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Abstract

A key issue when considering antihypertensives is patient tolerability, since the goal of treatment is to ensure that patients continue using their medication in the long term. A clinical audit of prescribing of antihypertensive medication was carried out using data from a single general practice with a patient population of 10,297.

Objectives: The aim was to provide an overall picture of prescribing patterns within the practice, focussing on tolerability of specific antihypertensive drugs.

Design: The audit was retrospective, and was carried out by extracting data from the practice computer system and clinical records.

Participants: Participants were selected by searching the database using the READ code G2 for diagnosis of hypertension, with the search restricted to patients with a current 'repeat prescription' for any antihypertensive drug. A further search looked at patients newly prescribed with antihypertensive drugs within an 18-month period.

Main outcome measures: The data were analysed for each drug looking at therapy discontinuation rates due to adverse effects, as a means of comparing tolerability.

Results: Within the calcium channel blocker class, lercanidipine was found to be better tolerated than amlodipine, with a much lower incidence of discontinuation due to ankle oedema. An intractable cough was the principal reason for discontinuing treatment with an angiotensin converting enzyme inhibitor, and within this class, lisinopril was considerably better tolerated than perindopril and ramipril.

Conclusion: In practice, certain antihypertensive agents within the same class are better tolerated than others by patients. This is an important consideration in our attempts to achieve therapeutic objectives in the long term.

Introduction

The British Hypertension Society and the National Institute for Health and Clinical Excellence (BHS/NICE) issued consolidated guidelines for the treatment of standard hypertension in 2006,[1] which contain updates to earlier guidance for the pharmacological management of hypertension.[2] These new guidelines recommend that use of beta-blockers should be reviewed with the result that other antihypertensive medication such as angiotensin converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs) and calcium channel blockers (CCBs) are preferred as first- and second-line therapies. Thiazide diuretics are recommended for patients aged more than 55 years or people of Afro-Caribbean origin as first-line therapy, or as a secondary add-on therapy for primary treatment with ACE inhibitors/ARBs or CCBs for all patients.[1]

An important issue when considering antihypertensive medication is patient tolerability because the goal of treatment is to ensure that patients remain using their medication in the long term. As with all long-term therapy any factor that may affect compliance, such as adverse reactions, is particularly pertinent. This is even more relevant in the treatment of essential hypertension because most patients do not have obvious troubling symptoms. Crucially, the BHS/NICE guidelines do not explicitly state which drugs within each class should be prescribed. Although the major classes of antihypertensives are associated with common class adverse-effect profiles, for example cough with ACE inhitors[3] or vasodilation and oedema with CCBs,[4] there may be subtle but clinically important differences between the different drugs within a class.

In the blood pressure clinic at the Village Green general practice in North Tyneside we have been following BHS/NICE guidelines.[1] We have introduced a system of assessment whereby pharmacological treatment is started with either an ACE inhibitor or an ARB principally for patients aged less than 55 years, or a CCB or a thiazide diuretic principally for patients aged more than 55 years.

Aims

To carry out a retrospective audit of data from a single general practice to review the prescribing of drugs in the management of hypertension. The objectives of this audit are:

- Examine prescribing of antihypertensives by a general practice.
- Identify the main agents used in newly diagnosed hypertensive patients.
- Assess tolerability of these agents, specifically focusing on individual drugs within each of the four main classes recommended by the consolidated BHS/NICE guidelines.[1]

