75 were examined (84 accounted for). Table II shows that at eight weeks, eight months, and four years there were significantly greater falls in both systolic and diastolic blood pressures in those taught relaxation than in the controls. This was true for men and women analysed separately.

TABLE II—*Blood pressure, plasma cholesterol concentration, and cigarette consumption in treatment and control groups at each examination*

	Initial	8 weeks	8 months	4 years
		Blood pressure		
Mean (SD) systolic pressure (mm Hg):				
Treatment group (n = 86)	146·5 (26·3)	132·0 (21·2)	130·3 (18·8)	139·4 (22·4)
Control group (n = 75)	144·1 (22·8)	140·2 (17·4)	139·1 (16·9)	145·7 (21·0)
p				0·015
Mean (SD) diastolic pressure (mm Hg):				
Treatment group (n = 86)	87·9 (15·2)	80·5 (13·0)	81·1 (11·4)	85·2 (13·6)
Control group (n = 75)	88·3 (12·3)	86·6 (10·8)	88·0 (11·4)	92·4 (12·8)
p				0·001
		Plasma cholesterol		
All subjects:				
Treatment group (n = 86)†	6·95 (0·92)	6·24 (1·13)	6·32 (1·00)	7·03 (1·25)
Control group (n = 75)‡	7·07 (1·00)	6·49 (1·39)	6·43 (1·15)	6·90 (1·16)
p		0·429	0·945	0·129
Initial concentration ⩾6·3 mmol/l:				
Treatment group (n = 74)§	7·19 (0·73)	6·30 (1·09)	6·43 (0·95)	7·13 (1·23)
Control group (n = 67)‖	7·27 (0·87)	6·73 (1·26)	6·62 (1·05)	7·09 (1·05)
p		0·051	0·451	0·587
		Smoking		
No (%) subjects stopped:				
Treatment group		9 (11·1)	8 (10·4)	20 (28·6)
Control group		5 (7·8)	3 (5·4)	13 (23·6)
No (%) subjects reduced:				
Treatment group		55 (55·6)**	52 (54·7)**	53 (60·9)
Control group		25 (27·2)	21 (25·3)	39 (48·1)
Reduction in No of cigarettes smoked/day:				
Treatment group		5·8**	4·8*	7·1
Control group		2·6	2·3	6·8

*p < 0·05; **p < 0·01.
†Values missing in one subject at eight weeks and three subjects at eight months and four years, respectively.
‡Values missing in two, six, and four subjects at eight weeks, eight months, and four years, respectively.
§Values missing in one, two, and three subjects at eight weeks, eight months, and four years, respectively.
‖Values missing in two, five, and three subjects at eight weeks, eight months, and four years, respectively.
Conversion: SI to traditional units—Cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml.

Both groups were given health education literature on stopping smoking, reducing dietary cholesterol and animal fats, and high blood pressure and its treatment. The treatment group also had group sessions of one hour a week for eight weeks to learn breathing exercises, deep muscle relaxation, and meditation as well as a stress management programme described previously.[19] They were asked to practise relaxation and meditation for 15-20 minutes twice daily and to try to relax during everyday activities, such as while waiting at red traffic lights, before picking up a telephone, and every time they looked at their wrist watches. The subjects were lent a tape recording on relaxation to use at home.

Assessments were made at eight weeks, eight months, and four years of smoking (by questionnaire); blood pressure, plasma cholesterol concentrations, and electrocardiograms were recorded. Four measurements of blood pressure were taken on two separate days. Three 24 hour dietary recall diaries were completed at eight weeks and eight months. The questionnaire at four years also included a medical history and record of current treatment. Subjects who did not attend the four year follow up examination were asked to complete the questionnaire. For those who could not be traced death certificates were sought at the central registry of the National Health Service. Of the five subjects who had left the country, three were traced.

Changes in blood pressure were also analysed separately for those with initially high pressures (⩾140/90 mm Hg) and those with initially normal pressures (< 140/90 mm Hg) (figure). The number of subjects in each group was small, but the group taught to relax showed a consistent advantage over the control group in both subgroups based on initial blood pressure.

