Stopping drug treatment of hypertension: experience in 18 British general practices

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SUMMARY

Background. *Of the many reports published describing the effect of withdrawing antihypertensive medication from patients who have well-controlled blood pressure, none have been major British general practice studies. Studies from other settings have shown that a substantial minority can do so without harm or resulting in the relapse of their hypertension.*

Aim. *To determine the proportion of hypertensive patients who could have their medication withdrawn without relapse, and to seek factors associated with success at withdrawal.*

Method. *A longitudinal observational study in 18 general practices in north-east England. Practices selected and managed patients to guidelines suggested by the study protocol. Data were abstracted from records by practice staff over three years of follow-up.*

Results. *A total of 196 out of 224 (88%) patients were followed up. Forty-three (22%) of these 196 remained normotensive off medication for the whole study. A total of 108 (55%) of the 196 had restarted medication by three months. Twenty-six (31%) of the 84 males, but only 17 (15%) of the 112 females, remained off medication. No differences in age, morbidity, symptoms, or biochemical parameters occurred between the group who stayed off medication and those who restarted it. Apart from male sex, no factors were found that enabled the prediction of patients more likely to succeed at stopping medication.*

Conclusions. *One-fifth of well-controlled hypertensives in British primary health care could have their medication withdrawn without the relapse of their hypertension or any harm. Of those that do relapse, over half are likely to have done so before three months. Life-long observation of all patients is essential.*

Keywords: hypertension; medication withdrawal; antihypertensive medication; Britain; general practice.

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Introduction

MANY reports have been published that describe the effect of withdrawing antihypertensive medication from patients who have well-controlled blood pressure.[1-3] The majority of these studies are from the United States of America and involve patients attending hospital outpatient clinics; whereas, in the United Kingdom (UK), uncomplicated, mild to moderate essential hypertension is treated mainly in general practice. Many British cases have been diagnosed as having hypertension many years before the current guidelines[4] were published and before the importance of lifestyle factors such as alcohol excess, stress, and depression[5] as causes of intermittent hypertension were widely appreciated.

There are three reports of British general practice populations in which hypertensive patients who were taking specific drugs were studied.[6-8] In a Medical Research Council study, 783 patients with mild hypertension who were taking either bendrofluazide or propranolol had their medication stopped.[6] Of these patients, 24 had their treatment restarted when either their systolic blood pressure rose above 200 mmHg or their diastolic blood pressure rose above 110 mmHg — figures that are well in excess of those now recommended.[4] A London general practice group withdrew medication from 17 patients taking angiotensin converting enzyme inhibitors (ACEIs) and, at two years, 15 were back on treatment.[7] In a third study from a British general practice, treatment was withdrawn from nine well-controlled hypertensives taking a variety of medication.[8] After one year of follow-up, one patient had relapsed and, although the blood pressure rose in the other eight, their diastolic blood pressure remained below 90 mmHg. These authors called for a larger study to be conducted in British general practice and pointed out the benefits to patients, doctors, and prescribing budgets.

This report describes the first major prospective study to evaluate the effect of stopping treatment of patients with controlled hypertension in primary care in the United Kingdom. Its aims were to determine, in that setting, what proportion of patients could have their medication withdrawn without the relapse of their hypertension over a three-year period, and to seek factors associated with success at withdrawal. It is a pragmatic, observational study describing how a group of general practices and their patients followed recommendations on the withdrawal of medication.

Method

Eighteen practices, 17 in Northumberland and one in Newcastle upon Tyne, agreed to participate in the project. Hypertensive patients aged 40 to 69 years were listed, excluding those who were poorly controlled (mean last three systolic blood pressures of 160 mmHg or diastolic blood pressures of 90), were on antihypertensive medication for less than two years, had a major cardiovascular event in the previous one year, had any indication in addition to hypertension for an antihypertensive drug (diuretic, beta-adrenergic, or calcium channel blocking agent, or ACEI), or had a previous relapse of hypertension after stopping treatment. The standardisation of blood pressure recording was improved

by a presentation by the research team to each practice, and by the provision of educational material on blood pressure measurement.

Practices selected patients from those with optimal blood pressure control and no reason for exclusion, and offered them entry into the programme. Patients who agreed to enter were given an information sheet explaining the care that they would receive and emphasised the importance of lifelong follow-up even if their medication was successfully stopped. Signed consent was given by participating patients who were then entered into the programme of stepping down and stopping medication. Those who were selected had an entry assessment, which included the recording of three sitting blood pressures during a 30-minute period, details of medication, cardiovascular history, risk factors, psychosomatic illness, and biochemical screening.

