A prescription survey in a hospital hypertension outpatient clinic

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Aims The objective of this study was to investigate drug utilization in the management of hypertension in Hong Kong.

Methods We conducted a prescription survey to examine the use of antihypertensive drugs in a hypertension clinic in a regional hospital and the resulting expenditure incurred. The use of concurrent medications such as antidiabetic drugs and lipid-lowering agents was also examined.

Results During a 7-week study period, 530 prescriptions were collected. All except 14 patients received antihypertensive drugs with 262 (50.8%) on monotherapy and 254 (49.2%) on combination therapy. Calcium channel blocking agents and β-adrenoceptor blocking agents were the two most popular antihypertensive drugs used in both monotherapy (38% and 31%, respectively) and combination therapy (27% and 33%, respectively). Forty-nine patients (19%) received three antihypertensive drugs or more. The number of antihypertensive drugs showed a significant positive correlation with the duration of attendance at the clinic ($r = 0.88$, $P < 0.001$). Of the total 530 prescriptions, 5.6% and 10% contained antidiabetic drugs and lipid-lowering agents, respectively. Calcium channel blocking agents, angiotensin converting enzyme (ACE) inhibitors and lipid lowering agents, accounted for 82% (HK\$211 654; £1 ≈ HK\$12) of the total drug expenditure (HK\$258 115). Seventy-nine percent of the lipid lowering agents prescribed were hydroxymethylglutaryl coenzyme A (HMG CoA) reductase inhibitors. Amlodipine accounted for 26% of usage but contributed to 41% of the overall costs of calcium channel blocking agents. α_1-adrenoceptor blocking agents were only used infrequently and were the most expensive class of drugs, due to the preferred use of doxazosin rather than prazosin which is far cheaper than the former.

Conclusions In view of the use of these often costly drugs for long-term therapy, monitoring of their use and its correlation with clinical outcomes and quality of life is essential to ensure the optimal use of health care resources.

Keywords: angiotensin converting enzyme inhibitors, antihypertensive drugs, β-adrenoceptor blocking agents, calcium channel blocking agents, diuretics, prescription survey

Introduction

The beneficial effects of the optimal control of blood pressure on mortality and cardiovascular morbidity have been confirmed in epidemiological and interventional studies [1, 2]. However, due to the high prevalence of hypertension and the requirement of chronic medications, the drug treatment cost represents a major issue in health economics. In developed countries, the expenditure on antihypertensive therapy has increased sharply in recent years due to the increasing use of the newer and more expensive drugs such as calcium channel blocking agents and angiotensin converting enzyme (ACE) inhibitors [3–5]. Furthermore, due to the frequent coexistence of hypertension, diabetes mellitus and hyperlipidaemia [6], the coprescribing of these long-term medications further increases the treatment costs for these patients.

In Hong Kong, the prevalence of hypertension has been reported to be 10–15% amongst subjects of working age [7]. Here, due to the lack of a comprehensive primary health care system and health insurance policy, many patients with chronic conditions such as hypertension seek treatment in public hospital clinics where they pay a nominal fee inclusive of consultation and drug costs (HK\$60 ≈ £5). We have previously reported that over 30% of prescriptions issued at a hospital medical clinic contained antidiabetic or cardiovascular drugs or both [8]. In this study, we examined the use of antihypertensive drugs and concomitant medications in a hospital hypertension clinic and the resulting expenditure incurred.

Methods

In Hong Kong, patients attending hospital outpatient clinics receive their medications from the pharmacy located on the same site and no extra fee is charged for the medications.

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Thus, data collection in prescription surveys largely reflect the pattern of drug utilization in these health care institutions. The present study was conducted in the specialist clinic of the Prince of Wales Hospital. The latter is the regional hospital of the eastern New Territories (NT) of Hong Kong with a catchment population of over 1 million. Patients attending the hypertension clinic are referred mainly from the community or discharged from the same hospital.

