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A study on pharmacoeconomics analysis of antihypertensive drugs

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Abstract
Hypertension is one of the leading cause of global burden of diseases and as it is a chronic condition with significant detrimental effects on the wide range of health outcomes, cost effective management of hypertension appears to be a great challenge for both developed as well as developing countries. Even though recently there have been lot of studies on pharmacoeconomics and outcome research in the field of hypertension globally, but the results cannot be exactly extrapolated to Indian scenario as the economic status and socioeconomic factors are different in India as compared to the countries. Hence a study was undertaken to evaluate the cost effective antihypertensive drugs in our hospital. An observational comparative study is planned on 100 patients attending the outpatient Department of General medicine with a follow up period of 6 months. Written informed consent is obtained from all the patients satisfying the inclusion criteria. Multitherapy was frequently prescribed (74%), out of that Atenolol with Amlong combination was most common (54%). Diabetes was the most common co-morbid condition (24%). Multitherapy was most frequently prescribed, and Amlodipine with Enalapril combination proved to be most cost effective therapy. HRQoL was not much different in all the treatment groups.
Keywords: Hypertension, pharmacoeconomics, quality of life (QoL), SF-36 questionnare, Cost Effective Ratio (CER)

Introduction

Hypertension (elevated blood pressure) is a major health problem and being the most common cardiovascular disease (CVD), it results in high morbidity and mortality in men as well as women[1, 2].

It has been estimated that 17.3 million people died from CVDs in 2008, representing 30% of all global deaths[3].The prevalence of these diseases is rising most quickly in Southeast Asia and the Eastern Mediterranean regions[4].

According to WHO health statistics 2012, the prevalence of hypertension in India was 23.1% in men and 22.6% in women in equal or more than 25 years age[5].

Epidemiological studies have shown that hypertension is present in 25% of urban and 10% of rural subjects in India. There is a difference in measurement methodology of BP in epidemiological studies as compared to clinic-based measurements. It has been reported that epidemiological studies that rely on single-session measurements over diagnose hypertension by 20-25%. If we discount this proportion, 19% adults in the urban and 7.5% in the rural areas shall be eligible for hypertension therapies. Translating these proportions into numbers reveals a massive burden of this disease in India[6].

Due to high prevalence of hypertension and the requirement of medications for prolonged periods, the drug treatment cost poses a major issue in health economics. In developed countries, the expenditure on antihypertensive therapy has increased sharply in recent years

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due to increasing use of newer and more expensive drugs[7]. As the expenses and costs for hypertension control are on the increase in developed and potentially also in the developing world, where resources are much more limited, Even in the most affluent countries, hypertension control needs to be considered in the context of other demands of society[8].

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[9, 10, 11].

In most western countries, the cost of hypertension treatment accounts for a substantial portion of health resources[12].

According to International Monetary Fund World Economic Outlook (April-2015), India is the 9th largest economy in the world but due to its huge population falls to 145th place for Gross Domestic product (GDP) with GDP of 87,748 INR. Per capita income of India is low by 6 times than world's average[13].

India expends only 5% yearly Gross Domestic Product (GDP) on health care. Of this, most of the expenditure (about 80%) is individuals out of-Pocket (OOP). The challenge before India is to attain health care accessible for the majority of its people at optimal cost[14].

Hence, studies that examine cost-effective approaches to control BP optimally among Indians are needed[15].

Pharmacoeconomics and Outcome Research (PEOR) is a part of health economics that focuses on the economic evaluation of pharmaceuticals.

Pharmacoeconomics and health outcomes research (PEOR) are playing an increasingly important role in informing clinical development and market access decisions of new innovative medicines. It is currently being used to make formulary decisions (complementing clinical data), design disease management programs and measuring the cost effectiveness of interventions and programs in managed care[16].

Methodology

Source of data

Patients attending OPD in General Medicine Department.

Inclusion criteria

- Patients aged > 35 years.
- Both male and female.
- Patients with co morbidity like diabetes, hypothyroidism, coronary artery disease and myocardial infarction.
- Patients with any grade of hypertension.
- Patients with or without complications of hypertension.

Exclusion criteria

- Pregnant women and lactating mother.
- Patient with psychiatric disorders.
- Patients with co morbidity such as renal transplant.

Sample size calculation

A study was conducted in Brazil, with the aim to assess the influence of hypertension control upon HRQoL in hypertensive patients with and without complications. In the study 77 hypertensive patients were observed for 12 months with special care program. The patients Health Related Quality of Life (HRQoL) assessed using Bulpitt and Fletchers specific questionnaire as well as Short Form (SF)-36 scores. Study concluded that special care program significantly controlled the hypertension but did not interfere with the health related quality of life (HRQoL).