Medication withdrawal followed a written protocol: diuretics being stopped at entry but other drugs stepped down in dose before withdrawal. Advice and literature on optimal weight, exercise, alcohol intake, salt reduction, and smoking were given to each patient at the entry assessment and reinforced throughout the study.

Antihypertensive medication was restarted whenever blood pressures rose to levels indicating treatment. Though the protocol gave practices guidance on when to restart, decisions were made by the patient's practitioner on the basis of individual risk profiles, of which blood pressure was only one. Patient follow-up data on blood pressures, medication, morbidity, and symptoms were collected on request at three and six months, and at one, two, and three years after entry. At three years, the data recorded at entry was assembled again at a final assessment. All results were filed and analysed on an Epi-Info database.[9]

Results

The total population aged 40 to 69 of the 18 practices was 35 341. A total of 2805 (7.9%) were on drug treatment for hypertension (Figure 1). Of these 2805 hypertensives, 723 (26%) had optimal blood pressure control and no exclusions. Two hundred and twenty-four of the 723 patients were recruited and followed up; this being 31% of the total who were listed for possible treatment withdrawal. A majority, 499 (69%) of the 723, were not selected on the basis of factors such as patient anxiety, doctor hesitancy, lifestyle, or health risk, and there was a degree of self-selection that was impossible to quantify. Twelve patients were lost to follow-up (four deaths and eight moved away), and incomplete data was filed for a further 16, resulting in an 88% follow-up rate. Table 1 shows the numbers (%) of the two groups of patients — those staying off medication and those restarting — using the denominator of 196 for which complete data was held.

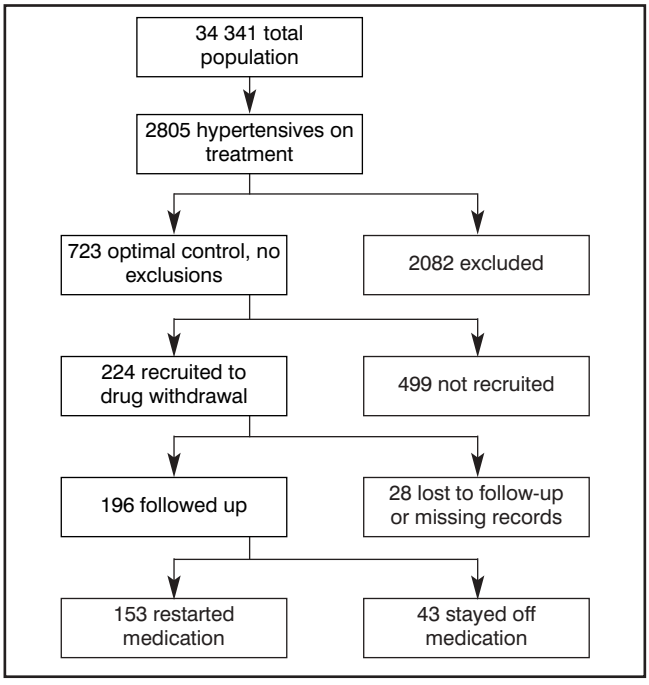

Figure 1. Profile of patient populations.

Systolic and diastolic blood pressures increased from entry to final assessments in both groups. At entry, 78% of both groups were optimally controlled (mean systolic <160 mmHg and mean diastolic <90 mmHg), but, at the final assessment, 57% of those who restarted but only 43% of those who remained off medication satisfied these criteria. Those who restarted medication reached three-year follow-up taking similar numbers of drugs (Table 2) but in smaller doses than at entry to the study, as shown in Figure 1. At three years, patients on thiazides had gone down from 31% to 22%, and on beta-blocking agents from 60% to 54%. Patients on calcium channel blockers had increased from 16% to 24%, and those on ACEIs from 4% to 10%.

Male sex, but not age, was associated with success at staying off treatment (Table 3). Comparing those who restarted medication with those who stayed off, there were only small changes in morbidity or cardiovascular symptoms, headache or insomnia. Male impotence did not differ between the groups. In the 59 males restarting medication, impotence increased from 13 to 17, and, in the 25 males who stayed off, it increased from two to five; slight increases possibly related to ageing. In the restarting medication group, mean body mass index (BMI) increased from 28.2 to 28.7, and, in those staying off, from 27.4 to 28.0. Smoking decreased from 18% to 16% in the restarting group and from 17% to 15.5% in those staying off.