Prescriptions issued from the hypertension clinic were collected consecutively during a 7-week period in 1996. Doctors were not informed of the survey to avoid possible changes in their prescribing habits. The clinic registration number, patient name, sex, age, duration of treatment, number of prescription items and treatment regimen were recorded. Since the prefix of the clinic number (e.g. 86/M1234) indicates the year when the patient first attended the clinic, the duration of follow up at the clinic was also estimated. In the case of 86/M1234, the patient would have been attending the clinic for 11 years in 1997. Antihypertensive drugs were categorized according to the British National Formulary [9]. The categories were diuretics, β-adrenoceptor blocking agents, calcium channel blocking agents, angiotensin converting enzyme (ACE) inhibitors, α_1-adrenoceptor blocking agents and centrally acting drugs (methyldopa). The unit cost of each drug was obtained from the Prince of Wales Hospital Drug Formulary [10] and the total drug cost was then calculated.

Statistical analysis

The statistical analysis was performed using the Microsoft Excel for Windows and Statistical Package for Social Science for Windows on an IBM-PC. Data are shown as mean ± s.d. or median (range) as appropriate. The Pearsons correlation analysis was used to calculate the correlation coefficient between the duration of attendance at the clinic and the number of drugs prescribed. Between group comparisons were performed using the Chi-square test, analysis of variance (ANOVA) or Student's *t*-test as appropriate. A *P* value < 0.05 (2 tailed) was considered to be significant.

Results

A total of 530 prescriptions were collected. Table 1 summarizes the information recorded from these prescriptions. All except 14 patients received antihypertensive drugs. β-adrenoceptor blocking agents (51%), calcium channel blocking agents (49%) and ACE inhibitors (27%) were the most popular drugs. There was also a significant number of patients receiving concurrent antidiabetic drugs or lipid-lowering agents. The number of antihypertensive drugs prescribed was significantly associated with the duration of attendance at the clinic ($r = 0.88$ $P < 0.05$).

There was a tendency for ACE inhibitors to be used more frequently (19.1% *vs* 15.5%) and diuretics less frequently (13.9% *vs* 16.6%) in men than women. Calcium channel blocking agents were used more frequently (36% *vs* 27.5%) and β-adrenoceptor blocking agents less often (28% *vs* 35%) in elderly patients (≥60 years).

A total of 262 patients (50.8%) were on monotherapy and 254 (49.2%) were on combination therapy. Calcium channel blocking agents (38%) and β-adrenoceptor blocking agents (31%) were the two most commonly prescribed antihypertensive drugs in monotherapy. Table 2 summarizes the pattern of use of antihypertensive drugs in patients receiving combination therapy, 19% of whom received three antihypertensive drugs or more. Calcium channel blocking agents and β-adrenoceptor blocking agents were

Number of prescriptions:	530
Male:	230
Female:	300
Age:	
Male:	54±13 years
Female:	53±12 years
% of patients over 60 years old	36%
Number of items:	2.3±1.2
Range	1–7
% of prescriptions >3 items	17%
Duration of the prescriptions (weeks):	15±5
Range	1–26
% of prescriptions with duration >16 weeks	37%
Number of prescriptions with antihypertensive drugs:	516
Patients treated with β-adrenoceptor blocking agents:	265 (51%)
Patients treated with calcium channel blocking agents:	255 (49%)
Patients treated with ACE inhibitors:	140 (27%)
Patients treated with diuretics:	126 (24%)
Patients treated with methyldopa:	18 (3.5%)
Patients treated with α_1-adrenoceptor blocking agents	13 (2.5%)
Number of patients treated with monotherapy:	262 (50.8%)
Number of patients treated with combination therapy:	254 (49.2%)
Number of patients treated with antidiabetic drugs:	29 (5.6%)
Number of patients treated with lipid lowering agents:	52 (10%)

Table 1 The details of 530 prescription collected from a hospital based hypertension clinic in Hong Kong during a 7-week study period.

Mean ± s.d.

Table 2 The patterns of use of antihypertensive drugs in patients treated with combination therapy.

