ORIGINAL ARTICLE

Pharmacoeconomics of antihypertensive drugs prescribed in a multispecialty hospital in South India

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The main objective of this study is to evaluate the most cost-effective therapy among the different group of antihypertensive prescribed in a multispecialty hospital. According to inclusion and exclusion criteria, 104 hypertensive patients were selected. Participants were interviewed at about the demographic data. Initial clinical assessment of blood pressure (BP) and pulse rate were done. They were prescribed monotherapy either with angiotensin receptor blocker (ARB) ($n = 7$) or beta blocker (BB) ($n = 23$) or calcium channel blocker (CCB) ($n = 9$). Angiotensin converting enzyme with BB ($n = 27$), ARB with CCB ($n = 17$) and ARB with BB ($n = 21$) were prescribed in combination therapy. The cost of antihypertensive drugs was calculated using incremental cost for "per mmHg" reduction and cost for "per patient" reaching target BP. The data are analyzed using suitable statistical methods. ARB with BB shows significant reduction in BP. To maintain the targeted BP, BB is found to be cost-effective in both systolic BP (SBP) and diastolic BP (DBP) as well as in the reduction of "per mmHg" of DBP. In case of reduction of "per mmHg" of SBP ARB is cost-effective. Treatment of hypertension with BBs is cost-effective.

Key words: *Antihypertensive drugs, beta blockers, cost effectiveness*

INTRODUCTION

Hypertension and its associated clinical conditions, in particular cardiovascular disease, place a great socioeconomic burden on the society.[1] Global burden of disease study reported that in 1990 there were 5.2 million deaths from cardiovascular diseases in economically developed countries and 9.1 million deaths from the same causes in developing countries.[2,3] Cardiovascular diseases caused about 2.3 million deaths in India in the year 1990 and are projected to double by the year 2020.[1,4] Persistent hypertension is one of the risk factors for stroke, myocardial infarction, failure and arterial aneurysm, and is a leading cause of chronic kidney failure.[5] While expenditures for hypertension are on the increase in developed countries, and potentially also in the developing world, resource constraints, even in the most affluent countries, need to consider hypertension control in the context of other demands of society. The population and the high-risk approach to hypertension control also have economic consequences; these may vary in different societies and need to be assessed to ensure appropriate allocation of resources. Pharmacoeconomic studies weigh the cost of alternative drugs and drug regimens against the outcomes they achieve to guide decisions.[6-9] Hence, it is very much necessary to assess the effective therapy and costs of the available intervention strategies to reduce the risks. The purpose of this study is to evaluate the effects and pharmacoeconomics of antihypertensive drugs prescribed in a multispecialty hospital.

MATERIALS AND METHODS

Prospective study was conducted for a period of 6 months in Cardiology Department of KMC Multi Specialty Hospital, Tiruchirappalli. The protocol was approved by Institutional Ethics Committee. Informed consent was taken from patients included in the study.

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Patient inclusion criteria

1. Both gender
2. Age between 18 and 80 years
3. Patients with co-morbid conditions such as diabetes, dyslipidemia, hypothyroidism, coronary artery disease and myocardial infarction.

Patient exclusion criteria

1. Patients who are pregnant and lactating women
2. Patients with any co-morbidity such as acute emergency hypertensive patients, renal transplant patients and malignancy condition.

Methods

On the basis of inclusion and exclusion criteria, 104 patients selected during the study period. At baseline visit apart from personal characteristics, BP and pulse rate was measured. According to the disease condition different groups of drugs were prescribed to the patients. Among monotherapy angiotensin receptor blockers (ARBs), beta blockers (BBs) and calcium channel blockers (CCBs) were prescribed to 7, 23, and 9 patients, respectively. Among 104 selected patients, 65 patients were treated with two antihypertensive drugs (combination therapy). Angiotensin converting enzyme (ACE) inhibitors with BBs (ACE + BB) were prescribed to 27 patients, ARBs with CCBs (ARB + CCB) and ARBs with BBs (ARB + BB) were prescribed to 17 and 21 patients, respectively. The BP and pulse rate of all the patients were again taken at the time of reviews. The side-effects reported by the patients during their reviews were also noted. In this study, initial readings were considered as base, first review values were taken at the end of 3rd month (Review I) and the second review at the end of 6th month (Review II).

