

Evaluation of anti-hypertensive drug utilisation and cost in Hospital Tengku Ampuan Afzan, Kuantan.

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ABSTRACT

Introduction: Hypertension is one of the most important risk factors for cardiovascular disease in Malaysia. The prevalence of hypertension nearly doubled over a ten-year period (1986 - 1996). This has resulted in a significant rise in its attendant cost. We aim to review the institutional anti-hypertensive use, the cost incurred and the implications on management in our local setting. **Materials and Methods:** A retrospective review of the annual cost (2006) of anti-hypertensive medications was undertaken at the Department of Pharmacy, Hospital Tengku Ampuan Afzan, a 600-bed major regional hospital on the east-coast of Malaysia. The total number of prescriptions given out and the total cost per drug is then factored to give the annual cost per drug per person in a percentage of the total annual expenditure. **Results:** The majority of patients were on either 2 (46.5%) or 3 (25.9%) anti-hypertensives. The most frequently prescribed medications were ACE Inhibitors (33.45%), Calcium channel blockers (29.63%), diuretics (16.67%) and B-blockers (13.64%). In terms of cost however, the Calcium channel blockers constituted the greatest percentage of the annual anti-hypertensive budget (63.67%) compared to ACE Inhibitors at just 20.04% of the annual expenditure. The least costly group of drugs is the diuretic making up 16.67% of the total annual prescriptions but only constituting 1.23% of the annual cost. **Conclusion:** The majority of patients were on ACE Inhibitors and/or Calcium channel blockers. This has huge monetary implications as they represent a large proportion of the annual antihypertensive allocation. There may be a need to reverse the trend in the developing world due to cost restrictions.

KEYWORDS: Hypertension, Medication, Cost.

INTRODUCTION

There is now an array of locally produced epidemiological data on the rise of hypertension prevalence in Malaysia. Over a ten-year period, there has been a doubling in its prevalence from a mere 14.4% in 1986 to 29.9% in 1997.¹ This is expected to increase further with the publication of the latest figures from the National Health and Morbidity Survey (2006). Although the data on hypertension control in the community is slightly fragmented, it does show a tiered pattern of progressively better control from the population study level (6%) to the public (26%) and private (59%) primary care clinics level.¹⁻³

The cost of hypertension to the community is two-fold; first is the actual cost of the drug and this is tied to the prevalence of hypertension in the community, and second is the cost of managing the complications associated with uncontrolled hypertension.

Studies have proven that once there is greater control of hypertension, the attendant costs associated with its complications will fall.^{4,7} In developing economies such as Malaysia where the majority of patients fall under public health care with finite annual budgets, greater emphasis should be placed on the control of hypertension.

There are several methodologies for evaluating patterns of drug use and its attendant cost.⁸ A quick and inexpensive method is a simple audit of the annual antihypertensive expenditure and the number of prescriptions given out. Data thus collected not only reflects on the prescribing habits of physicians but can also be used to assess the cost-effectiveness of the therapies used.⁸ In our study, we evaluated the total number of drug prescriptions given out in one year, the incurred expenditure and factored the two to give an annual (2006) cost per drug per person.

MATERIALS AND METHODS

The study was conducted in a medical outpatient clinic at the Hospital Tengku Ampuan Afzan, Kuantan, Malaysia. Kuantan is the capital of the east-coast Pen-

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insular Malaysia state of Pahang which has a predominantly agrarian economy. It serves a population of one and a half million people, the majority of whom are looked after in the public health care sector in view of the lack of a comprehensive medical insurance policy in Malaysia. These patients pay a nominal flat fee which covers both the cost of consultation and treatment.

The anti-hypertensive agents were classified into seven major groups; α -blockers (Prazosin), centrally acting agents (Methyldopa), diuretics (Chlorothiazide, Frusemide, Spironolactone), β -blockers (Propranolol, Metoprolol, Atenolol, Bisoprolol, Carvedilol), calcium-channel blockers (Nifedipine, Diltiazem, Amlodipine, Felodipine), Angiotensin converting enzyme (ACE) inhibitors (Captopril, Enalapril, Perindopril, Ramipril) and Angiotensin receptor (ARB) blockers (Losartan, Irbesartan, Valsartan, Telmisartan). Other drug classes such as the vasodilator Hydralazine was omitted due to its small utilisation.