	Number	
Drug classes combinations	*Total*	*% of prescriptions*
Two drugs combinations		(81)
Diuretic + methyldopa	3	1.2
β-adrenoceptor blocker + diuretic	38	14.9
β-adrenoceptor blocker + calcium channel blocker	81	32.0
β-adrenoceptor blocker + methyldopa	3	1.2
β-adrenoceptor blocker + α$_1$ -adrenoceptor blocker	4	1.5
★Calcium channel blocker + diuretic	8	3.1
Calcium channel blocker + α$_1$-adrenoceptor blocker	2	0.8
Calcium channel blocker + methyldopa	2	0.8
ACE inhibitor + diuretic	18	7.1
★ACE inhibitor + β-adrenoceptor blocker	16	6.3
ACE inhibitor + calcium channel blocker	25	9.8
ACE inhibitor + methyldopa	3	1.2
Diuretic + α$_1$-adrenoceptor blocker	2	0.8
Three drugs combinations		(18)
★β-adrenoceptor blocker + calcium channel blocker + diuretic	13	5.11
β-adrenoceptor blocker + calcium channel blocker + α$_1$-adrenoceptor blocker	1	0.4
β-adrenoceptor blocker + calcium channel blocker + methyldopa	3	1.2
Calcium channel blocker + α$_1$-adrenoceptor blocker + methyldopa	1	0.4
★ACE inhibitor + β-adrenoceptor blocker + diuretic	5	1.9
★ACE inhibitor + β-adrenoceptor blocker + calcium channel blocker	19	7.4
★ACE inhibitor + calcium channel blocker + diuretic	4	1.5
Four drugs combinations		(1)
★Diuretic + β-adrenoceptor blocker + calcium channel blocker + α$_1$-adrenoceptor blocker	1	0.4
★Diuretic + α$_1$-adrenoceptor blocker + calcium channel blocker + β-adrenoceptor blocker	2	0.7
Total	254	100

★less desirable combination.

% of prescriptions: Percentage of total prescriptions in the combination therapy.

the most popular drugs used in various combinations with other agents. The combinations were considered to be suboptimal in 26.8% of patients.

Twenty-nine patients (5.6%) were also receiving oral hypoglycaemic agents (OHA) and considered to have diabetes mellitus. In these patients, there was a tendency for calcium channel blocking agents (44.6% *vs* 30.4%) and ACE inhibitors (25.5% *vs* 16.7%) to be used more often than in patients not receiving OHA ($n = 487$). Moreover, β-adrenoceptor blocking agents (17.1% *vs* 33.2%) and diuretics (4.2% *vs* 15.7%) were used less frequently in these diabetic patients. Fifty-two patients (10%) were prescribed lipid-lowering agents and of these, the majority (79%) were given a HMG CoA reductase inhibitor. In these 52 patients, calcium channel blocking agents (37.5% *vs* 30.4%) and ACE inhibitors (20.8% *vs* 16.7%) were the preferred agents while the β-adrenoceptor blocking agents (25% *vs* 33.2%) and diuretics (12.5% *vs* 15.7%) were used less frequently than in the patients not treated with lipid lowering agents.

Table 3 summarizes the average monthly cost of prescriptions involving the various antihypertensive drug classes. Prescriptions just for diuretics were the cheapest while the use of ACE inhibitors and calcium channel blocking agents increased the treatment cost considerably especially when the duration of prescription was allowed for. Prescriptions containing α$_1$-adrenoceptor blocking agents were the most expensive, mainly due to the preferred use of doxazosin to prazosin, with the former being 20 fold higher in unit cost (doxazosin 2 mg HK\$4.00 *vs* prazosin 1 mg HK\$0.20).