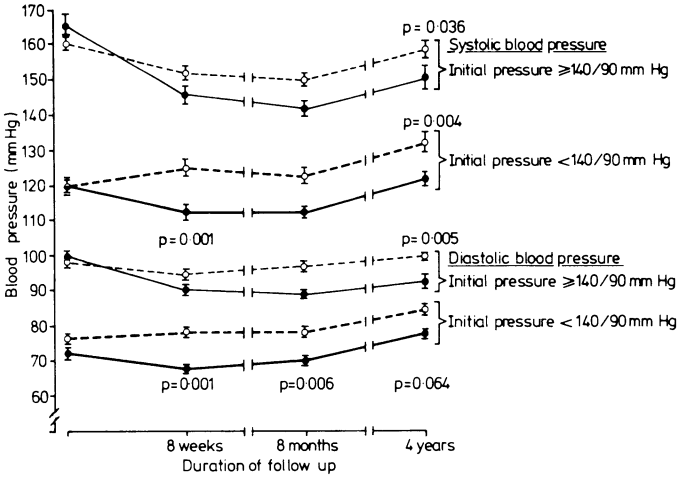
Plasma cholesterol concentration was reduced in both groups at eight weeks and eight months (table II). The mean fall in the group taught to relax was not significantly different from that in the control group. In those with an initial plasma cholesterol concentration of ⩾6·3 mmol/l (244 mg/100 ml), however, the fall was significantly greater in the group taught to relax than in the controls at eight weeks (fall of 0·89 mmol/l (34·4 mg/100 ml) *v* 0·53 mmol/l (20·5 mg/100 ml)).

The groups were comparable at entry to the study with respect to total energy and amount of different fats consumed. There were small changes in both the groups which were slightly greater in the control group at eight weeks, giving a ratio of polyunsaturated to saturated fat of 0·3 in the controls compared with 0·2 in the group taught to relax. Alcohol consumption was similar in both groups as was body weight, which did not change significantly. Thus the greater reductions in serum cholesterol concentration and blood pressure in the treatment group compared with the controls are unlikely to have been due to changes in diet or body weight.

TABLE III—*Incidence of morbidity and mortality at four year follow up*

	Subjects taught to relax (n = 88)	Controls (n = 81)
Self reported†		
Physician diagnosed:		
Angina	2	5
Heart attack	2	3
Heart failure		1
Kidney damage		1
Thrombosis of retinal vessels		1
Having treatment for:		
Angina	1	5
Coronary thrombosis		1
Heart failure		1
Hypertension	16	16
Independently established		
New electrocardiographic abnormality‡:		
Probable myocardial infarction		2
Possible myocardial infarction	1*	3
Fatal myocardial infarction		1
Other deaths	2	1

*One person taught to relax *v* six controls; $p < 0.05$ (Fisher's exact test).
†Some patients had more than one condition. When those taking antihypertensive drugs alone were excluded the actual numbers of patients affected were five of those taught to relax and nine controls.
‡Both initial and four year electrocardiograms were available in only 69 of those taught to relax and 57 controls.



Changes in blood pressure at each follow up in subjects with high and normal blood pressures initially. ●——● = Subjects taught relaxation. ○— — —○ = Controls. p values test differences between treatment and control groups in mean changes in blood pressure.

More people in the group taught to relax than the control group reduced their cigarette consumption (table II); this difference was significant at eight weeks and eight months. The reduction in the mean number of cigarettes smoked by those who were initially smokers was also significantly greater in those taught to relax than the controls.

At the four year follow up only 14 of 81 subjects in the group taught to relax said that they were regularly practising relaxation, and of these only three had practised at least once a day in the previous week. An additional 27 had practised relaxation in the last six months. However, 51 (63%) said that they sometimes and 16 (20%) that they often integrated relaxation into their everyday life, and 73 (90%) said that they often or sometimes told themselves to calm down under pressure. Thus most subjects were not spending the recommended 15-20 minutes daily relaxing and meditating, but many had changed their style of coping and were either cognitively or physically relaxing in their everyday life.

Those who had relaxed regularly showed greater reduction in mean systolic and diastolic blood pressures (10·9 and 7·0 mm Hg, respectively) than those who did not (6·3 and 1·7 mm Hg, respectively). Similarly, those who regularly integrated relaxation into their everyday life and those who told themselves to calm down under pressure (cognitive reappraisal) showed greater reduction in blood pressure compared with those who had not changed their behavioural or cognitive styles of coping.

Morbidity during the four years was assessed by a questionnaire and electrocardiograms (table III). More of the controls had symptoms of angina or possible myocardial infarction and were receiving long term treatment. Electrocardiograms were analysed blind using the Minnesota code. Five electrocardiographic abnormalities suggestive of ischaemia developed in the control group compared with one in the group taught to relax. There was also one fatal myocardial infarction in the control group proved at necropsy. Fisher's exact test for these objective data showed the difference between the groups to be significant ($p < 0.05$). Three deaths from cancer occurred, two in the treated and one in the control group. One of these deaths was in a subject in the treated group who was known to have had pneumonectomy for carcinoma of the bronchus before the study began.

Discussion

In our previous report we discussed the possibilities of bias and concluded that the changes in blood pressure were likely to have been the result of the treatment.[19] This study shows that a programme to modify behaviour of hypertensive patients can be delivered cost effectively. The total time spent per person was below one hour. This is not excessive for a newly diagnosed hypertensive patient when the therapeutic effect, without reinforcement, persists after four years. The treatment was evidently quite acceptable to this population of non-volunteers, 99% of whom consisted of white British men and women occupied in full time jobs.

