Oversight: a retrospective study of biochemical monitoring in patients beginning antihypertensive drug treatment in primary care

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Guidelines recommend biochemical monitoring of patients treated with antihypertensive agents, although there is little primary evidence for these recommendations.

WHAT THIS STUDY ADDS

- Patients treated for hypertension in general practice often have no biochemical tests before, or in the 6 months after, starting drug treatment.

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AIMS

Guidelines on the management of hypertension have recommended baseline testing of serum electrolyte and creatinine concentrations before treatment since the 1990s. We wished to examine the extent of laboratory monitoring in patients with newly diagnosed hypertension and newly treated with antihypertensive drugs.

METHODS

We carried out a retrospective analysis of 74 096 patients in the General Practice Research Database (GPRD) aged 18 years and older with newly diagnosed hypertension and prescribed a single antihypertensive agent. We determined the number of patients with a laboratory test for serum electrolyte and creatinine (or urea) concentrations prior to the first antihypertensive drug prescription and in the 6 months after and patient factors associated with subsequent monitoring.

RESULTS

Thirty-four thousand nine hundred and forty-seven patients (47%) had at least one biochemical test in the 12 months prior to beginning antihypertensive treatment, and 26 946 (36%) had at least one biochemical monitoring test in the 6 months after beginning antihypertensive treatment. Thirteen thousand five hundred and four (18%) had both baseline and monitoring tests. Baseline tests were normal in 11 671 patients (86%), of whom 10 213 (88%) had normal tests at first monitoring. Monitoring was significantly more likely in patients treated with ACE inhibitors than thiazides (adjusted OR 1.90; 95% CI 1.80, 2.00), older patients (adjusted OR 1.23; 95% CI 1.11, 1.36) [individuals aged 80–89 years compared with <40 years], and patients with diabetes mellitus (adjusted OR 2.03; 95% CI 1.91, 2.16).

CONCLUSION

Biochemical testing at baseline and monitoring after starting treatment is often omitted in newly diagnosed hypertensive patients. When both are tested, one in eight normal results becomes abnormal.

Introduction

Monitoring is a process of checking a system that changes with time, in order to guide changes to the system that will maintain it or improve it [1]. Monitoring of drug treatment can have several effects: improved adherence, better selection of drug therapy and better titration of treatment [2]. Monitoring can also, perhaps most importantly, identify potential adverse reactions to treatment.

Guidelines recommend that patients with newly diagnosed hypertension should have baseline biochemical tests of renal function and electrolyte concentrations before treatment, monitored again 1 week and 1 month after starting treatment, and at intervals following any dose changes [3–5]. These recommendations are based on the supposition that pre-treatment testing can discover rare secondary causes of hypertension and identify contraindications to treatment, and that post-treatment biochemical monitoring can identify changes related to adverse drug reactions (ADRs) before they have caused serious or permanent effects, and so avert them [1, 6]. However, primary evidence for the recommendations is lacking. A questionnaire survey suggested that general practitioners (GPs) often neglect biochemical monitoring [7].

We examined the extent and effect of laboratory monitoring in a cohort of patients in UK general practice with newly diagnosed hypertension and newly treated with antihypertensive drugs.

Methods

The study protocol was approved by the Independent Scientific Advisory Committee for Medicines and Healthcare products Regulatory Agency (MHRA) database research.

Data source

The GPRD is an automated medical record database that contains anonymized longitudinal records from over 460 general practices with approximately 3.5 million patients in the UK [8]. The computerized information includes demographic data, clinical history, laboratory tests and drug prescriptions. The age and sex distributions of patients in the database are representative of those of the UK general population [9], and its completeness and validity are well documented [10, 11].