With reference to the above article in our study we took sample size as 100.

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Sampling method

Observational comparative study

In the study two most frequently prescribed therapies, both in monotherapy and multitherapy group were compared for the cost effective ratio and quality of life.

Results

Out of 100 prescriptions, 74% were Multitherapy and 26% were Monotherapy.

Table 1: Type of antihypertensive therapy used by the study subjects

Therapy	Frequency	%
Monotherapy	26	26
Multitherapy	74	74
Total	100	100

Out of 100 prescription, 71% prescriptions had 2 drugs, 26% were monotherapy and only 3% prescriptions contained 3 drugs.

Table 2: Number of antihypertensive drugs used by the study subjects

No. of drugs	Frequency	Percent
1	26	26
2	71	71
3	3	3
Total	100	100

Out of 100 prescriptions, combination of AT+AM was most frequently(57%) prescribed, followed by AM (21%), AM+EN (9%), AT(5%), AT+AM+TL (3%), AT+TL (2%) and EN+DR (2%) and least percentage of AT+EN with (1%)

Table 3: Combination of antihypertensive drugs used among the study subjects

Combination of drugs	Frequency	Percent
AM	21	21
AT	5	5
AT,AM	57	57
AM,EN	9	9
AT,TL	2	2
EN,DR	2	2
AT,EN	1	1
AT,AM,TL	3	3
Total	100	100

Mean reduction in SBP in the group of patients treated with Atenolol is 8 mmHg± 5.4 mmHg compared to that of Amlodipine 6.6 mmHg ± 3.5 [p-0.477].

Table 4: Comparison of mean reduction of systolic BP among the two Monotherapy Treatment groups

Reduction in systolicBP(mmHg)	AT	AM	P value
Mean	8	6.6	0.477
SD	5.47	3.5	

Mean reduction in SBP in the group of patients treated with Multitherapy with Amlodipine and Atenolol combination is 9.54 mmHg ± 6.81 compared to that of Amlodipine and Enalapril 11.56mmHg ± 3.97 [p-0.207]

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Table 5: Comparison of mean reduction of systolic BP among the two Multitherapy treatment groups

Reduction in systolic BP(inmmHg)	AT,AM	AM,EN	P value
Mean	9.54	11.56	0.207
SD	6.81	3.97	

In Monotherapy group, Amlodipine is more cost effective with a mean CER of 8.93 rupees/mm of Hg whereas Atenolol group had a mean CER of 26.15 rupees/mm of Hg with [p-0.0059].

Table 6: Comparison of mean cost effective ratio for treating hypertension among the two monotherapy treatment groups

Monotherapy	No. ofcases	Mean	SD	P value
AT	5	26.15	22.43	0.0059
AM	21	8.93	7.57	

Combination of Amlodipine with Enalapril was more cost effective with a mean CER of 18.24 rupees/mm of Hg as compared to combination Amlodipine with Atenolol with mean CER of 27.73 rupees/mm of Hg with [p<0.057].

Table 7: Comparison of mean cost effective ratio for treating hypertension among the two multitherapy treatment groups

Multitherapy	No. ofcases	Mean	SD	P value
AT,AM	57	27.73	22.74	0.057
AM,EN	9	18.24	10.90	

Table8: Incremental Cost effective ratio in Monotherapy Group

Therapy	AT	AM	Difference	ICER
Cost(rupees)	126	54	72	51.42
SBP(mmHg)	8	6.6	1.4	

Table9: Incremental Cost effective ratio in Multitherapy Group

Therapy	AM with EN	AM with AT	Difference	ICER
Costs (rupees)	174	180	6	2.97
SBP (mmHg)	11.56	9.54	2.02	

Discussion

In a study conducted in Tanzania, Prescription patterns and the cost of some monotherapy were studied in 600 patients attending medical clinics at four private hospitals in Dar-es-Salaam. About 50% of the prescriptions contained 2 to 3 drugs. Antihypertensives prescribed as monotherapy included Atenolol(23.2%), Bendrofluazide(22%), Frusemide(19%), Hydralazine(11.2%), Nifedipine(9.8%), Amlodipine(9.5%) and Enalapril(9.3%). Among the combination therapy drugs were ACE inhibitors +diuretic (7%), BB+diuretic (4%), CCB + Losartan (2.3%), BB+ ACE inhibitor (2.2%), CCB + ACE inhibitor (1.8%) and Diuretic+Hydralazine (1.7%). The cost of Nifedipine, Bendrofluazide and Frusemide were about five to six times higher in the private hospitals than at the government owned medical stores department. This study reveals a need for continued education and standard treatment guidelines for rational prescribing of antihypertensive drugs[17].

