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ORIGINAL ARTICLE

An observational study of the medical events associated with clinician-initiated changes in treatment for essential hypertension

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We report a retrospective longitudinal observational study of co-morbidities and medical events associated with initiations and changes in antihypertensive therapy in 475 hypertensive patients of a large general practice. The median follow-up time was 7.0 years for males and 7.2 years for females. The data showed a low frequency of appropriate lifestyle recommendations (<30%), a gender-bias in lifestyle recommendations against women and that more than half of all patients' blood pressure (BP) was uncontrolled when last seen. Nearly half of all patients had co-morbidities relevant to essential hypertension (EHT) at first treatment for EHT and more than 11% of patients had more than one such co-morbidity. Whilst there was an increase in usage of ACE inhibitors and calcium channel blockers (CCB) as first treatment for EHT, there was also evidence that the existence of relevant co-morbidities rationally accounted for the majority of that increase. There were 5176 medical events relevant to EHT associated with change of drug or dosage treatment of EHT and the study provided evidence that the occurrence of such relevant medical events can rationally account for the majority of changes to EHT treatment. The study suggests that whilst general practitioners may fail to promote lifestyle changes to their patients with EHT, there is evidence that, when examined in sufficient detail, general practitioners' decisions to initiate changes in antihypertensive therapy are in keeping with the evidence base.
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Introduction

Much attention has been paid to developing guidelines,[1] disease management models, protocols and decision-trees in the treatment of essential hypertension (EHT). Such devices ignore the impact of broader socio-cultural factors on patient and health provider behaviours.[1,2] They tend to be disease-centred whilst general practitioners (GPs) tend to be patient-centred, as do their patients.

Recent criticism has questioned the disease-centred approach: 'Clinical trials—the fount from which most of our most sacred evidence springs—are largely unhelpful, because they are posing the wrong sorts of questions'.[3] It has even been suggested that 'being a good physician involves far more than an appeal to best evidence' and that 'a reliance on evidence alone forces us to stop too soon in our clinical reasoning'.[4]

We set out to discover what medical events were associated with GPs' decision-making in patients with EHT in the milieu of everyday practice. We retrospectively reviewed case records in fine detail to discover what clinically relevant information had been recorded by GPs and related it to recorded changes in antihypertensive regimen.

Such an observational view provides perspective, creating an evidence-base for understanding broader factors influencing, often paradoxically, outcomes of attempts to reduce morbidity and mortality associated with EHT.[5] It is a baseline for measuring effectiveness of interventions on prescriber and patient behaviours. From local or national health promotion to continuing medical education strategies, from new drugs to protocols and policy; observational data, despite its acknowledged vagaries, can inform decision-making.

We report evidence from a retrospective observational study of EHT treatment over more than 20 years in general practice which supports the hypoth-

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esis that GPs make rational decisions about antihypertensive therapy which are in line with best practice when sufficient information about the individual patient is considered.

Patients and methods

The setting was the Family Practice Unit (FPU) of Adelaide University's Department of General Practice, serving some 10 000 families. Functioning as a general practice, it has a database of patients held on computer and paper records, conforming to standards recommended by the Royal Australian College of General Practitioners (RACGP) beginning 1983. With few exceptions, the original record system is complete for more than 25 years.

The pattern of practice at FPU is similar to that of the National Morbidity Study.[6] Although not a random population, there is a high degree of confidence that the practice population is representative.

In a retrospective study, we identified all the patients whose records indicated mild to moderate EHT (systolic blood pressure (SBP) $\geqslant$160 mm Hg and/or diastolic blood pressure (DBP) $\geqslant$90 mm Hg). There were 475 patients in total, suggesting that not all patients had been properly screened for EHT. Trained nurses assessed their computer and paper records.

The date of diagnosis of EHT was recorded where possible. Where unclear the first date on which EHT was recorded or treatment for EHT given was used and age, gender, SBP and DBP were recorded as well as relevant co-morbidities (identified by review of the preceding medical record). The last date the blood pressure was recorded was noted. The date of last attendance of the patient was also noted.

Every subsequent visit to the FPU when there was any alteration of the antihypertension regimen (drug or dosage) was coded, along with the blood pressure and associated relevant medical events, forming a 'drug-event list' for each patient who had received drug treatment for EHT.

Nurses worked in pairs and conferred over doubtful or ambiguous entries. Where resolution was not obtained, the coding form and the medical record were reviewed by one of the authors (GB). Where doubt remained, the coding form entry was additionally coded as unreliable (less than 0.25% of entries—their inclusion or exclusion had negligible impact on the results).