Study population

We derived the study cohort from the full GPRD dataset. Selection into the cohort required patients to be 18 years or older and to have a Read or OXMIS (Oxford Medical Information System) code compatible with a diagnosis of essential hypertension, or three blood pressure measurements of greater than 160/100 mmHg (the threshold for initiation of antihypertensive treatment without other cardiovascular

risk factors at the time) on or within 365 days prior to the first prescription for a single antihypertensive drug (index date), or both. We then identified all patients in the cohort by selecting patients with a first prescription between 1 January 2000 and 31 December 2003 for a single antihypertensive drug from seven defined drug classes: angiotensin-converting enzyme inhibitors (ACE inhibitor), angiotensin-II (AT-II) receptor antagonists, calcium-channel blockers, thiazide diuretics, α -adrenoceptor blocking drugs (α -blockers), β -adrenoceptor blocking drugs (β -adrenoceptor antagonists), and loop or aldosterone antagonist/potassium-sparing diuretics. We defined this as a first prescription of antihypertensive drug therapy provided there had been no antihypertensive drug therapy in the preceding year.

Using methods described previously [12], we identified 1148 women who could have been pregnant between 1 January 2000 and 31 December 2003 and excluded them from the analysis because of potential differences in their clinical course, treatment and monitoring.

Assessment of covariates

Smoking status and body mass index (BMI) were used if recorded within 5 years of the index date and systolic blood pressure and diastolic blood pressure were used if recorded in the year prior to the index date. We used the British Hypertension Society guidelines to classify the severity of hypertension [13]. Socio-economic status was inferred from the social deprivation scores assigned to the postcode of each general practice using the Index of Multiple Deprivation.

Assessment of laboratory measurements

We defined baseline biochemical testing as a measurement of one or more of serum creatinine, urea, potassium or sodium concentrations between 365 days prior to the index date and 2 days following it, to allow for any delays in the uploading of laboratory test results to the general practice (prior to 2003 the majority of laboratory data entry was not automated). Follow-up monitoring was defined as a measurement of one or more of the serum concentrations between 3 days and 6 months after the index date. Where both urea and creatinine concentration were measured, we used only the latter in the analyses.

Assessment of abnormal values

Abnormal laboratory values at baseline and first follow-up monitoring test were determined using standardized reference ranges provided with the tests. Standardized reference ranges were 56–122 $\mu\text{mol}\cdot\text{l}^{-1}$ for creatinine, 2.6–7.2 $\text{mmol}\cdot\text{l}^{-1}$ for urea, 135–146 $\text{mmol}\cdot\text{l}^{-1}$ for sodium, and 3.5–5.1 $\text{mmol}\cdot\text{l}^{-1}$ for potassium. Where such ranges were missing, they were inferred from the patient's gender and age. Values outside the reference ranges for sodium or potassium concentrations, and above the reference ranges for creatinine or urea, were classified as abnormal.

Table 1

Baseline patient characteristics

Characteristic	Total (n = 74 096)	Any baseline testing (n = 34 947)	No baseline testing (n = 39 149)	P value
Male, n (%)	35 345 (47.7)	17 394 (49.8)	17 951 (45.9)	<0.0005
Mean age (years) (SD)	61.1 (12.8)	60.9 (12.5)	61.2 (13.1)	0.024
BMI (kg m ⁻²)				
Mean (SD)	28.5 (5.4)	28.5 (5.4)	28.4 (5.4)	0.0002
Underweight, n (%)	654 (0.9)	312 (0.9)	342 (0.9)	<0.0005†
Normal, n (%)	16 039 (21.6)	7 485 (21.4)	8 554 (21.8)	
Overweight, n (%)	25 392 (34.3)	12 426 (35.6)	12 966 (33.1)	
Obese, n (%)	20 606 (27.8)	10 115 (28.9)	10 491 (26.7)	
Smoking, n (%)				
Ever	33 118 (44.7)	16 256 (46.5)	16 862 (43.1)	<0.0005
Never	38 166 (51.5)	17 679 (50.6)	20 487 (52.3)	
Presence of diabetes mellitus, n (%)	6 437 (8.7)	4 565 (13.1)	1 872 (4.8)	<0.0005
SES quintile, n (%)				
0 (least deprived)	15 660 (21.1)	6 892 (19.7)	8 768 (22.4)	<0.0005†
1	13 205 (17.8)	6 575 (18.8)	6 630 (16.9)	
2	15 005 (20.3)	6 886 (19.7)	8 119 (20.7)	
3	14 154 (19.1)	6 034 (17.3)	8 120 (20.7)	
4 (most deprived)	16 072 (21.7)	8 560 (24.5)	7 512 (19.2)	
Blood pressure (mmHg) (SD)				
Mean systolic blood pressure	170.9 (20.1)	170.5 (19.5)	171.3 (20.6)	<0.0005
Mean diastolic blood pressure	97.2 (11.3)	97.0 (11.3)	97.5 (11.4)	<0.0005
Drug class initiated, n (%)				
ACE inhibitor	11 245 (15.2)	6 609 (18.9)	4 636 (11.8)	<0.0005
α-blocker	753 (1.0)	342 (1.0)	411 (1.1)	0.335
AT-II receptor antagonist	1 630 (2.2)	769 (2.2)	861 (2.2)	0.991
β-adrenoceptor antagonist	17 977 (24.3)	7 899 (22.6)	10 078 (25.7)	<0.0005
Calcium channel blocker	5 651 (7.6)	2 574 (7.4)	3 077 (7.9)	0.011
Loop or K-sparing diuretic	416 (0.6)	181 (0.5)	235 (0.6)	0.134
Thiazide diuretic	35 653 (48.1)	16 302 (46.7)	19 351 (49.4)	<0.0005
Combination preparation	771 (1.0)	271 (0.8)	500 (1.3)	<0.0005