Similarly in one more study conducted by De Gusmao JL *et al*., with the objective to assess the influence of hypertension control upon HRQoL in hypertensive patients with and without complications. In the study 77 hypertensive patients were observed for 12 month. In contrast to the above studies**,** our studyincluded 100 patients, out of which 51% were females and 49% were males.

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Prescription pattern analysis showed, multitherapy as major prescription pattern (74%) and monotherapy formed 24% of all prescriptions.

Most frequently used multitherapy was combination of Atenolol with Amlodipine(54%) followed by combination of Amlodipine with Enalapril (9%) and in monotherapy most frequently prescribed drug was Amlodipine (80%) followed by Atenolol (20%).

In a randomized control trial conducted by Tsuji RG *et al*., to evaluate the cost effective ratio of two antihypertensive therapeutic drug combination Hydrochlorothiazide plus Atenolol versus Losartan plus Amlodipine in patients with different grades of hypertension. Study showed, antihypertensive treatment that used Hydrochlorothiazide combined with Atenolol was more cost effective than the combination of Losartan and Amlodipine in patients with grade 1 and 2 hypertension, however there was no difference between cost effective ratio of these treatment regime in grade 3 hypertensive patients[18].

A study conducted by Mishchenko O, analysed the cost effectiveness of the new triple Fixed Drug Combination (FDC) Valsartan-Amlodipine- Hydrochlorothiazide compared with other antihypertensive regimes using dual FDCs Valsartan-Amlodipine, Valsartan-Hydrochlorothiazide, Amlodipine-Hydrochlorothiazide in terms of Ukraine payers. At the end of the study it has been found that triple FDC Valsartan-Amlodipine-Hydrochlorothiazide is more cost effective compared to the other regimes. But with the view of cost analysis, triple FDC is cheapest only to the dual FDC Valsartan-Hydrochlorothiazide[19].

In a comparative study conducted by Ikuo S *et al*., in 55 years old patients with moderate hypertension with presence or absence of concomitant diabetes, four treatment regimes were compared: initial Angiotensin receptor blocker (ARB) with calcium channel blocker (A+C), initial Calcium channel blocker with additional Angiotensin receptor blocker (C+A), initial ARB with additional Diuretics (A+D), initial Diuretics with additional ARB (D+A). Among patients without diabetes, expected survival and cost were similar in all treatment groups. Among the patients with concomitant diabetes expected survival was longest and expected costs were lowest in the group A+C. Expected survival decreased and expected costs increased in the order of A+D, C+A, D+A groups. The study concluded that presence of concomitant diabetes affected the cost effectiveness[20].

In our study patients with age >35 yrs were included. Majority of the patients (38%) were in the age group of 40-50yrs, (32%) in 50-60 yrs with the mean age as 55.17+10.3yrs.

Majority of the patients were in the initial stages of hypertension with prehypertension (49%), stage I (42%), stage II (4%), and stage III (2%).

Out of 100 patients, 24% patients had Diabetes mellitus as a comorbid condition along with hypertension and it was the most common comorbidity observed. 5% patients had Ischemic heart disease (IHD).

Outcomes were compared between the two most commonly prescribed therapies in monotherapy as well as in multitherapy. In monotherapy Amlodipine was compared with Atenolol and in multitherapy Amlodipine + Atenolol was compared with Amlodipine + Enalapril.(In multitherapy there were no FDCs).

Cost effective analysis in monotherapy showed Amlodipine to be more cost effective with mean CER of 8.93 rupees/mm of Hg than Atenolol with mean CER 26.15 rupees/mm of Hg with [p -0.0059]

In multitherapy, Amlodipine with Enalapril combination was more cost effective with mean CER 18.24 rupee/mm of Hg than Amlodipine with Atenolol combination with mean CER 27.73 rupees/mm of Hg, with [p-0.057].

Conclusion

- Multitherapy was most frequently prescribed, similar to the other studies suggesting that rational prescription and FDCs play an important role in effective management of hypertension.
- In monotherapy Amlodipine is more cost effective than Atenolol and in multitherapy Amlodipine with Enalapril combination is more cost effective than Amlodipine with Atenolol combination.

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