Pattern of use of anti-hypertensive drugs amongst hypertensive patients in a tertiary care hospital: a cross sectional, observational study

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ABSTRACT

Background: Hypertension is one of the primary modifiable risk factors for cardiac and renal diseases and is the single most important risk factor for stroke. Despite different guidelines for management of hypertension like Joint National Committee, British Hypertension Society, National Institute for Health and Care Excellence; there are still the clouds of controversy. The objective of the study was to evaluate the prescribing pattern of antihypertensive drugs among the patients attending medicine outpatient department of a tertiary care teaching hospital

Methods: A cross-sectional, observational study was conducted in our hospital over a period of six months. Relevant information was collected from medical records of 209 hypertensive patients fulfilling inclusion criteria. The collected data were sorted and analyzed.

Results: Out of 209 patients, maximum were of age group of 45-65 years (55.02%). 115 (55.02%) were male and 94 (44.97%) were female. Diabetes mellitus (24.4%) was the most common associated disease with hypertension. Most of the patients had received single antihypertensive drugs (49.28%). Among the monotherapy category calcium channel blocker (82.78%) was the most commonly prescribed antihypertensive drug class followed by angiotensin receptor blocker (36.36%). Amlodipine (81.82%) was the most common among calcium channel blockers. The most frequent fixed drug combination prescribed consisted of amlodipine and atenolol. Most of the drugs were prescribed in generic name (90.9%).

Conclusions: The treatment pattern, in general, conformed to standard treatment guidelines.

Keywords: Hypertension, Amlodipine, Generic

INTRODUCTION

Hypertension is one of the primary modifiable risk factors for cardiac and renal diseases and is the single most important risk factor for stroke. Hypertension has been described as the “largest epidemic ever known to mankind” and it is beyond doubt that hypertension is a serious threat to public health worldwide and most important non communicable disease leading to mortality and morbidity. During the last four decades, prevalence of hypertension raised from 594 million in 1975 to 1.13 billion in 2015. Not only that, highest blood pressure levels were shown in South Asia, Central and Eastern Europe areas. As per the study of 2015, South Asia accommodates about 258 million patients of which India shares 199 million. Different meta-analysis showed that usual blood pressure is strongly and directly related to vascular mortality amongst middle and old aged population. Every 20/10 mm Hg rise in BP results in two fold increased risk of cardiovascular mortality and morbidity above the BP threshold of 115/75 mm Hg. Hence reduction in BP reduces the risk of death due to stroke and cardiovascular disease (CVD) death.
Despite different guidelines for management of hypertension like Joint National Committee, British Hypertension Society, National Institute for Health and Care Excellence; there are still the clouds of controversy. However, the common link of all these guidelines is that definition of hypertension is ≥140/90 mm Hg and >130/80 mm Hg even in presence of diabetes mellitus, chronic kidney disease (CKD), heart failure. The basics of hypertension management include Life style modification and pharmacotherapy are common mission of all guidelines is to reduce the global burden of CVD.6

As the treatment of hypertension is lifelong and different classes of drugs are available, so aim of therapy should point ease of administration of drugs and also cost effectiveness for better therapeutic outcome vis a vis to reduce the pill burden and bill burden.

The present prescription monitoring study for antihypertensive drugs was undertaken with the purpose to investigate the use of antihypertensive drugs in hypertensive patients in order to establish the current trend of pattern of prescribing of antihypertensive drug; and to identify whether such pattern of prescription is appropriate and accordance with international guidelines for pharmacotherapy of hypertension with the emphasis on generic prescription to achieve the therapeutic goal of blood pressure control.

The objective of this study was to evaluate the drug prescribing pattern among hypertensive patients attending medicine OPD of our tertiary care teaching hospital (using WHO drug use indicator), to assess the number of anti-hypertensive drugs used per prescription, the rationality of drug prescription and the average cost per prescription.

METHODS

A cross-sectional, observational study was conducted by Department of Pharmacology in association with Department of Medicine in Midnapore Medical College and Hospital, Paschim Midnapore. The study was conducted over a period of 6 months after approval from Institutional Ethics Committee (Approval letter No. MMC/IEC-2017/2698, December 22, 2017).The patients included were those who were registered in the medicine OPD during the period 22 January 2018 to 22 July 2018. The diagnosis and line of treatment to be given was decided by the physician in charge of the Department of Medicine. No additional drugs or investigations were advised by us during the study period. Data of patients matching inclusion criteria were recorded after getting informed consent. Identity of patient was kept confidential.