P values presented are from the *t*-test for continuous variables and the Chi-squared test for binary variables. P values from the Chi-squared test for trend are indicated with a †. Some data for BMI and smoking status were missing.

Statistical analysis

We used Microsoft Access® to arrange data, and Stata® 10.0 to perform statistical analyses. We determined the relationships between patient variables and the probability of any monitoring within 6 months in univariable analyses, and then entered baseline characteristics that were statistically significant at the *P* < 0.05 level or were biologically plausible into a multivariable logistic regression model using backwards stepwise variable selection. Gender was forced into the model *a priori*.

Results

We identified 74 096 patients, 48% male, who were first prescribed a single antihypertensive agent between January 2000 and December 2003 (Table 1). Patients most often began treatment with a thiazide diuretic (48.1%), followed by β-adrenoceptor antagonists (24.3%), and ACE inhibitors (15.2%). A greater proportion of patients aged below 40 years was treated with an ACE inhibitor. Thirty-four thousand nine hundred and forty-seven patients (47.2%) had one or more laboratory tests in the year prior

to the index date. The majority of baseline testing (57%) occurred 1 month before the start of treatment, and the modal time interval was 0 (the day of the initiation of antihypertensive therapy). Patients with baseline testing were more likely to be male, younger, have diabetes mellitus or smoke tobacco.

In the 6 months after the date of first prescription 26 946 (36.4%) patients had at least one biochemical measurement. Of those patients who were monitored at least once within 6 months, 21 194 (78.7%) had all three tests of potassium, sodium and renal function and 1557 (5.8%) of those who were monitored had only one test. In patients with at least one follow-up test, 27% of patients had more than one follow-up monitoring test (Table 2). The mean number of repeat monitoring tests in those who had at least one test was 1.4 (Table 3). Patients started with an ACE inhibitor or a potassium-sparing diuretic had a greater mean number of follow-up monitoring tests. In 13 504/74 096 patients (18.2%), both baseline testing and follow-up monitoring were performed.

The median interval between first prescription and first biochemical monitoring was 35 days, and the modal interval was 7 days. The median interval between first pre-

Table 2

Summary for serum creatinine, concentration (micromoles per litre) and urea, sodium, and potassium concentrations (millimoles per litre) measured at baseline and in the 6 months after the initiation of treatment

