Discontinuation of and changes in treatment after start of new courses of antihypertensive drugs: a study of a United Kingdom population

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Abstract

***Objective*—To evaluate the incidence of discontinuation of and changes in treatment after newly prescribed courses of antihypertensive drugs of the four primary therapeutic classes: β blocker, calcium channel blocker, and angiotensin converting enzyme inhibitor.**

***Design*—A retrospective analysis of patients on an automated database of 1·2 million patients was conducted on visits between 1 October 1992 and 30 September 1993.**

***Setting*—General practices in the United Kingdom.**

***Subjects*—37 643 patients with hypertension receiving a relevant drug in the time period were identified. A new course of treatment in at least one of the four therapeutic classes, defined as a drug not prescribed in the previous four months, was observed in 10 222 patients aged ≥ 40 years.**

***Main outcome measures*—Patients changing to other treatment or discontinuing after initiating a new course of treatment, defined as the absence of a refill prescription for the new drug or another in its category within a six month observation period.**

***Results*—Changes in or discontinuation of treatment were frequently observed, and by month six continuation rates ranged between 40% to 50% for all four classes of drugs.**

***Conclusion*—Low rates of continuation with a newly prescribed antihypertensive drug exist regardless of which drug is prescribed.**

Introduction

Consistent drug treatment decreases both mortality and morbidity associated with hypertension.[1 2] In clinical practice, however, poor compliance, intermittent or switched prescriptions, and termination of use disrupts the consistency of treatment. The resulting suboptimal treatment is associated with progression of coronary atherosclerosis, congestive heart failure, and renal disease as well as considerably higher rates of readmission to hospital for hypertensive crises.[3 4]

Side effects may be one reason for changing or stopping the use of antihypertensive drugs, but the proportion of hypertensive patients who change or discontinue treatment because of side effects is difficult to estimate. Clinical trials suggest that discontinuation occurs in about 15% of patients randomised to angiotensin converting enzyme inhibitors, 15-20% of those taking diuretics, and 20-25% of those taking β blockers after six months to one year of treatment[5-7] and in about 20% of patients randomised to a calcium channel blocker after four years of treatment.[8] Rates of discontinuation observed in clinical trials, however, may not reflect everyday practice because of selection bias.[9 10]

Two studies in the United States investigated treatment for hypertension among Medicare patients and the California Medi-Cal population[11 12] but did not specifically assess discontinuation or substitution, although a high proportion of patients stopped treatment in the second study.[12] Although drugs with appreciable side effects, such as methyldopa and reserpine, are now less commonly prescribed, there is a paucity of data on acceptance by patients of the newer antihypertensive agents.

The computerised primary care databases in the United Kingdom provide a means by which patterns of treatment may be studied over extended periods. A substantial proportion of general practitioners have computerised medical records so a broad range of data is available. We characterised and quantified the time course of discontinuation of newly prescribed antihypertensive drugs.

Methods

DATA SOURCE

The United Kingdom MediPlus automated primary care database contains a broad range of information on patients, doctors, and medical practice for about 1·2 million patients and 500 physicians; it includes diagnoses (*International Classification of Diseases*, ninth revision (ICD-9) and Read codes) and prescriptions, which, since 1991, are linked to diagnoses for about 90% of patients. The data are recorded individually by date, providing longitudinal records of patients for the period of time they remain within the practice. A recent internal audit revealed that about 95% of prescriptions are captured in the data. The regional distribution of practices and doctors is representative of the United Kingdom as a whole, except that there is a higher proportion of younger physicians and an underrepresentation of practices in Scotland, (IMS International, personal communication).

DEFINITION OF STUDIED SUBJECTS AND OUTCOMES

The study patients were those who had an ICD-9 code for hypertension (ICD-9 codes 401-405) and a record of at least one prescription for a drug belonging to one of the four primary classes of antihypertensive drugs (diuretics, β blockers, calcium channel blockers, and angiotension converting enzyme inhibitors) within the defined one year study period from 1 October 1992 to 30 September 1993. Patients receiving a prescription for an antihypertensive drug in a therapeutic class which had not been prescribed during the previous four months were defined as undergoing a new course of treatment. This included both newly diagnosed patients as well as currently treated patients starting a new drug. The only combination drug analysed was

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co-amilozide because it is used widely. Patients eligible for the study were required to have a record of visits for at least six months after the initiation of the new treatment.

Changing or discontinuing treatment was defined as the absence of a prescription for the new antihypertensive drug or another in its class in the six month observation period with or without the presence of a prescription for another new drug outside its class. This could include termination of treatment or a change in treatment entailing a prescription for a drug from another class within six months after the receipt of the patient's initial prescription. Patients with more than one prescription were considered to be continuing unless there was a gap in treatment exceeding 60 days.

