ABSTRACT

Objective: Hypertension is the most common condition seen in primary care and leads to myocardial infarction, stroke, renal failure, and death if not detected early and treated appropriately. A large number of antihypertensive drugs alone or in various combinations are available, and physicians need to choose most appropriate drug for a particular patient. Pharmacoeconomic and drug utilization studies at regular intervals help physicians to prescribed rational drugs with high efficacy along with minimal cost.

Methods: The prospective observational study was conducted at Seth H. J. Mahagujarat Hospital from July to December 2013. 250 hypertensive patients, attending medicine outpatient department were included for drug utilization study and 100 hypertensive patients, attending in patients department were included for pharmacoeconomics analysis during the study period.

Result: The most frequently prescribed antihypertensive drug as monotherapy, as combination therapy and in fixed dose combinations was calcium channel blocker (Amlodipine). Generic drugs showed same efficacy as brand drug, but both drugs were significantly differed in the prize. Among 100 inpatients admitted for the hypertensive condition in general ward total of direct medical cost was 65.19% and total of indirect medical cost was 34.81%. β-blocker and diuretics were the most effective therapy which is followed by the clonidine, envas (Enalapril), and then, amlodipine.

Conclusion: We concluded from this study that use of β-blockers and diuretics were most cost-effective for the hypertensive patients in this study.

Keywords: Antihypertensive drugs, Drug utilization study, Pharmacoeconomics analysis.
Pharmacoeconomics consists of analysis and evaluation of outcomes (clinical, economic, or humanistic), cost consequences, and cost comparison. Pharmacoeconomic evaluations can be applied to assess the value of treatments, to compare the medical cost and health outcomes associated with new therapies/medicines to the cost and to determine the outcome of the existing alternative treatment. Currently European countries are making the maximum use of pharmacoeconomic data for reimbursement and other financial decisions, and most have officially introduced pharmacoeconomics guidelines in their countries. Australia in comparison with European countries has a relatively well-developed pharmacoeconomic structure. Countries in the North American continent, South American continent, and South Africa have introduced the concept of pharmacoeconomics and outcomes research data lately. Countries in Asia such as China, Hong Kong, Japan, Korea, and Singapore have a well-developed pharmacoeconomics and outcomes research structure [14]. In India, full proof system yet to be developed, where the majority of patients are below the poverty line and high cost of treatment is main reason for nonadherence to the treatment. This study was designed to analyze the drug utilization patterns and pharmacoeconomic analysis of antihypertensive drugs prescribed to hypertensive patients.

METHODS

The prospective observational study was conducted at Seth H J Mahagujarat Hospital during the period of July 2013 to December 2013. Ethical approval was obtained from the Institutional Ethics Committee of Rathi Hospital, Ahmedabad. Beer's criteria were used to analyze proportion distribution compare with standard guideline.

### Table 1: Demographical and clinical parameters of hypertensive patients

| Demographic characteristics | Gender | Number of patients | Mean±SEM | p value |
|-----------------------------|--------|--------------------|----------|---------|
| Age (years)                 | Male   | 136                | 61.448±0.889 | 0.499   |
|                             | Female | 114                | 56.543±0.880 |         |
|                             | Total  | 250                | 59.212±0.684 |         |
| DHTN (months)               | Male   | 136                | 49.65±4.506  | 1.601   |
|                             | Female | 114                | 42.798±4.937 |         |
|                             | Total  | 250                | 46.528±3.4685|         |
| BMI (kg/m²)                 | Male   | 136                | 23.305±0.436 | 1.764   |
|                             | Female | 114                | 24.735±0.5335|         |
|                             | Total  | 250                | 23.95±0.438  |         |
| SBP (mm of Hg)              | Male   | 136                | 143.23±1.616 | 0.499   |
|                             | Female | 114                | 149.34±1.969 |         |
|                             | Total  | 250                | 146.02±1.269 |         |
| DBP (mm of Hg)              | Male   | 136                | 84.338±0.743 | 0.024   |
|                             | Female | 114                | 85.394±0.758 |         |
|                             | Total  | 250                | 85.82±0.5319 |        |