	Creatinine		Urea		Urea (when creatinine missing)		Sodium		Potassium	
	Baseline testing	Monitoring 6 months after index date	Baseline testing	Monitoring 6 months after index date	Baseline testing	Monitoring 6 months after index date	Baseline testing	Monitoring 6 months after index date	Baseline testing	Monitoring 6 months after index date
Number of patients with at least one test, <i>n</i> (%)	33 976 (45.9)	26 282 (35.4)	28 331 (38.2)	22 456 (30.3)	794 (1.1)	524 (0.7)	31 615 (42.7)	24 853 (33.5)	31 404 (42.4)	24 804 (33.5)
Mean value	89.2	91.3	5.1	5.5	5.6	6.1	140.1	139.5	4.4	4.3
Median value	87.0	89.0	5.0	5.3	5.4	5.8	140.0	140.0	4.4	4.3
Range of values	23–905	25–1107	0.3–68	0.2–70	2.1–20	1.7–70	117–174	116–152	2.4–11.8	2.2–9.9
Number of patients who were monitored with										
one follow-up test, <i>n</i> (%)	–	19 146 (72.8)	–	16 441 (73.2)	–	469 (89.5)	–	18 116 (72.9)	–	18 154 (73.2)
two follow-up tests, <i>n</i> (%)	–	5 093 (19.4)	–	4 314 (19.2)	–	46 (8.8)	–	4 825 (19.4)	–	4 759 (19.2)
three follow-up tests, <i>n</i> (%)	–	1 384 (5.3)	–	1 157 (5.2)	–	5 (1.0)	–	1 296 (5.2)	–	1 293 (5.2)
four follow-up tests, <i>n</i> (%)	–	428 (1.6)	–	360 (1.6)	–	1 (0.2)	–	405 (1.6)	–	390 (1.6)
≥ five follow-up tests, <i>n</i> (%)	–	231 (0.9)	–	184 (0.8)	–	3 (0.6)	–	211 (0.8)	–	208 (0.8)
Abnormal test, <i>n</i> (%)	1 369 (4.0)	1 587 (6.0)	2 913 (10.3)	3 495 (15.6)	93 (11.7)	98 (18.7)	1 096 (3.5)	1 483 (6.0)	1 839 (5.9)	2 058 (8.3)

scription and first subsequent GP consultation was 23 days, and the modal interval was 28 days (Figure 1).

One or more test results were abnormal for 4 078/34 947 (11.7%) patients at baseline, and 4 775/26 946 (17.7%) patients at first monitoring. The distribution of abnormal tests before and after the initiation of antihypertensive treatment is presented in Figure 2. The proportion of patients with an abnormal creatinine value (4% at baseline to 6% at first follow-up monitoring) and with an abnormal urea value (10% at baseline to 16% at first monitoring) increased (Table 2). Similar increases in the proportion of patients with abnormal tests at baseline and first follow-up monitoring were seen with the sodium (4% to 6%) and potassium tests (6% to 8%). In the subset of 13 504 patients who had both baseline tests and at least one monitoring test, the proportion of abnormal results increased from 14% to 18% with treatment. Of the 11 671 patients with normal results at baseline, 1 458 (12.5%) developed abnormal results at first monitoring. Only 14 patients had a recorded baseline potassium value of less than 3 mmol·l⁻¹, of whom 8 (57%) had a follow-up serum potassium test. Eighty-five patients had a baseline creatinine value of greater than 200 µmol l⁻¹, of whom 50 (59%) had a subsequent creatinine measurement.

The percentage of patients who had biochemical follow-up monitoring in the first 6 months of treatment increased with time, from 25.6% in patients whose first prescription was in 2000 to 46.7% in patients whose first prescription was in 2003.

Logistic regression model

The patient factors associated with monitoring are shown in Table 4. Older patients, those with pre-existing diabetes, patients started on ACE inhibitors at baseline, and those with a first antihypertensive prescription in 2003 were more likely to be monitored at least once after starting antihypertensive treatment. In the multivariable model, monitoring was significantly associated with increasing age, the presence of diabetes, first-line antihypertensive therapy with ACE inhibitors and year of first prescription. Monitoring was also significantly associated with baseline testing and socio-economic status, being least likely for those of intermediate status.

Discussion

In a large cohort of patients with newly diagnosed hypertension, most patients began treatment with either thiazide diuretics or β-adrenoceptor antagonists, consistent with contemporaneous guidelines [14] and as previously demonstrated in the UK [15]. Only 34 947 patients (47%) had any baseline biochemical test in the 12 months prior to beginning antihypertensive treatment. A minority (36%) of our cohort had follow-up laboratory monitoring in the 6 months after the initiation of drug therapy. This compares

Table 3

Number of laboratory tests in the 6 months after first prescription by drug class in those patients who had at least one test (*n*, number of patients with at least one test)