The total drug expenditure in this clinic during the 7-week study period was HK\$258 115 (£21 510). Figure 1 shows the percentages of drugs used and the total drug expenditure. Compared with the β-adrenoceptor blocking agents and diuretics, the expenditure on ACE inhibitors, calcium channel blocking agents and α$_1$-adrenoceptor blocking agents were disproportionately higher in relation to their use. Metoprolol (44.8%) and atenolol (46.4%) were the two most commonly prescribed β-adrenoceptor blocking agents while the predominant ACE inhibitor used was enalapril (73%). Figure 2 shows the percentages of total prescribing and expenditure within the class of calcium channel blocking agents. Amlodipine and nifedipine (slow release) were the two main calcium channel blocking agents prescribed. Despite amlodipine only accounting for 26% of the calcium channel blockers used, it accounted for 41% of the overall expenditure on these agents.

Table 3 The expenditure, mean duration of prescribing and mean monthly cost of different classes of antihypertensive drug.

Number of prescriptions containing various antihypertensive drug type	★★Mean duration (months)	★Total expenditure (HK$)	†Mean monthly cost (HK$)
ACE inhibitors (n = 140)	3.5 ± 1.14	58 812	118 ± 54.4
β-adrenoceptor blocking agents (n = 265)	3.6 ± 1.19	24 116	24.0 ± 31.7
Calcium channel blocking agents (n = 255)	3.7 ± 1.06	100 911	113 ± 100
Diuretics (n = 126)	3.6 ± 1.21	2593	6.30 ± 5.7
α₁-adrenoceptor blocking agents (n = 13)	3.7 ± 0.93	7252	157 ± 122
Methyldopa (n = 18)	3.7 ± 1.16	1386	19.5 ± 7.74

£1 ≈ HK$12.

Mean ± s.d.

★Total expenditure due to that class of drug in the survey.

★★Mean duration of the prescriptions having that class of drug.

†Monthly cost of each prescription containing a particular class of antihypertensive drug =

$$\frac{\text{Total drug expenditure due to the antihypertensive drug class}}{\text{total number of prescriptions} \times \text{duration of prescription (months)}}$$
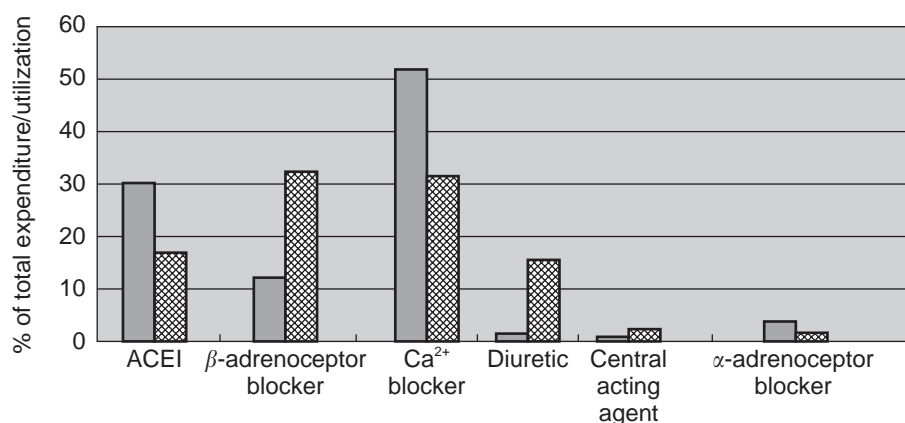
.

Figure 1 Utilization and expenditure patterns of antihypertensive drugs in this study.
▦ % of total antihypertensive drug cost
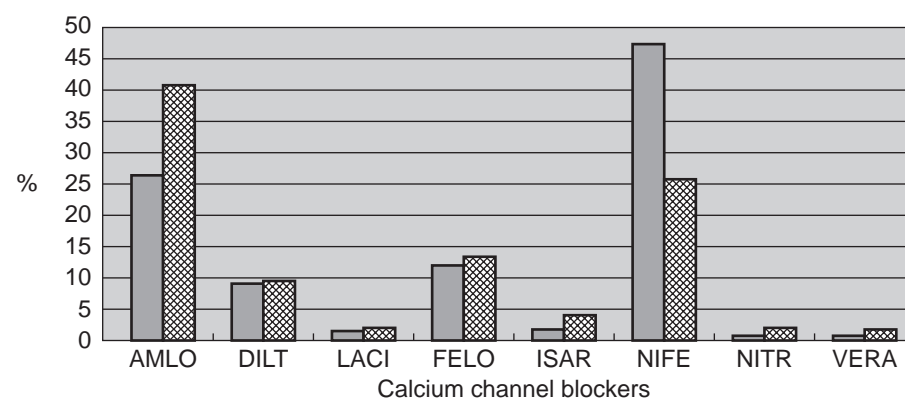▨ % of utillization