Experienced data-entry operators entered the data into a database. All drugs were recorded into the database under the name noted at each consultation (generic or brand name). During analysis, brand name drugs were 'mapped' onto their generic equivalent. Any generic drug could be included or excluded, as context required. For analysis, data were grouped into five categories representing the 'therapeutic group' (predominant mode of action) of the generic drug: thiazide diuretics (TZ), beta-adrenergic blocking agents (BB), ACE inhibitors (ACEi), calcium channel blockers (CCB) and other antihypertensive agents (Other).

Data were validated in three ways. Firstly, every change in antihypertensive regimen was confirmed to be linked to only one patient record. Secondly, patients who never received drugs were identified and their database entry confirmed. Finally, a range of maximum and minimum possible dosages for each drug was established. Exceptions were resolved by recourse to the coding form and to the clinical record. Intolerance, exacerbation of existing co-morbidities, the development of new co-morbidities and inadequate dose titration of a drug were identified. Some drugs with antihypertensive effects were specifically excluded (Table 1). Indapamide was subsequently analysed separately.

Table 1 Excluded drugs (generic)

acetazolamide
amiloride
bumetanide
clonidine
frusemide
hydralazine
indapamide
metolazone
spironolactone
triamterene

Our data are largely descriptive, being best described in tables associating categories (Tables 2–5). Where appropriate Students' *t*-test (unpaired, two-tailed, homoscedastic) and Chi-squared statistics were calculated.

Results

Mean age at intake into the study was 53.5 years for men (range 21.1–82.7) and 54.7 years (range 20.2–85.3) for women (difference NS $P = 0.31$). Mean treatment durations were males (M) 7.7 years (max 25.2) and females (F) 8.4 (max 27.6). These gender

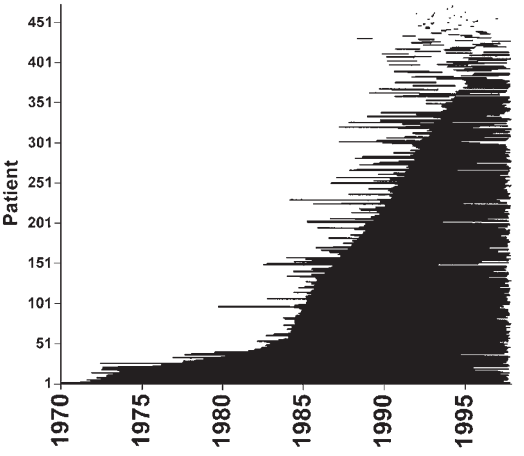

Figure 1 Patient enrolment throughout study period. Each fine horizontal line represents a patient: commencing when a patient was first seen and stopping when last seen.

differences were not significant (Students' *t*-test: $P = 0.31$ and $P = 0.22$ respectively).

These data do not describe a study population such as might be seen in a clinical trial. Figure 1 represents each of the patients in the study: illustrating its retrospectivity and observational view. It shows time passing from left to right. Each fine horizontal line represents a patient: commencing when a patient was first seen and stopping when last seen. Patient histories dating from the 1970s right through to the late 1990s are represented; some spanning the entire study period, others much less.

Of 475 patients (220 M 46.3%, 255 F 53.7%), 414 (87.2%, 186 M, 228 F) received drug treatment, and 61 (34 M 7.1% and 27 F 5.7%) did not. This difference was in keeping with the gender distribution of the intake population and was not significant ($\chi^2 = 0.31$, $P < 0.58$).

Only 140 patients (29.5%) had a record of appropriate changes in lifestyle being recommended (77 M, 63 F). Of these 140, only 67 (14.1% of study population) had a report that these recommendations were followed, in whole or part (37 M, 30 F). Lifestyle measures alone were effective in 21 (4.7%, 11 M and 10 F). In 1.1% of cases (2 M, 3 F) a drug with antihypertensive properties was prescribed anyway, for reasons other than hypertension. A gender-bias is evident in these results. Whilst males constitute the minority of the study population (46.3%), they are significantly in the majority with respect to lifestyle modification advice being recorded (57.9%, $\chi^2 = 5.99$, $P < 0.015$).

In 228 cases hypertension was unresolved (last blood pressure noted elevated (SBP $\geqslant$160 mm Hg or DBP $\geqslant$90 mm Hg, 55.1%, 108 M and 120 F). Mean ages M 57.7 years (median = 57.0, s.d. = 14.0) F 63 years (median = 63.1, s.d. = 13.0). This age difference was significant (Students' *t*-test: $P = 0.018$)

A total of 142 patients (29.9%) had relevant co-morbidities at intake into the study, 54 individuals (11.4%) having more than one. Table 2 shows these co-morbidites in decreasing frequency of occurrence.