HTN: Hypertension, SBP: Systolic blood pressure, BMI: Body mass index, DBP: Diastolic blood pressure

| Classification | Classification (BMI, kg/m²) | Male (%) | Female (%) | Total (%) |
|----------------|-----------------------------|----------|------------|-----------|
| Underweight    | <18.50                      | 22 (16.17)| 07 (6.14)  | 29 (11.60) |
| Normal range   | 18.50-24.99                 | 67 (49.26)| 57 (50.00) | 124 (49.60) |
| Overweight     | 25.00-29.99                 | 35 (25.73)| 33 (28.94) | 68 (27.2)   |
| Obese          | ≥30.00                      | 12 (8.82) | 17 (14.91) | 29 (11.6)   |
| Total          |                            | 136 (100.0)| 114 (100.0)| 250 (100.0) |

BMI: Body mass index

In the Table 2, showed that BMI of patients fall in normal range (49.6%). Although obese patient was more found in case of female compared to male patients and the mean BMI of the patients in our study were approximately 23.95 kg/m² which imply that the patients are normal range. While in one of the clinical work showed average BMI 27.16±2.85 in male patients and 26.40±3.65 in female patients during course of antidiabetic therapy, which implies that the patients were overweight (BMI ≥25 kg/m²) and were on the borderline of becoming obese (BMI ≥30 kg/m²), which in itself is a well-recognized significant risk factor for DM [15] and HTN. In most of the studies, being overweight was associated with a 2-fold to 6-fold increase in the risk of developing HTN. Framingham study suggests that 10% increase in weight a rise of 6.5 mm Hg in systolic pressure [16]. It also suggested that 65% of the risk for HTN in women and 78% in men can be related to obesity. The study done in Jaipur urban (both sexes) and rural studies (only males) [17], the Haryana rural study [18], the Chennai urban population study [19] as well as the Bombay executive study [20] have all shown a higher weight and BMI among hypertensive groups.

### Result and Discussion

In this study, 136 patients (54.4%) were males and 114 (45.6%) were females indicating 8.8% higher prevalence of HTN in male population. As shown in Table 1, the prevalence of HTN increases with age. Hence, age is one of the main factors for HTN. Our study showed that out of 250, 51 patients have hereditary condition of HTN. Hence, family history of elevated blood pressure is one of the strongest risk factors for future development of HTN in individuals. Among 250 patients, 112 patients have comorbid condition along with HTN. In our study, finding the majority of the patients 66 (57.89%) have diabetes mellitus (DM) followed by myocardial ischemia 26 (22.80%), thyroid complications 16 (14.03%), asthma 04 (3.50%), chronic obstructive pulmonary disease (COPD 1) (0.87%), and migraine 1 (0.87). The most frequently prescribed antihypertensive drug group was angiotensin 2 receptor blockers for patients who have comorbidity of DM (51.5%). Distribution of hypertensive patient according to age, duration of HTN, body mass index (BMI), systolic blood pressure, and diastolic blood pressure were showed in Table 1. The age difference between two gender groups (p<0.05) was statistically significant.

Distribution of drug in hypertensive patient – Monotherapy

A total of 187 (74.8%) patients received monotherapy. This study revealed that calcium channel blockers were the drugs of choice for hypertensive patients because it is prescribed to 54 (28.87%) patient...
of HTN as a single drug therapy, followed by the fixed dose combination (FDC) of β-blockers with amlodipine 42 (22.45%), β-blockers 37 (19.78), angiotensin 2 receptor blocker 23 (12.29%), diuretics 9 (4.81%), angiotensin converting enzyme inhibitors 9 (4.81%), centrally acting drug 2 (1.06%), and others. Diuretics are generally recommended as first-line therapy for treatment of HTN (JNC V; JNC VI) (Fig. 2). Utilization of diuretics in this study was 7.44% as monotherapy. Lesser use of diuretics in this study may be due to adverse effect of diuretics on glucose homeostasis and lipid profile [21]. In an Indian study, 49% of patients received monotherapy [22]. Tiwari et al. study also support this result of high use of calcium channel blockers as monotherapy (Fig. 2).