Factors that have enabled the prediction of success at the withdrawal of medication in previous studies were examined. The numbers of drugs being taken at entry were greater in patients who stayed off medication than in those who restarted it, but differences in drug type were small. Table 4 lists the possible predictive factors in the two groups.

During follow-up there were four cases of myocardial infarction (one death), six new cases of other symptomatic ischaemic heart disease (one death from congestive cardiac failure), one of stroke (died), two of transient cerebral ischaemic attack, and two of retinal haemorrhage. Of the 15 events detailed above, 11 patients had blood pressures in the normal range but the other four were suboptimally controlled with a mean last three blood pressures of 152/95, 176/90, 157/95, and 169/95 mmHg. Of these patients, one had been off medication for 10 months and the other three were back on treatment from 10 to 21 months. None of these events closely followed the stopping or restarting of drug treatment. None of these patients with poorly-controlled blood pressure had additional major risk factors, though one smoked cigarettes and two were overweight. There were two non-cardiovascular deaths: one from bronchial carcinoma and one from septicaemia following a perforated peptic ulcer.

Discussion

Great strides have been made in the organisation of the care of chronic illness by primary health care teams in recent years, and we believe that the results of this study can be generalised to the treatment of hypertension throughout primary care. Most prac-

Table 1. Number and percentage of patients staying off medication during three years of follow-up.

Duration off medication	At entry	3 months	6 months	12 months	24 months	36 months	
Number	196	108	102	75	45	43	
			Percentage	100	55	52 38	23

Table 2. Different numbers (%) of drugs taken by patients who restarted medication (n = 153) at entry and final assessments.

	At entry assessment	At final assessment
	n (%)	n (%)
Patients on one drug	104 (68)	114 (75)
Patients on two drugs	44 (29)	34 (22)
Patients on three drugs	5 (3)	5 (3)
Total patients	153 (100)	153 (100)

Table 3. Numbers (%) of males and females who stayed off or restarted medication.

	Males	Females
	n (%)	n (%)
Stayed off medication	26 (31)	17 (15)
Restarted medication	58 (69)	95 (85)
Total in each group	84 (100)	112 (100)

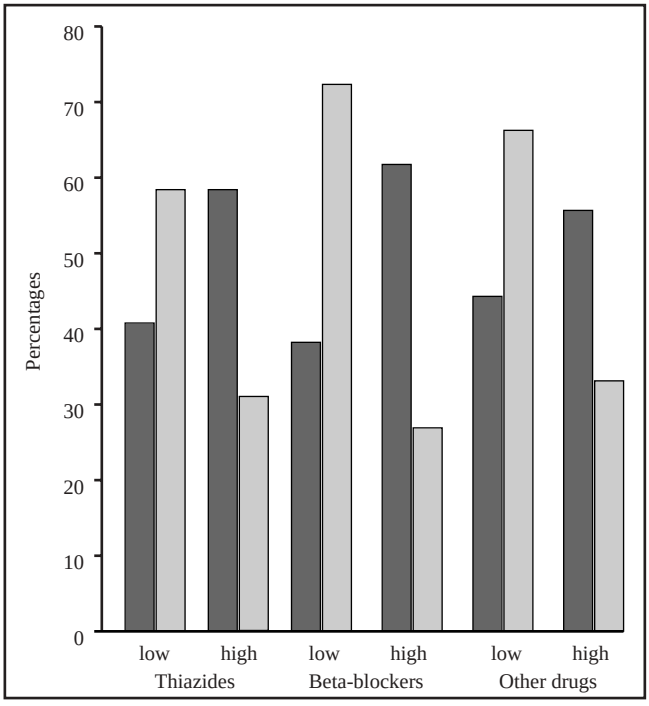

Figure 2. Drug dose comparisons (%) of restarters at entry and final assessment The percentages of patients, of those who restarted medication, taking either a low dose or a high dose at entry (dark bar) and at the end (light bar) of the study.

tices are now able to identify all of their hypertensive patients and give them structured, proactive care.