The Hospital Tengku Ampuan Afzan (HTAA) Formulary was used as a reference for drug cost. The total number of medications given out and the total amount expended for each medication per annum (2006) was obtained. The British National Formulary (BNF) was used as a reference for recommended dosage regimens.⁹ The annual cost for each medication per person was then derived in the national currency, Ringgit Malaysia - RM (1 USD = 3.4 RM)

Statistical analysis

Data for continuous, closely symmetrical variables were analyzed using standard descriptive methods to estimate means \pm SD. The total number of tablets issued by the HTAA Formulary and the total cost expended was derived. The total number of tablets was then divided by the recommended daily dosage based on the BNF over 365 days (1 year) to give the average number of individual prescriptions per year (e.g. 10950 tablets \div 3 [t.i.d. dosage according to the BNF] \div 365 = 10 individual prescription per annum). From here the total cost is then divided over the number of annual individual prescription to give the cost of an individual prescription per year (e.g. RM 2,000.00 per year \div 10 = RM 200.00 per prescription per year).

RESULTS

A total of 11,644.58 prescriptions were given out for the year 2006 at a total cost of RM 2,211,589.77 (USD 1 = RM 3.4). The pattern of antihypertensive prescription by different drug classes is illustrated in Figure 1. The most commonly used antihypertensives were the Angiotensin-converting enzyme (ACE) inhibitors at 33.46% followed by the Calcium-channel blockers at 29.63%.

The annualised numbers of individual prescriptions are detailed in Table 1. This is derived by dividing the total number of tablets with the common daily dos-

age requirement based on the British National Formulary over 1 year (eg Prazosin 344,000 tablets \div 3 (t.i.d. dosing) \div 365 days = 314.15). The commonest medications to be utilised in order of frequency are Perindopril, Amlodipine, Frusemide, Metoprolol and Spironolactone, making up 68.26 % of the total number of annual prescriptions and incurring 76.24 % of the total annual budget (RM 1,686,182.91).

The proportion of each individual drug class to the annual antihypertensive budget is illustrated in Table 2. The two costliest drug classes are the Calcium-channel blockers (63.67 %) and the ACE inhibitors (20.05 %), together taking up 83.72 % of the total annual budget. When we compare the proportion of drug utilisation (annualised number of individual prescriptions - Table 1, Column 5) against the proportion of drug cost (Table 2, Column 5), it is evident that the least 'economical' or 'cost-effective' drugs are the Calcium-channel blockers. Despite only representing 29.63 % of the annual prescriptions, they take up 63.67 % of the annual antihypertensive budget. The least costly class is the diuretic which supply 16.67 % of the prescriptions but garner a mere 1.23 % of the cost. This is better illustrated in Figure 2.

We then factored the total annual cost per drug to the total annual number of prescriptions (Total annual cost \div Total annual prescription = Total annual cost per prescription i.e. the cost in RM of each drug per prescription, per year). We have ranked it in the order of most expensive to least expensive and highlighted the 5 most frequently used anti-hypertensive medications (Table 3).

This figure does not represent the true cost as it is derived from the total annual (2006) tablets given out which is then averaged over the optimal dosage regimen according to the British National Formulary and then factored against the total annual expenditure. In reality some prescriptions may differ from the optimal dosage regimen e.g. Prazosin is optimally prescribed as a t.i.d. (3 x / day) dose, however in reality patients may be on b.i.d. (2 x / day) or q.i.d. (4 x / day) doses. This will result in a difference compared to the actual per tablet cost over one year.

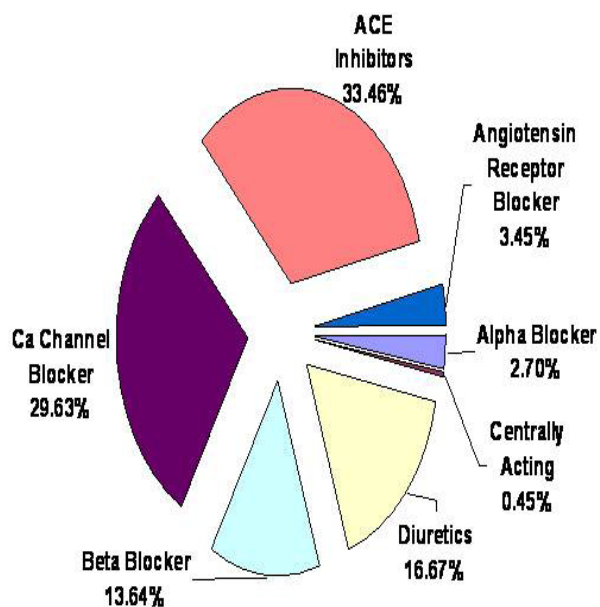


Figure 1. Pattern of anti-hypertensive prescription cost.