The following data were collected: age, sex, registration number, height, weight, diagnosis, duration of illness. Each drug prescribed to the patient was noted as follows: brand/generic name, indication, route of administration, dose and frequency of administration and date of starting the drug.

Inclusion criteria

All patients >30 yrs, patients with diagnosis of hypertension, able to communicate, treatment naive patients were included in this study.

Exclusion criteria

Pregnancy induced hypertension example eclampsia/ pre-eclampsia; malignant hypertension; hypertensive emergency were excluded in this study.

Descriptive statistics like mean and percentages were used for the analysis for the interpretation of results. Statistical analysis was performed using SPSS version 21.

RESULTS

Demographic details

During the study period, a total of 209 hypertensive patients fulfilled the criteria for inclusion in the study analysis. Among them 115 (55.02%) patients were male and 94 (44.97%) were female. Male:female ratio was 1.223:1 (approx.) indicating that hypertension is slightly more prevalent in the male gender. The mean age of the study population was found to be 57.14 years with a standard deviation of 0.693 years (Table 1).

Table 1: Mean age, systolic, diastolic blood pressure of the subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>57.14</td>
<td>0.693</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>142.26</td>
<td>17.71</td>
</tr>
<tr>
<td>Female</td>
<td>143.85</td>
<td>18.74</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>89.48</td>
<td>11.33</td>
</tr>
<tr>
<td>Female</td>
<td>88.60</td>
<td>10.32</td>
</tr>
</tbody>
</table>

In this study, more than two-third (70.2%) of the patients were illiterate. 64.3% of the patients were non-smokers and 35.7% of the patients had smoking history present. More than half (64.7%) of the patients belonged to rural areas. Most of the respondents were engaged (68.4%) in one of the other occupation.

Almost half of the patients were found to be obese (48.6%) and 29.3% were overweight as per Asia Pacific perspective for Asians (WHO IOTF 2003).7

The age distribution of hypertensive patient was 33 (15.8%) below the age of 45 years, 115 (55.02%) were between 45 and 65 years and 61 (29.19%) were above 65 years (Figure 1).
In our study most of the patients were suffering from hypertension for a period of 1-5 years (56%) followed by 0-1 year (29%) and more than 5 years (16%) duration (Figure 2).

Comorbidities

Total 134 patients (74.0%) were suffering from only hypertension. Diabetes 51 (24.40%) was the commonest comorbidity followed by dyslipidemia 27 (12.92%), cerebrovascular disease 22 (10.53%), thyroid disorders 10 (4.78%), coronary artery diseases 9 (4.30%) and others 13 (6.22%) like neuropathy, COPD, seizure disorder, hyperuricemia etc (Table 2).

Table 2: Significant comorbidities.

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>51</td>
<td>24.40</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>27</td>
<td>12.92</td>
</tr>
<tr>
<td>CVA</td>
<td>22</td>
<td>10.53</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>10</td>
<td>4.78</td>
</tr>
<tr>
<td>CAD</td>
<td>9</td>
<td>4.30</td>
</tr>
<tr>
<td>Others</td>
<td>13</td>
<td>6.22</td>
</tr>
</tbody>
</table>

Pharmacotherapy

For the purpose of analyzing the prescriptive patterns of antihypertensive drugs in the treatment of hypertension the pharmacotherapy was classified as monotherapy, dual therapy, triple therapy and four drug therapies, where single antihypertensive, two, three and four antihypertensives respectively were used for the treatment. Table 3 shows the number of patients who underwent treatment under different groups.

Table 3: Number of drugs prescribed.

<table>
<thead>
<tr>
<th>No. of drugs</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single drug</td>
<td>103</td>
<td>49.28</td>
</tr>
<tr>
<td>Two drugs</td>
<td>100</td>
<td>47.84</td>
</tr>
<tr>
<td>Three drugs</td>
<td>5</td>
<td>2.39</td>
</tr>
<tr>
<td>Four drugs</td>
<td>1</td>
<td>0.48</td>
</tr>
</tbody>
</table>

About half of the patients had received one antihypertensive drug 103 (49.28%), followed by two 100 (47.84%), three 5 (2.39%) and four 1 (0.48%) antihypertensive drugs. 49.28% of the patients were on mono therapy and 50.72% were on combination therapy.

Pattern of drug use

Calcium channel blockers (CCBs) was the most preferred anti-hypertensive drug class 173 (82.78%) prescribed followed by angiotensin II receptor blockers (ARBs) 76 (36.36%), diuretics 40 (19.14%), Beta blockers 33 (15.79%), and angiotensin-converting-enzyme inhibitors (ACEIs) 26 (12.44%) in that order.