In this study, the practices selected only 31% of those patients who qualified for treatment withdrawal; the other 69% not being included for complex reasons. We had to exclude 16 patients with incomplete data, and it was clear from details of non-attendance that this was a problem of practice rather than patient non-compliance. There are therefore many confounding factors in any comparisons made between those who stayed off medication and those who restarted it. Because of the way our patients were selected, comparisons of the groups using statistical analyses would be inappropriate and misleading.[10,11] We emphasise that this is a pragmatic study, the value of which lies in its likelihood of generalisation to other primary care settings. Pragmatic trials measure the effectiveness and the benefit that a treatment produces in routine clinical practice rather than in an experimental setting.[11]

The numbers of deaths and major events during the three years were as expected for the groups of patients with their particular profile of cardiovascular disease risk factors. We compared them with the incidence of events in those with similar risk factor profiles in the active treatment arms of major antihypertensive drug therapy trials. Nevertheless, it is of concern that four cardiovascular events occurred when blood pressures were at suboptimal levels, even though none had other major cardiovascular risk factors. In these cases, practices allowed blood pressures to continue above advised target levels.

Our findings that 22% of patients remained normotensive off medication at three years were in keeping with those previously reported from other settings where about a quarter of patients have been able to stop treatment without hypertensive relapse.[1,2] Because most other studies followed up patients for periods of only one or two years, we would expect fewer in our study to succeed in medication withdrawal. In common with other studies, the mean blood pressures of both groups — those who restarted medication and those who stayed off — increased, and the proportion of patients with optimally controlled blood pressure fell. The increase in mean blood pressure was greater in those staying off, and it was accepted that, although few of the blood pressures at the final assessment appeared to indicate starting or increasing medication, levels were higher and there was probably a small increase in overall cardiovascular risk. The increase in mean blood pressure of those who restarted medication appeared to show an association with a reduction in the proportion of patients taking higher doses of drugs. A common criticism of prescribing for hypertension is that drugs are not prescribed in high enough doses, and this is an important cause of suboptimal blood pressure control. Some other studies have found that those on fewer drugs before withdrawal were more likely to succeed in staying off medication, but we found the reverse to be true in our patients. Apart from male sex, no factors were found that would have predicted success at stopping medication. There is evidence from other sources that ambulatory blood pressure monitoring or echocardiography may have a place in deciding whether to attempt drug withdrawal from some patients.[12]

This study showed that, in the primary care setting where most patients with hypertension are exclusively treated, withdrawing medication from those with optimal control will result in four-fifths having to restart treatment within three years; half of them

Table 4. Possible predictive factors. Factors at entry of those who stayed off and those who restarted medication.

Factor at entry	Stayed off medication n = 43 (%)	Restarted medication n = 153 (%)
Male sex	26 (60)	58 (38)
Taking one drug	30 (70)	107 (70)
Taking a thiazide	18 (42)	69 (45)
Taking a beta-blocker	27 (63)	94 (61)
BP[a] <160 and <90	31 (72)	119 (78)
Mean blood pressure	136/82 mmHg	140/83 mmHg
Mean body mass index	27.4	28.2
Cigarette smoker	5 (12)	24 (16)
History of anxiety-depression	5 (12)	21 (14)

[a]Blood pressure.

within three months. The fifth that remain normotensive on no treatment suffer no discernible deterioration in health, and we conclude that a trial of withdrawal of medication is appropriate in all optimally controlled cases unless there are firm reasons for not doing so. Patient and doctor cooperation and consent are important, and follow-up for life is essential. Non-drug strategies, which have been shown to increase the number who remain normotensive without drugs,[13] should always be employed.

The prevalence of hypertension in the UK in 1991/92 was 41 per 1000 or 74 per general practitioner,[14] though these figures include some patients not on antihypertensive medication. Screening has increased since then and the 1996 figure for Northumberland is 52 per 1000 or about 90 per practitioner.[15] Extrapolating from our results, one-fifth of optimally controlled hypertensive patients could have their medication withdrawn. If a trial of withdrawal was a more prominent feature of current guidelines, as it is in some countries,[16] the attitude of many doctors to withdrawing medication might change, and as many as 0.54 million (20%) of the 2.7 million patients on treatment nationally might have their medication stopped. The tendency for recent guidelines to recommend starting treatment at lower levels of blood pressure will also increase the numbers of those optimally controlled and suitable for a trial of drug withdrawal. Patients with no other cardiovascular risk factors comprise a group that should have high priority for attempting to stop their drugs, and those with only mild hypertension at the commencement of treatment have also been shown in most other studies to have a greater chance of success at withdrawal.[1,2]

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