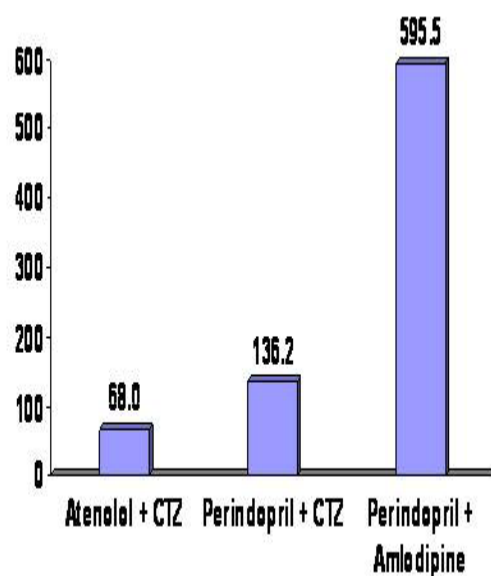


Figure 3. The difference in prices (in RM) between different drug combinations based on the annual cost per person (Table 3).

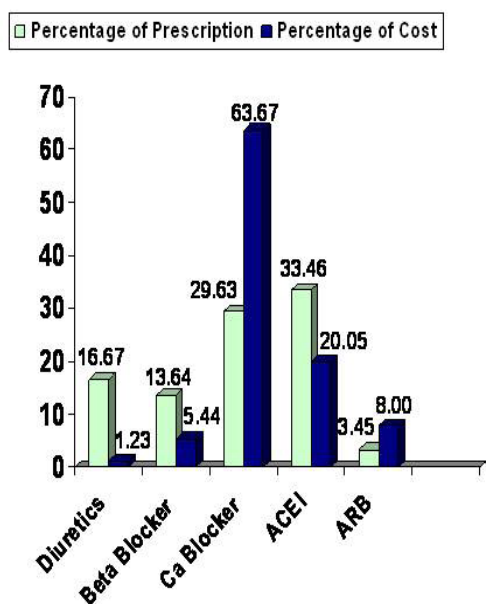


Figure 2. Comparison between the proportion of prescription and cost for the 5 most used drug classes.

Table 1. Number of individual prescriptions per annum for different drug classes

Drug Class	Dosage	Number of Tablets	Annualised Number of Individual Prescriptions		Percentage of total annual prescriptions
α-blocker					
Prazosin	1,2,5 mg	344,000		314.15	2.70%
Centrally acting					
Methyldopa	250 mg	57,000		52.05	0.45%
Diuretics					
Chlorothiazide	500mg	3,750 x 30		312.5	
Frusemide	40mg	605,000		828.76	
Spirolactone	25mg	146,000	800	1941.2	16.67%
B-blocker					
Propranolol	10,40mg	52,250		71.57	
Metoprolol	100mg	597,000		817.8	
Atenolol	100mg	217,000		594.52	
Bisoprolol	2.5,5mg	11,800		32.32	
Carvedilol	6.25,25mg	18,100	72.6	1588.81	13.64%
Ca²⁺ channel blocker					
Nifedipine	10mg	532,000		485.84	
Diltiazem	30mg	131,000		119.63	
Amlodipine	5,10mg	31,417 x 30		2618.08	
Felodipine	5,10mg	2,727 x 28	227.25	3450.8	29.63%
ACE Inhibitor					
Captopril	25mg	378,000		690.41	
Enalapril	5,10,20mg	219,550		300.75	
Perindopril	4mg	69,231 x 30		2884.62	
Ramipril	5mg	245 x 28	20.41	896.19	33.46%
Angiotensin receptor blocker					
Losartan	50	1,166 x 30			
	50+12.5	389 x 30			
	100+25	40 x 30			
Valsartan		1595 x 30		132.91	
	80	664 x 28			
	80+12.5	110 x 28			
Irbesartan		774 x 28		64.5	
	150	160 x 28			
	300	1,305 x 28			
Telmisartan		40 x 28		125.41	
	40	606 x 28			
	80	296 x 28			
	80+12.5	40 x 28			
		942 x 28		78.5	
				401.32	3.45%
				11,644.58	100.00%