Figure 2 Percentage of utilization and expenditure for different calcium channel blockers in the study.
AMLO: Amlodipine DILT: Diltiazem
LACI: Lacidipine FELO: Felodipine
ISAR Isardipine NIFE: Nifedipine
NITR: Nitrendipine VERA: Verapamil
Rx / %(▦): Percentage of total prescribing
Exp / %(▨): Percentage of total expenditure

Discussion

Patients' characteristics and prescribing patterns

Drug utilization has been defined by the World Health Organization (WHO) as the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences [11]. Prescription surveys are one of the pharmacoepidemio-logical methods which provide a relatively unbiased picture of prescribing habits. This kind of survey allows the identification of areas of aberrant or suboptimal prescribing for further evaluation. The advantages of being able to evaluate large numbers of prescriptions cost-effectively offsets the disadvantages of not having details such as outcome indicators and patient histories. The resources required to review case notes and clinic records reliably also greatly reduces the number of patients who can be surveyed.

In this study, ACE inhibitors were preferred to diuretics in men compared with women. A higher incidence of coronary arterial disease has been reported in men [14]. In light of the putative cardioprotective effects of ACE inhibitors post myocardial infarction [15], this may account for their higher use in the male group. Another reason for this gender difference may be related to the adverse effects of diuretics on sexual dysfunction which occurs less frequently with ACE inhibitors [12, 13]. Compared with the younger patients, elderly patients (≥ 60 years) were prescribed calcium channel blocking agents more frequently and β-adrenoceptor blocking agents less frequently. Side-effects such as fatigue and postural hypotension are not uncommon in elderly patients treated with β-adrenoceptor blocking agents and older subjects appear to respond less well to such agents [16]. Furthermore, elderly patients are claimed to have a better blood pressure response to calcium channel blocking agents probably due to their low renin and salt replete state [17–19]. These various factors may contribute to the increased use of calcium channel blocking agents in the elderly population.

Monotherapy vs combination therapy

Nearly half of the patients attending this clinic received combination therapy. Although monotherapy is associated with improved patient compliance and a lower incidence of side-effects, combination therapy is often required for the optimal control of blood pressure and other cardiovascular complications. When combination therapy is required, drugs with synergistic actions are preferred enabling low dosages to be used [20]. A calcium channel blocking agent is often coadministered with a β-adrenoceptor blocking agent to counteract the tachycardia associated with the former. Similarly, the use of an ACE inhibitor may attenuate the stimulation of the renin angiotensin system by diuretic therapy. However, some combination therapies are generally considered to be less desirable such as the use of an ACE inhibitor with a β-adrenoceptor blocking agent and the combination of a calcium channel blocking agent with a thiazide diuretic. These combinations appear to have little if any additive effects in blood pressure reduction and in the case of patients treated with α_1-and/or β-adrenoceptor blocking agents, the efficacy of centrally acting adrenergic agents may be reduced [19].

In our survey, the combination of antihypertensive drugs prescribed was considered to be suboptimal in 26.8% of patients although it is possible that these combinations were prescribed for treatment of concomitant diseases rather than to control blood pressure. Nevertheless, it was not practical to retrieve the medical records to see if there were any clues to explain the prescribers' decision. Irrespective of the underlying reasons for these therapeutic regimens, in a busy clinic like the one in the present survey, doctors often have little incentive to change therapeutic regimens despite their suboptimal nature, when patients appear to be clinically stable since this will lead to more frequent clinic visits. We also found that the longer the patients had been attending the clinic, the more antihypertensive drugs were being prescribed. This finding suggests that therapy tended to be stepped up rather than down in these busy clinics which may reflect deteriorating patient compliance rather than attenuation in drug efficacy. Although treatment compliance was not assessed in this study, poor treatment compliance is well recognized amongst patients taking long-term medications especially in those on complex regimens [22].