The total number of relevant medical events in the study was 5176. Of these, 2569 (49.6%) were antihypertensive drug initiations or continuations. On 504

Table 2 Co-morbidities present at intake

Co-morbidity name	*Total*	*F*	*M*
Lipids elevated	50	24	26
Asthma/COPD	34	21	13
Diabetes type II	20	10	10
Angina	20	9	11
Gout	16	4	12
Myocardial infarction	12	2	10
Left ventricular hypertrophy	11	5	6
Dyspnoea (not asthma)	9	5	4
Impotence	7	—	7
Proteinuria	5	1	4
Libido lowered	4	2	2
Heart failure	3	2	1
Glucose intolerance	2	1	1
Diabetes type I	2	—	2
Urate/uric acid elevated	1	1	—
Total	196	87	109

Co-morbidities present at intake into study listed in order of decreasing frequency. Some patients had more than one co-morbidity: see text.

Table 3 Drug initiations by therapeutic group over 15-year period

Drug	*5-Year periods commencing*		
	1983	*1988*	*1993*
Thiazide diuretics	13	15	6
Beta blockers	63	59	25
Angiotensin converting enzyme inhibitors	0	18	27
Calcium channel blockers	2	22	19
Other antihypertensives	9	4	6
Total	87	118	83

First-ever recorded drug treatment for EHT by therapeutic group for each of three consecutive 5-year periods.

Table 4 Medical events associated with drug withdrawals in decreasing order of frequency

Medical event	*Total*	*TZ*	*BB*	*ACE*	*CCB*
Non-compliance	175	39	58	26	35
Ineffective treatment	109	15	32	27	19
Headache	63	8	17	9	19
Lethargy	58	13	30	7	5
Dizziness	53	8	15	12	14
Cough	45	1	9	33	2
Heart failure/peripheral oedema	29	9	9	1	8
Hypotension	27	9	4	5	5
Nausea	23	3	7	6	5
Angina	15	1	5	2	5
Cerebro-vascular event	15	3	4	3	2
Constipation	15	1	5	1	7
Impotence	14	3	6	4	1
Dyspnoea (not asthma)	13	1	7	2	2
Left ventricular hypertrophy	12	3	2	1	6
Libido lowered	11	1	6	3	
Lipids elevated	8	3	3	1	1
Asthma/COPD	6		5		1
Bad dreams	6		5	1	
Diabetes type II	6	1	2	1	1
Nocturia	5	2			2
Gout	5	4		1	
Proteinuria	3		1	2	
Urate/uric acid elevated	3	2			1
Myocardial infarction	3	1			1
Glucose intolerance	2	1	1		
Diabetes type I	1				
Totals	725	132	233	148	142

Medical events which were recorded by clinicians contemporaneously with a record of drug withdrawal by therapeutic group of drug changed. TZ, thiazide diuretics; BB, beta-adrenergic blocking agents; ACEi, ACE inhibitors; CCB, calcium channel blockers.

Table 5 Medical events associated with the simultaneous decrease of a drug in one therapeutic group and an increase in a drug in another therapeutic group

Drug group decreased *Drug group increased*		*TZ* *BB*	*TZ* *ACE*	*TZ* *CCB*	*BB* *TZ*	*BB* *ACE*	*BB* *CCB*	*ACE* *TZ*	*ACE* *BB*	*ACE* *CCB*	*CCB* *TZ*	*CCB* *BB*	*CCB* *ACE*
	Total	44	44	30	56	191	133	14	59	138	10	83	124
Angina	14									6		8	
Asthma/COPD	5					5							
Bad dreams	6					3	3						
Cerebro-vascular event	21		5	2	3	2	2						7
Constipation	37	3				8			8	3		5	10
Cough	63	2				2	7	3	17	32			
Diabetes type II	10			2			5					3	
Dizziness	60	2	8	2		17				14		10	7
Dyspnoea (not asthma)	42					18	9	4		3			8
Glucose intolerance	0												
Gout	18	3	3	3		3	3			3			
Headache	70		2		10	10	8		3	9		14	14
Heart failure/oedema	51				7	14	12		2	6		2	8
Hypotension	21	6		3		3	2			4			3
Impotence	20			2		9	3			3			3
Ineffective treatment	168	7	12	4	5	25	23		21	23	4	11	33
Left ventricular hypertrophy	34	3		3		10	4				4	6	4
Lethargy	79	3	6	4	7	32	15			7			5
Libido lowered	8					3	5						
Lipids elevated	16		5			6							5
Myocardial infarction	0												
Nausea	31	4				5	8		3	6		5	
Nocturia	3												3
Non-compliance	135	8	3	2	24	14	24	7	5	16	2	16	14
Proteinuria	5					2				3			
Urate/uric acid elevated	9	3		3								3	

Medical events which were recorded by clinicians contemporaneously with a record of the simultaneous decrease of a drug in one therapeutic group and an increase in a drug in another therapeutic group by therapeutic group of drugs changed. TZ, thiazide diuretics; BB, beta-adrenergic blocking agents; ACEi, ACE inhibitors; CCB, calcium channel blockers.