DATA ANALYSIS

A descriptive analysis characterised the population of hypertensive patients overall and the subsample of hypertensive patients undergoing new treatment. Within each class of drug the monthly rate of continuation of new treatment versus changes of treatment to another class of antihypertensive or discontinuation was analysed over six months. Among continuers and those changing or discontinuing treatment with a new course of drugs age and sex adjusted estimates of the total number of antihypertensive prescriptions and number of contacts with a general practitioner are presented. We used two way analysis of variance to compare continuers with those changing or discontinuing treatment on each outcome.

Results

We identified 37 643 patients with treated hypertension within the study period (table I). As the prevalence of treated hypertension among patients under 40 years of age was low (less than five per 1000) subsequent analyses focused on those aged ≥40.

TABLE I—*Prevalence of treated hypertension in the MediPlus population: age and sex distribution*

		Women		Men	
Age (years)	Total No	No	Rate/1000	No	Rate/1000
0-19	18	9	0·1	9	0·1
20-39	1 116	548	4·7	568	4·9
40-64	14 681	7 632	66·4	7 049	60·2
≥65	21 828	14 116	185·5	7 712	145·4
Total	37 643	22 305		15 338	

For patients with ongoing treatment in one or more of the four study categories during the study, treatment with diuretics was most common (31% of all patients), with women accounting for over two thirds of the total use, most in the over 65 age group. Treatment with angiotensin converting enzyme inhibitors was the least common (15%), with 24% and 18% of patients on β blockers and calcium channel blockers, respectively.

During the one year study period 10 222 patients started a new course of treatment with at least one of the four primary classes of drugs. There was a total of 14 740 new courses of treatment among these patients, as some patients started more than one course of treatment in the study period (table II). Of patients prescribed new treatment, 50·6% (n=5171) were prescribed diuretics, 35·4% (n=3615) β blockers, 31·7% (n=3244) calcium channel blockers, and 26·5% (n=2710) angiotensin converting enzyme inhibitors, which corresponds to the overall proportional use.

Table II also shows rates of continuation of treatment for each of four primary classes of drug among new courses of treatment. Continuation of all four types decreased progressively over the course of six months. By month one the rate of changing or discontinuing treatment was between 15% (β blockers) and 22% (calcium channel blockers). By month six, 50-60% of new treatment had been changed or discontinued in all four drug classes.

The overwhelming proportion of these changes (greater than 96% of all changes) entailed substitution or switching to drugs outside the therapeutic class of the original antihypertensive drug (table III). After initiation of any one of the three non-diuretic drugs change was most likely to result in a switch to a diuretic; this was true after discontinuation of β blockers (53%), calcium channel blockers (47%), and angiotensin converting enzyme inhibitors (55%). A change after initiation of a diuretic, however, led to a more evenly distributed switch to other drugs, with 40% changing to β blockers, 26% to calcium channel blockers, and 30% to angiotensin converting enzyme inhibitors.

The total number of consultations and prescriptions for hypertension in the six months after new treatment were compared for patients who continued taking treatment versus those who discontinued it (table IV). Overall, those changing or discontinuing had more prescriptions (mean=6·7) than did continuers (5·0). Patients starting with calcium channel blockers (6·4) and angiotensin converting enzyme inhibitors (6·2) ultimately had more antihypertensive prescriptions

TABLE II—*Monthly continuation rates for new courses of treatment with antihypertensive drugs. Figures are numbers (percentages) of patients continuing treatment* by month*

Class of drug	Total exposed	No of users	First month	Second month	Third month	Fourth month	Fifth month	Sixth month
Diuretics	12 157	5 171	4 205 (81)	3 211 (62)	2 668 (52)	2 372 (46)	2 230 (43)	2 131 (41)
β blockers	9 348	3 615	3 075 (85)	2 523 (70)	2 215 (61)	1 983 (55)	1 858 (51)	1 779 (49)
Calcium channel blockers	7 176	3 244	2 539 (78)	1 877 (58)	1 598 (49)	1 450 (45)	1 367 (42)	1 323 (41)
Angiotensin converting enzyme inhibitors	5 811	2 710	2 232 (82)	1 760 (65)	1 501 (55)	1 367 (50)	1 275 (47)	1 211 (45)

*Includes those continuing with drug identified as new course of treatment.