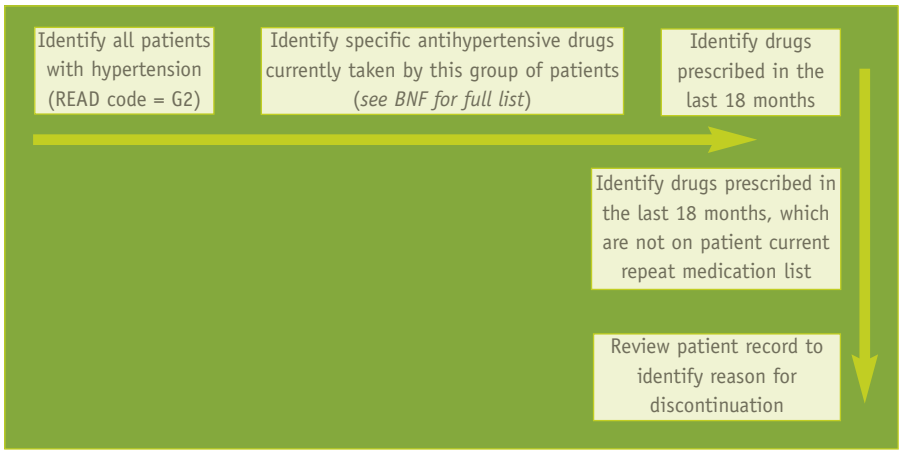


Figure 1. *Flow chart showing search strategies for data collection.*

Methods

The practice computer system and clinical records (EMIS PCS) were used to initially identify the prevalence of hypertension, stratified by age and sex, and to quantify the practice's compliance with the three hypertension quality and outcome framework (QoF) markers, which are:

- number of patients on the hypertension register
- blood pressure (BP) check in the last nine months
- BP less than 150/90mm/Hg.

A structured search of the practice electronic records using the hypertension READ code (G2) and specific drug names was undertaken to assess the number of patients prescribed treatment with antihypertensive drugs as illustrated in Figure 1. Data were exported into a separate database for further analysis, which enabled assessment of the number of patients on each treatment and particular treatment combinations. Data extraction was restricted to patients with a current repeat medication for any antihypertensive drug.

A further search was undertaken of new prescriptions for specific ACE inhibitors, ARBs, CCBs and thiazide diuretics and whether these were continued or discontinued. Searches were restricted to identifying patients who had started taking an antihypertensive agent in the previous 18 months and the starting dose was recorded. Where the antihypertensive agents were discontinued we ascertained the reasons, such as adverse events from the patients' medical records.

Results

1. Patients diagnosed with hypertension

Age and sex distribution

Analysis by READ code identified 1,507 patients with hypertension (14.6% of practice population of 10,297) with the greatest proportion being found in the 60–79 year age range for both sexes, as shown in Figure 2. The QoF data identified that of these patients, 90% (1,355 patients) had undergone a BP check within the previous nine months, and 72% (1,090 patients) had a BP measurement below the QoF audit standard of 150/90mmHg.

2. Current prescriptions for patients with hypertension

Of the hypertensive population of 1,507 patients, 9.1% (137 patients) were not prescribed antihypertensive medication. In total 2,657 medicines were prescribed to the remaining 90.9% of the hypertensive population (1370 patients). The distribution of antihypertensive medicines, by class, prescribed to these patients is shown in Table 1. These patients received one or more medicines as follows: one drug, 35.5% (487 patients); two drugs, 41% (559 patients); three drugs, 18% (252 patients); four drugs, 5% (65 patients); five drugs, 0.4% (six patients); six drugs, 0.1% (one patient). Thus the largest proportion (41%; 559 patients) were taking two antihypertensive drugs.

3. Patients who started and discontinued antihypertensive agents during the previous 18 months

Over the 18-month period 453 patients were started on treatment with an antihypertensive drug from at least one of the four classes recommended in the BHS/NICE guidelines (ie. at least one of a CCB, ACE inhibitor, ARB or thiazide