Cost analysis

In pharmacoeconomics, cost effective analysis was performed. The cost of the antihypertensive drug therapies were calculated as a function of the dosage prescribed and the price in current index of medical specialties. The overall cost of each class of antihypertensive drugs was estimated as the mean cost of that class. The cost-effectiveness was calculated by using incremental cost for per mmHg reduction and cost for per patient reaching target BP was calculated.[10] This evaluates cost-effectiveness of antihypertensive drugs in monotherapy and in combination therapy.

Data analysis

The values of systolic BP (SBP), diastolic BP (DBP) and pulse rate were evaluated by intragroup comparisons made between the values obtained under base and reviews. These values were statistically evaluated by a repeated measures analysis of variance (ANOVA). ANOVA is used to compare the (BP or pulse rate) It can compare overall longitudinal BP (variables or values) Change between two or more groups using repeated measures with addition of interaction between the groups For this purpose Dunnett's multiple comparison was used. Statistical significance was achieved with $P \leq 0.05$.

RESULTS

The 6 months study was completed by all 104 patients. Of selected 104 patients, 63 patients were male and 41 were female. The average age of the patients was 53.17 ± 1.21 years. The age groups of 41-60 years patients were more hypertensive compared with 21-40 and above 60 years. The detail characteristics of patients included in this study are given in Table 1.

Table 1: Demographic characteristics of patients involved in the study (*n*=104)

Characteristics	Number of patients
Age (in years)	
21-40	9
41-60	54
61-80	41
Gender	
Female	63
Male	41
BMI	
18.5-25 (normal)	
Male	43
Female	21
Total	64
25.1-30 (overweight)	
Male	186
Female	8
Total	24
30.1-40 (obese)	16
Male	4
Female	12
Total	16
Social habits	
No habits	95
Habits (smoker, alcoholic and both)	9
Co-morbid diseases	
Diabetes	40
Dyslipidemia	37
CAD	52
Myocardial infraction	24
Angina	8
Anemia	6
Hypothyroidism	3
Hyperuremia	1
Osteoarthritis	1
COPD	4
APD	7
Acute gastritis	2
Asthma	1

BMI: Body mass index, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, APD: Advanced pulmonary disease

The effects of monotherapy antihypertensive drugs are represented in Table 2. In monotherapy only BB showed a significant reduction of DB*P* values after 6 months. However, SBP and pulse rate values were almost stable at Review I and Review II with BB treatment. Though the other two groups of drugs ARB and CCB showed reduction of both BP and pulse in ReviewI and Review II phases, but that reductions were not significant at any stages.

The results on combination therapy with ACE + BB, ARB + CCB and ARB + BB are showed in Table 3. A significant reduction in BP (both SBP and DBP) was achieved in the treatment with ARB + BB after 6th month. The pulse rate values showed almost stable during the reviews in this group of treatment. The reductions of BP of the other two groups (ACE + BB and ARB + CCB) were not significant from base to reviews. At base level, the pulse rates of ARB + CCB group were higher than the other two combination therapy group. After 6 months, the pulse rate of ARB + CCB significantly reduced and at that stage the pulse rate of all groups became same.

Of 104 patients, 13 patients reported side-effects. This analysis revealed that one patient had headache in ARB with CCB group, two patient reported cough in BB and ACE with BB group, one patient reported increased appetite in ARB group, five patient had giddiness (two on CCB, one on ACE with BB, one on ARB with CCB, and one on ARB with BB), two patients reported vomiting on CCB group, one patient reported insomnia on BB and one patient had loose stool on ARB with CCB group [Table 4].