TABLE III—*Types of change of treatment among patients changing between classes of drug within six months of initiating new course of treatment. Figures are numbers (percentage) of patients*

		Present drug				
Class of former drug	Total changing treatment	Diuretic	β Blocker	Calcium channel blocker	Angiotensin converting enzyme inhibitor	Drug combination
Diuretic	2 545 (49)	2 616*	1 015 (40)	660 (26)	756 (30)	114 (4)
β Blocker	1 556 (43)	828 (53)	2 059*	395 (25)	234 (15)	99 (7)
Calcium channel blocker	1 680 (52)	788 (47)	452 (27)	1 564*	308 (18)	132 (8)
Angiotensin converting enzyme inhibitor	1 296 (48)	713 (55)	209 (16)	272 (21)	1 417*	102 (8)

This does not include 93 patients whose former antihypertensive treatment was a combination of drugs. Numbers under each medication class are not mutually exclusive due to use of drugs in >1 class.
*Those continuing on treatment in that class.

TABLE IV—*Differences in use of health care in those who discontinued and changed or continued treatment for hypertension*

Drug class	Mean (SE) No of contacts with general practitioner in first six months		Mean (SE) No of prescriptions for antihypertensive drugs in first six months	
	Continuers	Discontinuers	Continuers	Discontinuers
Diuretics	2·2 (0·08)	1·7 (0·04)	4·7 (0·13)	6·6 (0·08)
β blockers	2·6 (0·08)	1·5 (0·05)	4·8 (0·14)	6·0 (0·08)
Calcium channel blockers	2·7 (0·08)	1·9 (0·05)	5·6 (0·15)	7·1 (0·09)
Angiotensin converting enzyme inhibitors	2·9 (0·09)	2·3 (0·05)	5·2 (0·17)	7·2 (0·1)

than patients taking either diuretics (5·7) or β blockers (5·4).

There were consistently more visits to general practitioners in the group continuing treatment across drug classes. Continuers had a significantly greater number of contacts with their doctors (2·6) during the six months after start of treatment than those changing or discontinuing (1·8). Patients starting treatment with angiotensin converting enzyme inhibitors had significantly more contacts (2·5) than patients starting with either diuretics or β blockers (both 1·8) or calcium channel blockers (2·1).

Discussion

Our main finding was the consistent decrease in the frequency of continuation after initiation of the four most commonly prescribed classes of antihypertensive drugs. Although each displayed a slightly different pattern over the course of six months, initiation of all four classes resulted in a similar incidence of continuation at six months of between 40% and 50%.

The reasons for the relatively poor continuation are unclear. The findings are consistent with those of McCombs *et al* in California[12] but not of the older Medicare population in the United States.[11] This latter study, however, did not examine patterns of continuous use over time.

Many physicians recommend an orderly step by step approach to the treatment of hypertension, with diuretics and β blockers preferred over calcium channel blockers or angiotensin converting enzyme inhibitors[13] except for in specific populations (for example, hypertensive patients with compromised ventricular functioning).[14] In practice, however, there seems to be a more chaotic pattern, and, although 40% of those taking diuretics did change to a β blocker, the next treatment was also often noted to be the other drugs (table II).

As the patients represented here were not primarily newly diagnosed, the results do not seem to reflect a possible resistance to being newly diagnosed as ill with an asymptomatic but chronic hypertensive disease.[15] Such patients might attribute any adverse signs or symptoms to drugs rather than to the diagnosis itself.

Key messages

- Suboptimal compliance with treatment for hypertension can lead to further complications
- Up to half of new courses of treatment studied were changed or discontinued treatment over six months
- Patients were more likely to switch to a different class of drug rather than to a different drug within the same class
- The recommended step by step treatment for hypertension did not seem to be followed
- Research on why so many patients discontinue treatment is indicated

The finding of reduced numbers of visits for those changing or discontinuing treatment is not surprising if a proportion of the patients are avoiding treatment or have borderline hypertension not requiring continued treatment, or both. This would be consistent with the findings of Psaty *et al*, in which lower systolic blood pressure at baseline predicted discontinuance of antihypertensive drugs at one year's follow up.[11] In contrast those switching from the angiotensin converting enzyme inhibitors, and to a lesser extent from the calcium channel blockers, in the present study had higher rates of contacts with their general practitioners than those changing from diuretics or β blockers. This may suggest differences in severity of disease among those treated with the different drug classes. For example, it is likely that hypertensive patients with additional heart failure might be treated with angiotensin converting enzyme inhibitors.[13]

These results generate several questions about the possible causes of such high rates of discontinuation of treatment from newly prescribed antihypertensive drugs. To what extent are side effects of drugs of sufficient magnitude to warrant discontinuation of treatment? The greater numbers of prescriptions, on average, among patients changing or discontinuing versus those continuing treatment in the present study may suggest that the patients are terminating treatment early because of side effects rather than terminating at the end of the prescription because of poor efficacy. The overwhelming evidence in this study for changes to be interclass rather than intraclass may suggest that side effects are operative and that physicians may be deciding that drugs within the same therapeutic class will share common side effects. To study these issues prospective research of the perspectives of patients and physicians on the reasons behind the decision to discontinue the current antihypertensive treatment is warranted.

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