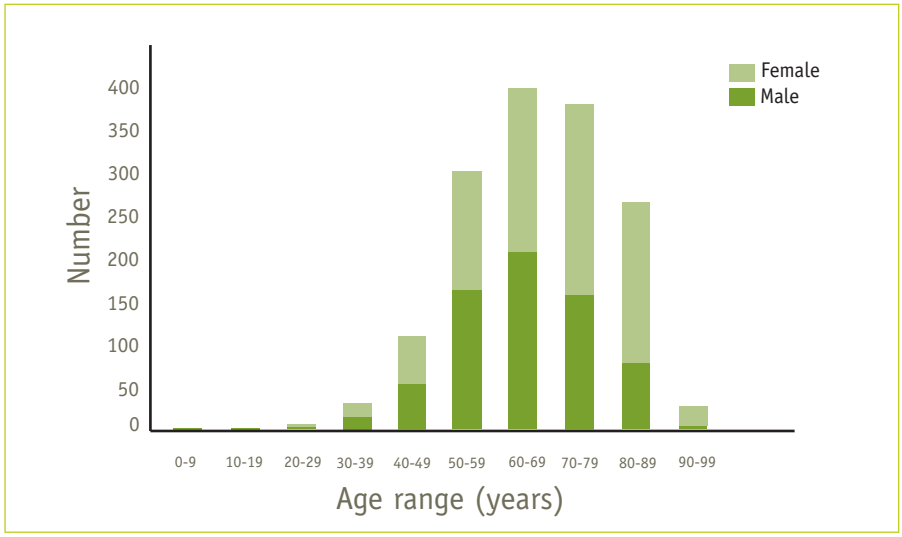


Figure 2. *Age and sex distribution of practice patients with hypertension (n = 1,507).*

Table 1. Antihypertensive drugs prescribed for patients with hypertension who currently received medication

Antihypertensive drug class	Proportion of patients receiving drug	Number of medicines
Angiotensin converting enzyme (ACE) inhibitors	26%	690
Thiazide diuretics	25%	659
Calcium channel blockers (CCBs)	19%	512
Beta blockers	19%	499
Angiotensin receptor blockers (ARBs)	7%	194
Others	4%	103
Total	**100%**	**2657**

diuretic).[1] All patients were started on treatment using a dose defined in practice protocols, as detailed in Table 2. The number of newly prescribed antihypertensive agents and the number of these that were discontinued during the previous 18-month period are also shown in Table 2. CCBs were the most frequently prescribed antihypertensive drug for newly diagnosed patients with hypertension (43%), followed by ACE inhibitors (33%), thiazide diuretics (13%), and ARBs (10%) during the 18-month period (Table 2).

Of the four classes of antihypertensive drugs recommended by the BHS/NICE guidelines, CCBs were also the most commonly discontinued for patients newly diagnosed with hypertension (29% of patients who were newly prescribed CCBs), followed by thiazide diuretics (19%), ACE inhibitors (17%) and ARBs (11%).

Table 2. Antihypertensives newly prescribed to patients over an 18 month period, and percentage of patients who discontinued treatment

Antihypertensive class/drug	Protocol-defined starting dose (mg)	Number*	Proportion discontinued**
Perindopril	2	80	21% (17)
Lisinopril	10	65	11% (7)
Ramipril	1.25	5	20% (1)
Imidapril	5	1	0% (0)
Total ACE inhibitors		**(33%) 151**	**17% (25)**
Losartan	50	6	0% (0)
Valsartan	80	7	14% (1)
Candesartan	8	7	0% (0)
Irbesartan	150	24	17% (4)
Total ARBs		**(10%) 44**	**11% (5)**
Amlodipine	5	67	46% (31)
Lercanidipine	10	127	21% (26)
Nifedipine	20	3	0% (0)
Total CCBs		**(43%) 197**	**29% (57)**
Bendroflumethiazide	2.5	61	20% (12)
Total thiazide diuretics		**(13%) 61**	**20% (12)**
Total patients		**(100%) 453**	

*Number of patients started on drug in previous 18 months (percentage of all drugs prescribed)
**Proportion of the patients started who subsequently discontinued their treatment

4. Reasons that newly started antihypertensives were discontinued

The reasons given in the clinical records for discontinuation of treatment are shown in Table 3. In some cases, the reason given was not attributable to tolerability of antihypertensives. In some cases data were not available — ie. no specific reason was documented. For some patients, therapy was discontinued because a satisfactory level of BP control had been achieved and the drug was no longer required (normotensive). No precise information was available in situations where a drug was discontinued during a hospital admission. However, some patients discontinued because of specific adverse effects, namely oedema, cough, changes in electrolyte balance, and other adverse effects as shown in Table 3.

Discussion

Comparison of data from our practice with statistical data from the EPIC GP database[5] and the UK Government Office of National Statistics (ONS)[6] showed a typical distribution of age and sex demographics for the incidence of hypertension in a UK clinical practice population (illustrated in Figure 2). The data presented in this audit show that there was variation in discontinuation rates of newly prescribed antihypertensive agents, and in reasons given for discontinuation of individual drugs within the same class.