The cost for reduction of per mmHg of SBP and cost required to maintain the targeted SBP is given in Table 5 for monotherapy. This shows that ARB is comparatively cost-effective in the reduction of per mmHg of SBP. In order to maintain the target SBP in hypertensive patients, BB is found to be the cost effective drug to maintain a target SBP for the patients included in the study. In case of combination therapy, ARBs with BB are comparatively cost-effective in the reduction of per mmHg of SBP. In order to maintain the target SBP ARB with CCB is found to be the cost-effective drug.

The cost for reduction of per mmHg of DBP and cost required to maintain the targeted DBP is given in Table 6. This shows that BB is comparatively cost-effective in the reduction of per mmHg of DBP. In order to maintain the target DBP BB is found to be the cost-effective drug in monotherapy. In case of combination therapy, ARBs with BB are comparatively cost-effective in the reduction of per mmHg of DBP. In order to maintain the target DBP ARB with CCB is found to be the cost-effective drug for the patients included in the study.

Table 2: Effect of antihypertensive drugs on blood pressure and pulse rate (monotherapy)

Group	SBP (mmHg)				DBP (mmHg)				Pulse rate/min			
	Base	Review I	Review II	% mean change between base and review	Base	Review I	Review II	% mean change between base and review	Base	Review I	Review II	% mean change between base and review
ARB (*n*=7)	138.60±4.04	146.40±10.39	128.60±4.04	7.21	84.29±2.02	82.86±2.85	80.00±0	5.08	72.00±1.06	72.57±1.49	70.00±0	2.77
BB (*n*=23)	125.70±2.16	125.70±3.00	124.80±1.76	0.71	81.74±1.26	81.74±1.73	76.00±0.99*	7.02	71.17±0.50	70.90±0.51	71.52±0.72	−0.49
CCB (*n*=9)	134.00±5.03	142.00±4.00	132.20±4.90	1.34	82.22±2.22	87.78±3.20	80.00±1.66	2.70	73.78±1.68	72.67±0.94	71.78±1.12	2.71

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, ARB: Angiotensin receptor blocker, BB: Beta blocker, CCB: Calcium channel blocker

DISCUSSION

Hypertensive patients are high in the age between 41 and 60 years in this study. The same finding was also reported

Table 3: Effect of antihypertensive drugs on blood pressure and pulse rate (combination therapy)

Group	SBP (mmHg)				DBP (mmHg)				Pulse rate/min			
	Base	Review I	Review II	% mean change between base and review	Base	Review I	Review II	% mean change between base and review	Base	Review I	Review II	% mean change between base and review
ACE+BB (*n*=27)	137.00±3.45	133.30±3.24	128.50±2.04	6.20	83.70±1.52	82.96±1.17	80.37±0.37	3.97	70.74±0.34	70.48±0.33	70.44±0.66	0.42
ARB+CCB (*n*=17)	132.40±4.73	127.60±4.73	121.20±3.03	8.61	82.94±2.05	78.82±2.25	77.65±1.06	6.37	73.41±1.40	71.88±0.84	70.24*±0.23	4.31
ARB+BB (*n*=21)	144.30±5.99	136.20±4.22	130.00*±2.07	9.90	95.24±7.02	84.29±1.03	81.43±0.78*	14.50	71.14±0.76	72.29±0.83	70.00±0.13	1.60

Data presented are mean±SE. Analysis of data was done by one-way ANOVA by Dunnett's multiple comparison test. This comparison is done between base and review values. *Significant $P>0.05$. ARB: Angiotensin receptor blocker, BB: Beta blocker, CCB: Calcium channel blocker, ACE: Angiotensin converting enzyme, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SE: Standard error

Table 4: Side effects of different antihypertensive drug therapies (*n*=104)

Side effects	ARB (*n*=7)	CCB (*n*=9)	BB (*n*=23)	ACE+ BB (*n*=27)	ARB+ CCB (*n*=17)	ARB+ BB (*n*=21)
Headache	0	0	0	0	1	0
Cough	0	0	1	1	0	0
Increased appetite	1	0	0	0	0	0
Giddiness	0	2	0	1	1	1
Vomiting	0	2	0	0	0	0
Insomnia	0	0	1	0	0	0
Loose stool	0	0	0	0	0	1