Table 2. Cost of individual medications per annum for different drug classes

Drug Class	Individual Drug Cost Per Annum (RM)	Percentage of Total Cost	Class Cost Per Annum (RM)	Percentage of Total Cost
α-Blocker				
Prazosin	29,552.30	1.34%	29,552.30	1.34%
Centrally acting				
Methyldopa	5,928.57	0.27%	5,928.57	0.27%
Diuretics				
Chlorothiazide	7,837.50	0.35%		
Furosemide	10,049.05	0.45%		
Spironolactone	9,287.06	0.42%	27,173.61	1.23%
β-Blocker				
Propranolol	431.46	0.02%		
Metoprolol	78,027.90	3.53%		
Atenolol	25,519.20	1.15%		
Bisoprolol	6,834.21	0.31%		
Carvedilol	9,430.16	0.43%	120,242.93	5.44%
Ca²⁺ Channel Blocker				
Nifedipine	14,592.76	0.66%		
Diltiazem	7,231.20	0.33%		
Amlodipine	1,268,279.37	57.35%		
Felodipine	118,105.90	5.34%	1,408,209.23	63.67%
ACE Inhibitor				
Captopril	80,506.44	3.64%		
Enalapril	34,431.05	1.56%		
Perindopril	320,539.53	14.49%		
Ramipril	7,913.50	0.36%	443,390.52	20.05%
Angiotensin Receptor Blocker				
Losartan	62,463.75	2.82%		
Valsartan	29,426.10	1.33%		
Irbesartan	56,602.20	2.56%		
Telmisartan	28,600.56	1.29%	177,092.61	8.00%
			2,211,589.77	100.00%

Table 3. Annual cost per drug, per prescription

Medication	Total annual prescription	Total annual cost	Annual cost per person (RM)
Felodipine	227.25	118,105.90	519.71
Amlodipine	2618.08	1,268,279.37	484.43
Losartan	132.91	62,463.75	469.97
Valsartan	64.5	29,426.10	456.21
Irbesartan	125.41	56,602.20	451.33
Ramipril	20.41	7,913.50	387.6
Telmisartan	78.5	28,600.56	364.33
Bisoprolol	32.32	6,834.21	211.39
Carvedilol	72.6	9,430.16	129.88
Captopril	690.41	80,506.44	116.6
Enalapril	300.75	34,431.05	114.48
Methyldopa	52.05	5,928.57	113.9
Perindopril	2884.62	320,539.53	111.12
Metoprolol	817.8	78,027.90	95.41
Prazosin	314.15	29,552.30	94.07
Diltiazem	119.63	7,231.20	60.44
Atenolol	594.52	25,519.20	42.92
Nifedipine	485.84	14,592.76	30.03
Chlorothiazide	312.5	7,837.50	25.08
Fruzemide	828.76	10,049.05	12.12
Spironolactone	800	9,287.06	11.6
Propranolol	71.57	431.46	6.02

DISCUSSION

Pattern of antihypertensive prescription

In this audit, the most commonly used antihypertensives were the Angiotensin-converting enzyme inhibitors (ACEI) and the Calcium-channel blockers (CCB). This seems to reflect the prevailing trend in antihypertensive prescription patterns around the world especially that of the United States (US).⁸ In the US there has been a reduction in the use diuretics and β -blockers followed by a corresponding rise in the use of ACEI and CCBs.^{8,10} This runs contrary to current recommendations on the use of antihypertensives in hypertension.⁴

The Malaysian Clinical Practice Guidelines for the management of Hypertension which mirrors the World Health Organisation's (WHO) recommendations closely underlines the use of specific agents for particular compelling indications without which monotherapy with diuretics or β -blockers is suggested.¹¹ The US guidelines also favor the use of thiazide diuretics in uncomplicated monotherapy for hypertension.¹² The British guidelines have moved away from diuretics and incorporated the AB/CD concept in which those younger than 55 to initiate therapy with ACEI or ARB and those older than 55 to initiate CCB or diuretics.¹³

In Malaysia, the adoption of diuretics as the principle monotherapy in uncomplicated hypertension not only reflects the recommendations of other internationally available guidelines but also reflects the realities of

cost limitations in a developing economy such as ours. This has not been borne out by this study however as the data shows that the more expensive ACEI and CCBs are most widely prescribed (63.09%). There could be several reasons for this discrepancy.