ACE inhibitors

Our audit showed that among all three ACE inhibitors studied, lisinopril was considerably better tolerated than the other two ACE inhibitors, with a discontinuation rate due to adverse effects of 9.1% (6 of 65 patients), in comparison to 16.4% (13 of 80 patients) for perindopril and 20.0% for ramipril. The most common reason for ACE inhibitor discontinuation was an intractable cough. The incidence of discontinuation due to cough was markedly lower with lisinopril (4.6%; 3 of 65 patients) than perindopril (13.8%, 11 of 80 patients) and ramipril (20.0%; one of five patients). However, it should be noted that the population size newly started on ramipril was small (five patients).

Table 3. Reasons for discontinuation of antihypertensive medication they had been newly prescribed within an 18-month period

Reason for discontinuation	CCB		ACE inhibitor			TD
	Amlodipine	Lercanidipine	Lisinopril	Perindopril	Ramipril	Bendroflumethiazide
Oedema (ankle/leg/foot)	14.9% (10)	3.9% (5)	0% (0)	0% (0)	0% (0)	0% (0)
Cough	0% (0)	0% (0)	4.6% (3)	13.8% (11)	20% (1)	0% (0)
Changes in electrolyte balance	0% (0)	0% (0)	1.5% (1)	1.3% (1)	0% (0)	4.9% (3)
Other adverse effects	10.5% (7)	7.2% (9)	3.0% (2)	1.3% (1)	0% (0)	4.8% (3)
Total due to specific adverse effects	**25.4% (17)**	**11.1% (14)**	**9.1% (6)**	**16.4% (13)**	**20% (1)**	**9.7% (6)**
Hospital discontinuation	17.9% (12)	2.4% (3)	1.5% (1)	1.3% (1)	0% (0)	1.6% (1)
Normotensive	0% (0)	6.3% (8)	0% (0)	0% (0)	0% (0)	0% (0)
No reason documented	3.0% (2)	0.8% (1)	0% (0)	3.8% (3)	0% (0)	8.2% (5)
Overall total discontinued	**46.3% (31)**	**20.5% (26)**	**10.8% (7)**	**21.3% (17)**	**20.0% (1)**	**19.7% (12)**
Total patients started on drug	**67**	**127**	**65**	**80**	**5**	**61**

Reasons for patients discontinuing specific antihypertensive drugs that they had been newly prescribed within an 18-month period were extracted from patients' clinical notes. Data are shown for specific drugs from each of the three most commonly prescribed classes (CCB = calcium channel blocker; ACE inhibitor = angiotensin converting enzyme inhibitor; TD = thiazide diuretic). Rates of discontinuation for each reason are expressed as a percentage of the total number of patients started on each specific drug. Numbers of patients are shown in parentheses.

Calcium channel blockers

CCBs were the most commonly prescribed class of drug to patients newly diagnosed with hypertension. We compared the two most widely-used drugs within this class, namely amlodipine and lercanidipine, among patients newly diagnosed with hypertension in our practice, for therapy discontinuation rates and the underlying reasons. Adverse effects resulted in discontinuation in 25.4% of patients taking amlodipine (17 of 67 patients) compared with 11.1% (14 of 127 patients) taking lercanidipine — representing 2.3-fold fewer patients who stopped taking lercanidipine. This clearly demonstrates that lercanidipine was considerably better tolerated than amlodipine in our practice patients.

In examining the reasons given for discontinuation of CCBs, we uncovered a marked difference between amlodipine and lercanidipine. Although a range of specific adverse effects were reported as reasons for CCB discontinuation (such as nausea, dermal irritation, hot legs and dizziness), the majority of these were experienced by only a low proportion of patients. However, ankle oedema was cited as the reason for discontinuation by the greatest proportion of patients for both of the CCBs studied. It was given as the reason for discontinuation by 14.9% of patients who were newly prescribed amlodipine (10 of the total 67 patients) compared with 3.9% who were newly prescribed lercanidipine (5 of 127 patients). This 3.8-fold lower incidence of ankle oedema cited as a reason for discontinuing lercanidipine compared with amlodipine is a key finding of our study and is in accord with previous studies that have shown ankle oedema to be an issue with many CCBs.[4,7,8]