	Creatinine			Urea			Sodium			Potassium		
	<i>n</i>	Mean (median)	Range	<i>n</i>	Mean (median)	Range	<i>n</i>	Mean (median)	Range	<i>n</i>	Mean (median)	Range
ACE inhibitor	5 962	1.56 (1)	1–9	4 887	1.56 (1)	1–9	5 542	1.55 (1)	1–9	5 540	1.55 (1)	1–9
α-blocker	213	1.37 (1)	1–8	172	1.36 (1)	1–6	196	1.33 (1)	1–5	195	1.32 (1)	1–5
AT-II receptor antagonist	564	1.31 (1)	1–7	474	1.29 (1)	1–5	528	1.31 (1)	1–7	525	1.31 (1)	1–7
β-adrenoceptor antagonist	5 298	1.31 (1)	1–15	4 526	1.30 (1)	1–15	5 071	1.31 (1)	1–15	5 055	1.31 (1)	1–15
Calcium channel blocker	1 734	1.38 (1)	1–12	1 500	1.38 (1)	1–12	1 625	1.37 (1)	1–12	1 631	1.37 (1)	1–12
Loop or K-sparing diuretic	146	1.62 (1)	1–8	115	1.44 (1)	1–8	133	1.56 (1)	1–8	129	1.57 (1)	1–8
Thiazide diuretic	12 167	1.35 (1)	1–14	10 617	1.34 (1)	1–9	11 566	1.35 (1)	1–14	11 541	1.35 (1)	1–14
Combination preparation	198	1.29 (1)	1–8	165	1.30 (1)	1–8	192	1.29 (1)	1–8	188	1.30 (1)	1–8
Total	26 282	1.40 (1)	1–15	22 456	1.38 (1)	1–15	24 853	1.39 (1)	1–15	24 804	1.38 (1)	1–15

Figure 1

Time to first monitoring and first GP consultation in the 6 months after the first antihypertensive prescription (index date). GP consultation (—); any biochemical monitoring(—)

with similar poor rates of follow-up reported in other studies of antihypertensive drugs [16–19] and in other drugs such as statins [20, 21], thiazolidinediones [22] and allopurinol [23]. Half the cohort had a GP consultation within 24 days of starting treatment, so the lack of monitoring was likely not to be due to non-attendance but because only a small proportion of patients was monitored. We found older patients and those with diabetes mellitus were more likely to have either baseline testing or follow-up monitoring, which is consistent with the results of other smaller studies [16, 19].

The use of the GPRD allowed for the examination of real-life data on monitoring by UK GPs. Our work is, we believe, the first to look at monitoring in a range of antihypertensive medications in UK general practice. Although we have shown some similarities to previous studies, the results from prior work is of limited relevance to UK primary care as such research has been restricted to specific drug classes or to data from health maintenance organizations, where monitoring is often protocol-driven.

We used standardized reference ranges to define abnormality and identified that as many as one in eight

Figure 2

Distribution of any baseline test or any follow-up monitoring test in the 4 weeks before and after the first antihypertensive prescription (index date). Total number of tests (■); number of abnormal tests (■)

patients will have an abnormal baseline test, although many of these abnormalities may be clinically insignificant. Given that 5% of the normal population will have a result outside the reference range, and 2.5% will have results above normal, the expected rate of abnormal creatinine, potassium or sodium results as we defined them was $[1 - (0.975 \times 0.95 \times 0.95) = 0.12]$, that is, 12%. This implies that the observed rate of abnormal results at baseline is no different in antihypertensive-treated patients from normal subjects.

According to a questionnaire survey, a minority of European GPs (17%) routinely request the laboratory tests recommended to assess hypertensive patients [24]. Absence of baseline testing is inconsistent with standard guidelines. Hypertension guidelines have, for more than 15 years, stated that the measurement of serum electrolyte and urea or creatinine concentrations is 'essential' [25]. Simple baseline investigations allow the detection of some causes of secondary hypertension, associated cardiovascular risk factors, evidence of target organ damage, and co-morbid diseases, all of which can influence treatment decisions. Absence of baseline testing also makes changes in renal function and electrolyte concentrations more difficult to assess.