Firstly, the availability of recent data on 'newer' antihypertensive agents such as ACEIs, ARBs and CCBs have added to the compelling evidence for their use in hypertension especially when associated with cardiovascular disease (CVD) prevention.¹³ Secondly, the high prevalence of CVD (20-25% of total in-hospital mortality in Malaysia) and diabetes mellitus in our population makes a compelling argument for the initiation of ACEI in these patients. Thirdly, wider use of diuretics and β -blockers could be limited by their potential adverse effects on glucose tolerance, lipid metabolism, hyperuricaemia and sexual dysfunction.¹³⁻¹⁵ Finally, the reduced human resource and limited consultation time may have induced medical practitioners to prescribe CCBs ahead of other more indicated medications in order to effectively reduce blood pressure quickly.

Implications on the cost of antihypertensives

In a recent survey on antihypertensive prescription patterns of 331 patients in the Cardiology outpatient clinic Hospital Tengku Ampuan Afzan, the mean systolic (SBP) and diastolic blood pressure (DBP) among

hypertensive patients was 139.3 ± 21.0 mmHg / 81.6 ± 10.4 mmHg and the majority of patients were on either 2 (46.5%) or 3 (25.9%) antihypertensives. This has costly repercussions as, 24.17 % of patients were on both ACEI/ARB and CCBs and a further 67.67 % were on either ACEI/ARB or CCBs in combination with other medications. A staggering 91.54 % were on either ACEI/ARB and/or CCBs.¹⁶

The cost of keeping a patient on an Amlodipine 10 mg and Perindopril 8 mg (based on the cost derived from Table 3) is RM 595.55 per annum. When compared to keeping the same patient on Perindopril 8 mg and Chlorothiazide 500 mg (RM 136.20) or Atenolol 100 mg and Chlorothiazide 500 mg (RM 68.00) the difference is almost exponential as illustrated in Figure 3. The implication is, for the same cost of keeping 1 person on an Amlodipine / Perindopril combination per annum, we can keep 8.7 persons on an Atenolol / CTZ combination or 4.4 persons on the Perindopril / CTZ combination per annum.

This is compounded by the fact that the median price ratio (MPR) for many drugs in Malaysia, including generics are higher than the International Reference Price (IRP) across all sectors. Therefore, an unskilled government worker commanding the lowest pay in the public sector would require 4.9 days of wages to pay for 1 month treatment with Amlodipine 5 mg from private retail pharmacies.¹⁷ This is offset by the fact that most patients are managed under the public health service with nominal fees for consultation, treatment and medications. However the implication on the burgeoning annual health budget will be tremendous.

Recommendations

The rationale for making a particular selection when initiating antihypertensive therapy should as in any other aspect of medicine, be evidence-based and clinically impartial. Increasingly however, the cost-related implication of treatment is having an impact on the choice made by physicians especially in resource-poor or developing economies with publicly funded health care.

Insofar as this consideration does not run contrary to the prevalent volume of evidence or guidelines, this consideration should not only be accepted but promoted to ensure optimal population coverage. When these considerations do collide, measures need to be put in place in order to limit the macroeconomic impact. In our practice, a true cost-effectiveness analysis should follow before any changes to the current CPGs are implemented. This is due to the fact that our study was conducted in a tertiary referral center and may not reflect the majority of hypertensive patients.

In conclusion, the most commonly prescribed antihypertensives in our setting are the ACEIs and CCBs which is in keeping with the prevailing international

trend. These medications however take up the majority of our annual antihypertensive budget and a true cost-effectiveness analysis need to be undertaken to ascertain the sustainability of this trend, its macroeconomic implications and whether the same level of blood pressure control could be achieved with cheaper alternatives.

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