Table 4: Frequency of administration of individual drugs.

<table>
<thead>
<tr>
<th>Antihypertensive group</th>
<th>Name of drug</th>
<th>Number of prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium channel blockers (173)</td>
<td>Amlodipine</td>
<td>171</td>
</tr>
<tr>
<td></td>
<td>Cilnidipine</td>
<td>2</td>
</tr>
<tr>
<td>ARB (76)</td>
<td>Losartan</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Telmisartan</td>
<td>26</td>
</tr>
<tr>
<td>Diuretics (40)</td>
<td>Hydrochlorothiazide</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Chlorthalidone</td>
<td>14</td>
</tr>
<tr>
<td>Beta blockers (33)</td>
<td>Atenolol</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Metoprolol</td>
<td>12</td>
</tr>
<tr>
<td>Ace inhibitors (26)</td>
<td>Enalapril</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Ramipril</td>
<td>3</td>
</tr>
</tbody>
</table>

Amlodipine 171 (81.82%) was the most commonly prescribed antihypertensive agent both as mono therapy and combination therapy followed by losartan 50 (23.92%). The most prevalent combination of drug was a 2-drug therapy of CCBs and ARBs which was found to be 47 (22.4%) followed by CCB and diuretics 17 (8.13%). Among the three drug combinations, diuretics, ARB and CCBs comprised the most commonly prescribed combination 4 (1.91%) (Table 4).

Other drugs co-prescribed

Oral hypoglycemic drugs were prescribed very commonly as diabetes was the most frequent associated comorbidity.
in the study samples. Among them metformin was given in 51 patients (34.80%). Glimepiride were given in 38 (16%) cases. Glytirins were prescribed in 11 cases (10.49%).

Anticoagulants were prescribed to 22 patients (10.53%). Among them aspirin 75 mg was given most commonly (15 cases) and clopidogrel 75 mg was given only in 7 cases. HMG-Co A reductase inhibitors were given in 47 patients (22.49%). Atorvastatin was given to 36 patients and rosuvastatin in 11 patients.

Antimicrobials were prescribed in 28 encounters only (13.4%). Antibiotics were given to patients who had some infections e.g. urinary tract infection, respiratory tract infection, etc. Azithromycin (21.42%) and levofloxacin (17.6%) was used most commonly among antibiotics.

A total of 22 fixed dose combinations were prescribed of which amldipine and atenolol was most commonly prescribed (n=12).

Table 5: Frequency of co-prescribed drugs.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Number</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td>47</td>
<td>12.91</td>
</tr>
<tr>
<td>OHA</td>
<td>100</td>
<td>47.84</td>
</tr>
<tr>
<td>Anti-coagulants</td>
<td>22</td>
<td>10.53</td>
</tr>
<tr>
<td>L-thyroxine</td>
<td>11</td>
<td>4.87</td>
</tr>
<tr>
<td>Others</td>
<td>62</td>
<td>29.67</td>
</tr>
</tbody>
</table>

Key prescribing indicators

Average number of drugs per prescription (encounter) was around 3.22 whereas, average number of antihypertensive drugs per prescription (encounter) was around 1.96±0.79. 90.9% prescriptions were in generic name. 13.4% of encounters were with an antibiotic and 17.7% with injection. 42.31% of the drugs prescribed were from essential drugs list (NLEM 2011). Average drug cost per encounter 13.50 INR and average cost of anti-hypertensive/prescription/day- 5.5±0.79 INR.

Patient care indicators

Average consulting and dispensing time was 8.48 minutes and 1.26 minutes respectively.

85% of drugs were actually dispensed. 69.06% of the patient’s had knowledge of correct dosage.

Facility indicators

Copy of essential drug list or formulary was present. Availability of key drugs was 90%.

DISCUSSION

Hypertension is a worldwide problem with an alarming increase in its prevalence. Appropriate antihypertensive drug therapy is important as any deviation from evidence based guidelines in hypertension treatment contributes to high economic burden to the population.8

This study is essentially an observational, cross-sectional study on the prescribing pattern of drugs for the treatment of hypertension carried out over a period of six months (January 22, 2018- July 22, 2018). A prescription-based survey is regarded as one of the most effective methods to assess and evaluate the prescribing attitude of physicians.