It has been recommended that all hypertensive patients given an ACE inhibitor should have their renal function measured before and after 1 week of treatment [4]. This is because a rise in previously normal serum creatinine concentration of $\geq 30\%$ after starting treatment with an ACE inhibitor may suggest renovascular disease. Few

patients had both baseline testing and subsequent monitoring, depriving their doctors of the opportunity to assess intra-individual changes within the reference range. Even for those patients treated with an ACE inhibitor, only 38% had both baseline testing and any follow-up monitoring. In patients who did have at least one follow-up monitoring test, we found that less than a third of patients did not have a second follow-up test. This limits the ability of GPs to judge sequential changes in serum concentrations.

A trade-off exists between monitoring too frequently and not enough. Too frequent monitoring may identify short-term changes in renal function, which may lead to the inappropriate cessation of antihypertensive therapy to the detriment of blood pressure control. Too few monitoring tests would fail to identify significant adverse effects of treatment.

The proportion of patients monitored after starting treatment increased over the 4 year period that we examined. This improvement was similar to the pattern demonstrated in the proportion of patients with a record for weight and smoking, and may reflect a general improvement in standards in general practice [26], or in the electronic recording of test results, or in the way guidelines are implemented.

Although patients treated with diuretic drugs and those acting on the angiotensin system were more likely to be monitored than those treated with drugs such as calcium antagonists that have fewer biochemical adverse effects, many patients treated with drugs with a potential to cause biochemical harm went unmonitored. The odds of

Table 4

Logistic regression model of any monitoring in 6 months following first prescription (*n* is the number of patients who exhibited the characteristic from *N*, the total population assessed for this characteristic)

Characteristic	<i>n/N</i>	Unadjusted OR 95% CI		<i>P</i> -value	Adjusted OR* 95% CI		<i>P</i> value
Gender							
Female	13 768/38 751	1			1		
Male	13 178/35 345	1.08	1.05, 1.11	<0.0005	1.00	0.97, 1.03	0.955
Age (years)							
<40	1 122/3 492	1			1		
40–49	3 599/10 388	1.12	1.03, 1.22	0.007	1.08	0.99, 1.18	0.086
50–59	7 118/20 360	1.14	1.05, 1.23	0.001	1.13	1.04, 1.23	0.004
60–69	7 214/19 312	1.26	1.17, 1.36	<0.0005	1.22	1.12, 1.33	<0.0005
70–79	5 830/14 971	1.35	1.25, 1.46	<0.0005	1.33	1.22, 1.44	<0.0005
80–89	1 936/5 190	1.26	1.15, 1.38	<0.0005	1.23	1.11, 1.36	<0.0005
90–100	127/383	1.04	0.84, 1.31	0.683	1.19	0.92, 1.53	0.191
Smoking status							
Never	13 710/38 166	1			1		
Ever	12 537/33 118	1.09	1.05, 1.12	<0.0005	1.06	1.03, 1.10	<0.0005
Diabetes status							
No	23 271/67 659	1			1		
Yes	3 675/6 437	2.54	2.41, 2.67	<0.0005	2.03	1.91, 2.16	<0.0005
SES quintile							
0 (least deprived)	5 823/15 660	1			1		
1	5 011/13 205	1.03	0.98, 1.08	0.182	1.03	0.98, 1.09	0.206
2	5 318/15 005	0.93	0.89, 0.97	0.002	0.90	0.85, 0.94	<0.0005
3	4 760/14 154	0.86	0.82, 0.90	<0.0005	0.86	0.82, 0.91	<0.0005
4	6 034/16 072	1.02	0.97, 1.06	0.508	1.03	0.98, 1.08	0.232
Hypertension							
Normal or mild	4 147/11 373	1			1		
Moderate	10 836/30 241	0.97	0.93, 1.02	0.232	1.09	1.03, 1.14	0.001
Severe	11 098/28 529	1.27	1.13, 1.45	<0.0005	1.34	1.27, 1.40	<0.0005
BMI							
Underweight	243/654	1.01	0.86, 1.19	0.860	–		
Normal	5 905/16 039	1			–		
Overweight	9 334/25 392	1.00	0.96, 1.04	0.907	–		
Obese	7 840/20 606	1.05	1.00, 1.10	0.016	–		
Drug therapy							
Thiazide diuretic	12 492/35 653	1			1		
ACE inhibitor	6 049/11 245	2.16	2.07, 2.25	<0.0005	1.90	1.80, 2.00	<0.0005
α-blocker	220/753	0.71	0.65, 0.90	0.001	0.76	0.64, 0.90	<0.0005
AT-II receptor antagonist	576/1 630	1.01	0.91, 1.12	0.804	0.97	0.87, 1.09	0.641
β-adrenoceptor antagonist	5 441/17 977	0.80	0.77, 0.84	<0.0005	0.86	0.82, 0.90	<0.0005
Calcium channel blocker	1 808/5 651	0.87	0.82, 0.93	<0.0005	0.89	0.83, 0.94	<0.0005
Loop or K-sparing diuretic	149/416	1.03	0.85, 1.27	0.740	1.29	1.03, 1.62	0.029
Combination preparation	211/771	0.70	0.60, 0.82	<0.0005	0.73	0.62, 0.87	<0.0005
Any baseline testing							
No	13 442/39 149	1			1		
Yes	13 504/34 947	1.20	1.17, 1.24	<0.0005	0.91	0.88, 0.94	<0.0005
Year of first antihypertensive prescription							
2000	4 251/16 508	1			1		
2001	5 742/17 927	1.36	1.30, 1.44	<0.0005	1.33	1.27, 1.40	<0.0005
2002	7 543/19 532	1.81	1.73, 1.90	<0.0005	1.76	1.68, 1.85	<0.0005
2003	9 410/20 129	2.53	2.42, 2.65	<0.0005	2.51	2.39, 2.63	<0.0005