(9.7%) of these occasions, the SBP or DBP was uncontrolled. In total, 3111 medical events (60.1%) were relevant to antihypertensive treatment.

Practitioners' first choice of drug for EHT changed over the years covered by the study: Table 3 showing the therapeutic grouping from which practitioners' first treatment choice was made. In the first quinquennium, BB and TZ diuretics predominated. Over the next 10 years ACEi and CCB became preferred.

Of the total of 3111 relevant medical events, 725 (23.3%) were associated with cessation of a drug. They are shown in decreasing order of frequency in Table 4

Of the 3111 relevant medical events, 926 (29.8%) were associated with the simultaneous decrease of a drug in one therapeutic group and an increase in a drug in another therapeutic group. They are shown in alphabetical order in Table 5.

Discussion

Observational studies rely on records written with no knowledge of their future use. Weaknesses of such an approach are the inevitable omissions, inaccuracies, and ambiguities in clinician's recording. Intrinsic strengths of this study are that a full population of patients presenting with EHT is included. Longitudinal data are tracked on patient-by-patient basis for up to 25 years and fine granularity of medical detail is available. Every drug event recorded by clinician, every associated relevant medical event and the blood pressure at that time (where recorded by clinician) is included and medical review of inadequate dose titration occurred. Most importantly, a retrospective study avoids influencing prescribing behaviours of clinicians.

The gender-bias in lifestyle recommendations may reflect a true difference in the rate of discussion of lifestyle issues with patients but may be as a result of more males having lifestyle factors requiring modification or males requesting information about lifestyle factors more frequently. Alternatively males may be more reluctant to take drugs and be offered alternatives more frequently (consistent with the greater proportion of men remaining untreated), or there could be bias towards the recording of lifestyle information given to males.

More than half of all patients' blood pressure remained uncontrolled when last seen. However, this figure may not be as surprising as it seems. It includes patients still in the process of stabilization at the last visit recorded, patients who failed to return for follow-up and the common practice of practitioners opting for partial control of BP, 'titrating' treatment against side effects to obtain a relative reduction in risk.

There is a dramatic change in the choice of first drug for the treatment of EHT over time. Since the introduction of ACEi and CCB, these agents have come to represent the majority of initial prescribing despite evidence that uncomplicated EHT is best initially treated with TZ and/or BB. However, there were only 288 initiations of antihypertensive treatment (the remaining patients being on treatment at the start of their record) and 142 patients had one or more initial relevant co-morbidities. When co-morbidities are taken into account, the high rate of initial prescription of ACEi and CCB may simply reflect good management.

Nearly 25% of 3111 relevant medical events was associated with drug withdrawal, the pattern of those events generally demonstrating sound clinical practice. For example, five of six BB withdrawals were associated with asthma and 33 of 45 ACEi withdrawals were associated with cough and nine of the remaining 12 withdrawals for cough were of BB.

Even finer resolution of the association of events with changes in antihypertensive drug therapy is possible. Nearly one-third of relevant medical events was associated with the simultaneous increase of one antihypertensive and the decrease of another. Again, sound therapeutic principles are evident in practitioner behaviours, eg 47 of 79 instances of lethargy were associated with the reduction or withdrawal of a BB and the simultaneous initiation or increase of either an ACEi or CCB.

In conclusion, the data in Table 3 might be viewed as supporting the prevailing view that ACEi and CCB are increasingly being prescribed as first-line treatments, perhaps inappropriately. But a deeper review of relevant co-morbidities present at intake suggests that practitioners may not simply be using new drugs for old. Finally, the association of medical events with logical changes in antihypertensive therapy indicates that prescribers' behaviours generally fit well with sound clinical practice. It is not too great an extension to postulate that, were the data to include even greater detail of patients' individual medical and psycho-social circumstances, prescriber behaviour would be seen to be more rational again. We argue that it is necessary to take such a detailed view into account when formulating drug policy and prescribing protocols.

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