Drug utilization and expenditure pattern

Calcium channel blocking agents and β-adrenoceptor blocking agents were the two most commonly prescribed antihypertensive agents used for both monotherapy and combination therapy. However, the former accounted for 50% of the total drug expenditure compared with 12% for the β-adrenoceptor blocking agents. Much of the expenditure on calcium channel blocking agents was also due to the high cost of amlodipine. Although this drug has been shown to be well tolerated in patients with heart failure [23], there are to date still no long-term data on clinical end points such as cardiovascular events for the calcium channel blocking agents as a therapeutic class [24]. The use of calcium channel blocking agents as a first line therapy is therefore much debated.

Similarly, ACE inhibitors were used in 17% of the prescriptions but accounted for 30% of the total expenditure. The cardio-[15] and renoprotective effects [25] of ACE inhibitors independent of blood pressure reduction have now been confirmed in some patient groups. However, unlike β-adrenoceptor blocking agents and diuretics [1, 2], long-term mortality data are also lacking for this class of agents in patients with essential hypertension.

Despite the infrequent use of α_1-adrenoceptor blocking agents in this study, the preferred usage of doxazosin to prazosin, with a 20 fold difference in terms of unit cost, has led to the disproportionately high overall expenditure due to prescriptions containing this class of agents. In Western countries, the use of diuretics and β-adrenoceptor blocking agents is declining while that of the calcium channel blocking agents and ACE inhibitors is increasing [26]. However, in view of the lack of long-term morbidity and mortality data with these newer agents in patients with essential hypertension, the cost effectiveness of this trend is still very much in question [24, 27, 28].

Hypertension, diabetes and hyperlipidaemia frequently coexist [6]. In our study, 16% of patients were receiving concurrent antidiabetic or lipid lowering agents, the latter mainly involved the HMG CoA reductase inhibitors. This class of drug accounted for 17.7% of the total drug expenditure in spite of only 6% of total drug usage. Due to their relatively neutral effects on glucose and lipid metabolism [29], calcium channel blocking agents and ACE inhibitors were the preferred antihypertensive drugs in these patients. Furthermore, due to the increased risks of complications such as proteinuria and cardiovascular diseases in these patients, the use of ACE inhibitors may have additional advantages [15, 25]. However, there is some evidence that ACE inhibitor monotherapy is relatively less efficacious in reducing blood pressure than calcium channel blocking agents in NIDDM patients who are often salt replete [30].

Since these patients were attending a 'Hypertension Outpatient Clinic', the majority were assumed to have hypertension. However, in this study, only limited patient

information such as sex and age were recorded. Hence, without reviewing the medical records and previous drug history, the rationale of the therapy could not be fully ascertained. However, as pointed out earlier, an attempt to reliably obtain this data and comprehensively, would not have been practical if the sample size was to be maintained. The coexistence of other conditions such as cardiovascular and renal complications might also influence therapeutic decisions. The effects of these treatments on blood pressure responses as well as their adverse effects were unknown. All these factors would also influence the interpretation of the expenditure incurred.

Despite these limitations, results from this drug utilization survey confirmed the preferred use of the newer and more expensive antihypertensive drugs in a hospital based clinic. Most of the drug expenditure were due to the calcium channel blocking agents, ACE inhibitors and lipid lowering agents. While the use of these expensive agents have been shown to be beneficial in certain patient groups especially those with end organ damage, the extensive use of these agents in a hypertension clinic suggest that their use might have been less judicious than they should have been. In view of the use of these medications for long-term therapy and the resulting expenditure incurred, monitoring of their use as well as their correlations with clinical outcomes and quality of life, is important to ensure optimal use of health care resources.

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