*Adjusted for gender, age, smoking status, diabetes, socio-economic status (SES), hypertension, drug therapy, any baseline testing and year of first antihypertensive prescription.

being monitored were not significantly influenced by gender but were increased in older patients and those with diabetes, even when adjustment was made for other factors.

Limitations

Coding for hypertension may not have been consistent across general practices. We may also have missed patients

treated with antihypertensive agents at blood pressures lower than we defined. We relied on records of issued prescriptions, but we did not know whether the patient collected, or took, the medicine. We might therefore have over-estimated the number of patients taking medicines, and so over-estimated the 'non-monitoring' rate [27].

The general practice records may not have captured all the monitoring in secondary care. However, most patients

with hypertension, especially those with 'simple' hypertension requiring therapy with a single agent, are treated in the community. The GP who initiated treatment would usually be responsible for monitoring.

We did not include renal function at baseline as a potential predictor of subsequent monitoring in our models. That would have required a measurement of serum creatinine or urea concentration and biased the results by restricting the analyses to patients who already had a laboratory test and might be more likely to be monitored.

Our data were collected during a time of change in United Kingdom general practice that resulted in improvements in the management of hypertension as judged by the increased recording of blood pressure measurements [28]. The proportion who had at least one monitoring test increased during the survey period. Although we cannot be sure our data reflect current practice in biochemical monitoring, the differences in monitoring between drug class and among patients are likely to persist.

Finally, we considered results abnormal if they fell outside the reference range for serum sodium or potassium concentrations or above the upper limit of the reference range for serum creatinine or urea concentrations. In practice, clinicians do not act on every abnormal result, and the threshold values for action will often be some way outside the defined reference range. Therefore, there will be fewer patients with results sufficiently abnormal to warrant clinical intervention than with abnormal results as we defined them. We were able to allow for this to some extent in estimating renal function. Serum urea concentration was often outside the reference range, but where both urea and creatinine concentrations were measured, we used only the latter.

Guidelines recommend baseline and post-treatment biochemical testing of patients with hypertension. Judged by these standards, current practice represents an oversight ('an accidental omission; a mistake made through inadvertence or negligence') rather than oversight ('the action of overseeing something; supervision, inspection') [29]. The elderly, those with diabetes, and those on ACE inhibitors were more likely to be monitored. Few patients had both baseline tests and subsequent monitoring, limiting the ability of GPs to assess changes in serum biochemical measurements for each patient. Future studies are necessary in order to determine whether more frequent or more assiduous biochemical monitoring in hypertensive patients in general practice would reduce harm from adverse drug reactions. Results from such studies would help to devise rational monitoring schemes.

Competing interests

There are no competing interests to declare.

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