ARB: Angiotensin receptor blocker, BB: Beta blocker, CCB: Calcium channel blocker, ACE: Angiotensin converting enzyme

by Sur *et al*., 2010.[11] Male patients are affected more than females by hypertension. The same results are also reported by By *et al*., 2010.[12,13] Normal BMI patients are more likely to have hypertension, which is similar to the result of clinical study reported by Ifeoma L *et al*., 2011[17] Obesity is a risk factor for hypertension, especially in female. The same results are also reported by Sur *et al*., 2010.[11] No impact on incidence of hypertension with social habits in my study. There is an association between cardiovascular disease, diabetes and dyslipidemia. The results obtained similar to earlier work done by Xavier *et al*., 2004.[18] From this study it is found that side effects were more with CCB compared to other monotherapy and combination therapy. In case of monotherapy antihypertensive drugs, BBs are more prescribed compared with ARB and CCB. In case of combination therapy antihypertensive drugs, ARB with BB are more prescribed compared with ACE inhibitor with BB and ARB with CCB. ARB is found to be more effective in the reduction of SBP compared with CCB and BB. BB is found to be more effective in the reduction of DBP compared with ARB and CCB. In case of combination therapy of antihypertensive drugs, ARB with BB are more effective in reduction of SBP and DBP compared to ACE inhibitor with BB and ARB with CCB.[14]

In pharmacoeconomic study, among the monotherapy and combination therapy ARB shows cost effective in the reduction of per mmHg reduction of SBP, BB shows cost-effective in order to maintain the target SBP, BB shows cost-effective in the reduction of per mmHg reduction of DBP and BB shows cost-effective in order to maintain the target DBP.[15,16]

CONCLUSION

Angiotensin receptor blocker with BB shows significant reduction in BP. ARB shows cost-effective in the reduction of per mmHg reduction of SBP and BB shows cost-effective in order to maintain the target SBP. BB shows cost-effective in the reduction of per mmHg reduction of DBP and BB shows cost effective in order to maintain the target DBP.

Table 5: Cost effectiveness of antihypertensive drugs based on SBP

Drug	Half yearly cost (Rs.)	Average reduction (mmHg)	Percentage of patients with target SBP	Cost/average reduction (Rs.)	Cost/target SBP (Rs.)
ARB (*n*=7)	881.36	10.00	43	88.13	20.49
BB (*n*=23)	391.92	0.86	56	455.72	6.99
CCB (*n*=9)	360.64	2.22	22	162.45	16.39
ACE+BB (*n*=27)	1251.20	8.15	52	153.52	24.06
ARB+CCB (*n*=17)	1230.96	11.17	65	110.20	24.06
ARB+BB (*n*=21)	1293.52	14.28	38	90.58	34.04

ARB: Angiotensin receptor blocker, BB: Beta blocker, CCB: Calcium channel blocker, ACE: Angiotensin converting enzyme, SBP: Systolic blood pressure

Table 6: Cost effectiveness of antihypertensive drugs based on DBP

Drug	Half yearly cost (Rs.)	Average reduction (mmHg)	Percentage of patients with target DBP	Cost/average reduction (Rs.)	Cost/target DBP (Rs.)
ARB (*n*=7)	881.36	4.28	100.00	205.92	8.81
BB (*n*=23)	391.92	5.73	100.0	68.39	3.91
CCB (*n*=9)	360.64	3.33	80.00	108.30	4.50
ACE+BB (*n*=27)	1251.20	3.33	96.29	375.73	12.99
ARB+CCB (*n*=17)	1230.96	5.29	100.00	232.69	12.30
ARB+BB (*n*=21)	1293.52	13.80	100.00	93.73	12.93

DBP: Diastolic blood pressure, ARB: Angiotensin receptor blocker, BB: Beta blocker, CCB: Calcium channel blocker, ACE: Angiotensin converting enzyme

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