The evidence that reductions in blood pressure were genuine and not the result of relaxation at the time of measurement is supported by the favourable trend in plasma renin activity and aldosterone concentration.[6 12 19] Further support comes from the recent report by Little *et al*, which showed that relaxation treatment for hypertension during pregnancy can almost halve the incidence of admission to hospital without compromising the outcome for the mother and fetus.[20]

We were disappointed with the effect of our study on smoking as our pilot study in a volunteer group had shown a quite dramatic reduction in smoking.[18] From this we have learnt not to extrapolate results from studies of volunteers. Differences between the groups, however, were significant at eight weeks and eight months. The greater reduction in cigarette smoking could not have been responsible for the greater reduction in blood pressure in the group taught to relax as, in general, blood pressure in smokers is not higher than that in non-smokers.

Morbidity data at the four year follow up were intriguing. Self reported events are subject to bias, but blindly coded electrocardiograms showed that new ischaemic events were significantly more common in the control than the treatment group. Numbers were small and electrocardiograms were not available in all subjects, so the estimate of benefit is imprecise. If this trend could be confirmed in a large study of morbidity, however, the financial and health care implications would be enormous.

Roughly 20% of the population is likely to have mild hypertension. Blood pressure in this group can be reduced either by modifying behaviour alone or by a judicious combination of this treatment with antihypertensive drugs. When this is considered together with the reduction in blood pressure in normotensive subjects who, nevertheless, were at risk because of two other cardiac risk factors it seems that we may indeed have found a mass strategy for primary prevention[21] that is safe, cheap, effective, and acceptable.

On the basis of changes in risk factors we estimated that there

was a 22%, 15%, and 12% reduction in risk of coronary heart disease at eight weeks, eight months, and four years, respectively, using a multiple logistic function from the London Whitehall study. The reduction in the incidence of new electrocardiographic abnormalities at four years was greater than predicted. This may have been the result of chance variation, but it may suggest that relaxation affects pathways other than the established cardiac risk factors.

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Short course chemotherapy for tuberculosis of lymph nodes: a controlled trial

BRITISH THORACIC SOCIETY RESEARCH COMMITTEE

Abstract

One hundred and fifty two patients with tuberculosis of lymph nodes were enrolled in a randomised trial of nine versus 18 months' chemotherapy. The regimens consisted of rifampicin plus isoniazid for nine or 18 months, supplemented initially by ethambutol for eight weeks. At 36 months data from 113 patients were available for analysis, of whom 56 had received the short course regimen. Progress during chemotherapy was uneventful in 84 of the 113 patients. Fresh nodes appeared in 13 patients and existing nodes increased in size in 13; these events occurred within the first eight months of treatment. In 10 patients residual nodes were palpable at the end of chemotherapy. Events including enlargement of nodes, appearance of new nodes, fluctuation, and formation of sinuses occurred in 12 patients after the end of chemotherapy. The incidence of these events was similar in both groups, and they did not result in an unfavourable outcome.

Nine months' treatment with rifampicin and isoniazid supplemented initially by ethambutol should be adequate for tuberculosis of lymph nodes, but confirmation must await a longer period of follow up.

Introduction

A survey of notifications of tuberculosis in England and Wales in 1978 showed that disease of the lymph nodes was the commonest form of non-respiratory tuberculosis.[1] The British Thoracic Association's first controlled trial of chemotherapy for tuberculosis of lymph nodes compared two 18 month regimens in 99 patients.[2 3] The regimens comprised either rifampicin plus isoniazid or ethambutol plus isoniazid, both supplemented with streptomycin for the first two months. A satisfactory response to chemotherapy was seen, and microbiological relapse did not occur when treatment was stopped. In a retrospective study of lymph node tuberculosis Summers and McNicol reported no relapse in 239 patients, some of whom were treated with nine month regimens incorporating rifampicin and isoniazid.[4]

Our study compares treatment with rifampicin and isoniazid given for either nine or 18 months, supplemented initially by eight weeks' treatment with ethambutol. We describe the state of patients 36 months after entry to the study.

The study was organised by a subcommittee of the research committee of the British Thoracic Society, whose members were: Dr I A Campbell (chairman), consultant in thoracic medicine, Llandough and Sully hospitals, Cardiff; Dr C R McGavin (coordinator and compiler of the report), chest physician, Plymouth Chest Clinic; Dr J A R Friend, consultant in thoracic medicine, City Hospital, Aberdeen; Dr R M Greenwood, member of scientific team, Division of Computing and Statistics, Clinical Research Centre, Harrow, Middlesex; Dr P A Jenkins, head of department, Mycobacterium Reference Unit, University Hospital of Wales, Cardiff; and Dr A R Somner, consultant physician, Chest Clinic, Wallsend, Tyne and Wear.

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