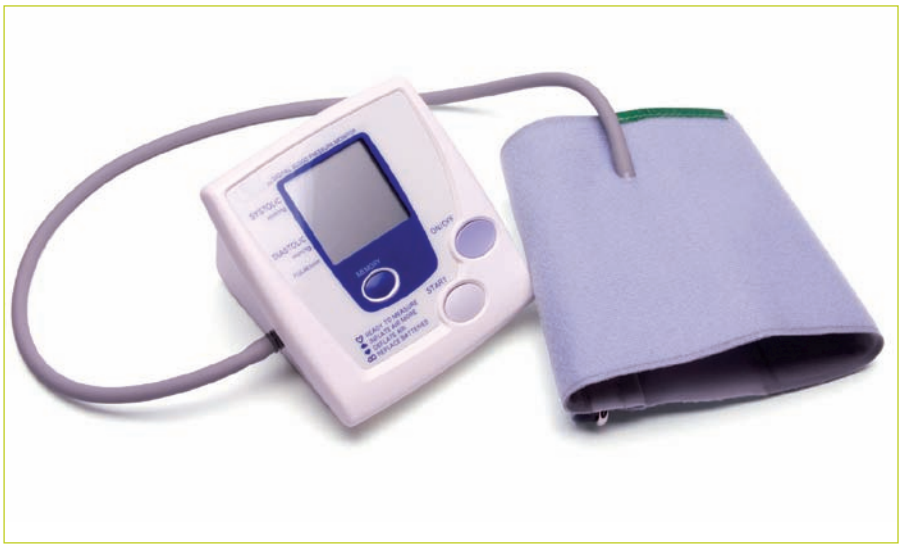
Goals in treating hypertension

Recent updates to NICE clinical guidelines will inevitably lead to a change in prescribing patterns of different classes of antihypertensive drugs, with increases in the use of CCBs, ACE inhibitors, ARBs and thiazide-type diuretics.[1] When newly starting a patient on an antihypertensive drug, two essential goals are achieving an acceptable level of BP control and ensuring that the patient is able to continue using the drug over a prolonged period. Tolerability is therefore a key factor in selecting the most appropriate medication, since troubling adverse reactions may reduce compliance, particularly given that essential hypertension is frequently asymptomatic.

Our retrospective audit provides valuable data on tolerability of the four main classes of antihypertensives specified in the updated NICE guidelines,[1] and shows clinically important distinctions between specific drugs within these classes. The audit suggest that use of lercanidipine in preference to amlodipine at our practice, could result in fewer treatment discontinuations, particularly with respect to ankle oedema. This in turn may result in improved compliance and patient outcomes. Our data also indicate that perindopril is associated with a high frequency of cough compared to lisinopril, and so lisinopril use in preference to perindopril may result in fewer discontinuations. The key message from this audit is that in practice certain antihypertensives within the same class are better tolerated by patients than others. It is important to consider these when making prescribing decisions because they can impact upon long-term therapeutic objectives.

Polypharmacy and patient compliance

The data from this audit raise a number of interesting points, and highlight areas which merit further investigation. For example, the majority (64%) of our hypertensive patient population who were prescribed medication (883 of 1370) took more than one antihypertensive with 41% of these taking two drugs (559 patients). These figures raise the questions of whether polypharmacy aids patient care, and what



affect it may have on patient compliance, which might be worthy of future study. An ideal antihypertensive drug regimen should provide patients with medication that is easy to take, ensuring that it is used long-term without the patient experiencing troubling adverse effects, while achieving an acceptable level of BP control.

Study limitations and future work

It is important to recognise the limitations of our study. This was a retrospective audit from a single clinical practice, which showed the outcomes of following our standard clinical procedures. However, by conducting a prospective audit, it would be possible to standardise various key factors. These include controlling for age and sex of patients; the length of time for which they have been diagnosed as hypertensive; whether they are affected by other illnesses; and stratifying patients by antihypertensive drugs. Furthermore, it would be of interest to compare our audit data with that of other general practices to identify any potential areas for future investigation.

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