Distribution of drugs in hypertensive patients

A total of 49 (19.6%) patients received dual therapy. Among them, 15 patients received Ca\(^2+\) channel blocker along with other drugs such as atenolol, revolol, enalapril, telmisartan, and clonidine, (telmisartan +atenolol) (losartan + hydrochlorothiazide). Other 14 patients received combination of FDCs (Ca\(^2+\) channel blocker + β-blocker) along with other drugs such as enalapril, clonidine, losartan, telmisartan, while 9 patients received combination of diuretics (furosemide) along with other drugs such as amlodipine, atenolol, and telmisartan. The remaining 11 patients prescribed β-blocker along with telmisartan, losartan, enalapril, clonidine, and amlodipine (Table 3). Only one patient prescribed the quadruple therapy with combination of amlodipine, hydrochlorothiazide, clonidine, and metoprolol.

Associated comorbidity with HTN

In our study, finding the majority of the patients 66 (57.89%) have DM followed by myocardial ischemia 26 (22.80%), thyroid disease 16 (14.03%), asthma 04 (3.50%), COPD 1 (0.87%), and migraine 1 (0.87). A study carried out by Olusegun Adesola found 43 hypertensive patients (n=240) had coexisting DM [23]. In one clinical study, found that the most common comorbid in HTN was DM, 98 (38.6%); followed by dyslipidemia in 50 (19.6%), bronchial asthma in 28 (11.0%), and renal diseases in 12 (4.7%) [24]. Another study showed that the highest comorbid condition found with HTN were diabetes (13%), followed by hyperlipidemia (7.5%), renal disease, and obesity (6.5% each). Peptic ulcer disease and stroke (4% each) and congestive cardiac failure (3.5%) [25].

Pharmacoeconomic study

Cost minimization

There is no significant difference between efficacies of these two drugs (branded vs. generic drugs) (p>0.05), these drugs do significantly differ in the prices. Hence, prescribing generic as their cost is low compared to branded products which is a good option for trust based hospital and also beneficial for rural people (Table 4).

Cost of illness

Total of direct medical costs among 100 inpatients admitted due to hypertensive crises in general ward was 65.19%, among them, cost of health personnel (physician and nursing charges) constituted 25.43%, cost of medication constituted 28.53%, and laboratory cost constituted 11.24% of from the direct medical costs for the hypertensive condition.

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**Fig. 1: Overview of methodology (CRF – Case record form, BMI – Body mass index, BP – Blood pressure)**

**Fig. 2: Drug utilization of antihypertensive drug as a monotherapy**
Total of indirect medical costs among 100 inpatients admitted for the hypertensive condition in general ward is 34.81%, among them, cost of loss of productivity (missed earning days) constituted 15.29, cost of transportation, and meal are 19.51% from the indirect medical costs for hypertensive condition.

Cost-effectiveness analysis

Diuretics and β-blockers were the most effective therapy which is followed by the clonidine, enalapril, amlodipine, and other class of drugs. The cost-effectiveness studies alter with comorbidities associated with HTN. In this study, the majority of patients associated with CV disorders so β-blocker is most cost-effective drug in this study.

Cost effectiveness is dependent on QALYs. Higher the QALYs better the cost effectiveness which directly affects the total cost and ultimately benefited to patients and overall economic burden of therapy is reduced (Table 5).

CONCLUSION

The most frequently prescribed antihypertensive drug group was calcium channel blocker as monotherapy, though diuretics are the first line choice of drug therapy for the HTN. Lesser use of diuretics in this study may be due to adverse effect of diuretics on glucose homeostasis and lipid profile. The most prevalent combination of drugs prescribed were calcium channel blockers + β-blockers as dual, triple, and as FDCs.

In pharmacoeconomics study, we concluded that it is beneficial for developing countries where the majority of people below the poverty line and nonadherence to therapy are observed only because of the high cost of the treatment. By the cost minimization, we concluded that use of generic drug significantly affects the cost of medication without change in the safety and efficacy. In cost of illness, we concluded that indirect cost was invisible to the patient but it covers near to 30% of the total cost, by proper knowledge of pharmacoeconomics we can minimize the indirect cost of treatment by minimizing the duration of stay depending on disease condition. Finally, we concluded from this study that use of β-blockers and diuretics were most cost-effective for the hypertensive patients in this study.

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