Demographic characteristics

In this study of 209 patients, 115 (55.02%) were male and 94 (44.97%) were female. A relative male preponderance was also observed in other studies.9,10 However, some studies have shown relatively higher incidence of hypertension in females than in males.9,11

Maximum patients belonged to age group of 45-65 years 115 (55%), followed by >65 years 61 (29.2%) and <45 years 33(15.8%). A study in India found most common age group 50-59 years (33.3%) followed by 60-69 years and 40-49 years (26.7%).11 Another study reported most common age group 60-69 years (34%) followed by 70-79 years (23%) and 40-49 years (22%).12 In current study, mean age of study subjects were 57.14±0.693 years similar to that found in other study.13

In these patients, the duration of hypertension ranged from newly diagnosed hypertension up to 25 years, with a median duration of five years. In this study most of the patients were suffering from hypertension for a period of 0-6 months (26.8%).

The mean systolic blood pressure (mm Hg) of the study population was found to be 146±19.318, mean diastolic blood pressure (mm Hg) was 89.5±10.184 and mean pulse pressure (mm Hg) was 54.77±18.450.

Co-morbid conditions

Patients with chronic diseases like hypertension usually suffer from other associated conditions. In our study, majority of the patients were suffering from concurrent diabetes (24.4%). Other commonly associated conditions were dyslipidemia (12.92%), CVD (10.53%), thyroid disorder (4.78%), CAD (4.3%) and others disease (6.22%). Sakthi et al reported diabetes mellitus (35%) as the most frequent co-morbidity followed by asthma (5%) and ischemic heart disease (1.6%).14

Pattern of anti-hypertensive prescriptions

In this study, all the prescription patterns of antihypertensive drugs prescribed conform to the oral route of administration. In general the prescription patterns reported so far, highlight the importance of monotherapy and combination therapy.
Monotherapy implies the use of an individual drug selected from the respective generic group (eg. amlodipine from the group CCBs and losartan from the group ARB). Combination therapy means the use of two or more anti-hypertensives at a time, chosen from appropriate different groups (eg. amlodipine as a CCB and telmisartan as an ARB).

The present study observed that multiple drug therapy (50.72%) was more common than single drug therapy (49.28%). Combination therapy seems to be a rational approach to reduce the cardiovascular mortality.\(^\text{15}\)

The increasing use of combination therapy as compared to monotherapy in this study is similar with the JNC7 Report which states that most hypertensive patients with diabetes or renal disease will require two or more antihypertensive drugs to achieve the target blood pressure of <130/85 mm Hg.\(^\text{16}\)

Since large number of patients were suffering from concomitant diabetes, coronary artery disease, and dyslipidemia, they are likely to have required multiple anti-hypertensives to achieve optimal blood pressure control and impede end organ damage.

In this study, the choice of amlodipine, losartan, hydrochlorothiazide, atenolol, and enalapril in preference to other drugs from the same respective groups is overwhelming and noteworthy. Thus the importance of amlodipine (a long acting CCB), losartan (an ARB), hydrochlorothiazide (a diuretic), atenolol (a cardio-selective beta blocker), and enalapril (an ACEI) either individually and or in appropriately chosen combination is realised.

In our study, among the antihypertensive drug classes a long acting CCB was the most preferred anti hypertensive 173 (82.78%) followed by an ARB 76 (36.36%), a diuretic 40 (19.14%), a beta blocker 33 (15.79%) and an ACEI 26 (12.44%) in that order.

A study reported ACEIs (47%) were most commonly prescribed drug followed by CCBs (25.85%), beta blockers (12%), angiotensin receptor blockers (10.8%) and diuretics (3.7%).\(^\text{17}\)

Other study reported calcium channel blockers (49%) were the most commonly prescribed drugs followed by diuretics (43.5%), angiotensin converting enzyme inhibitors (29.5%) beta blockers (29%), angiotensin receptor blockers (21%), alpha adrenergic blockers (2%) and central sympatholytics (2%).\(^\text{12}\)

This difference might be due to physician’s choice with relation to the characteristics of patients, their concurrent illness, as well as the availability of medicines.

Among the individual antihypertensive drugs, amlodipine (CCB) was the most commonly prescribed drug 171 (81.82%) followed by losartan (ARB) 50(23.92%). Solanki et al reported enalapril (ACE inhibitor) as the most commonly prescribed drug (79.66%) followed by atenolol (beta blocker) (49.66%).\(^\text{18}\)

CCBs, both as monotherapy and in combination, have been used most frequently. The share of the CCBs 173 (81.82%) in terms of total number of drugs prescribed is more than twice as much as the second largest antihypertensive group of ARBs 76 (36.36%). The use of amlodipine as an individual antihypertensive drug far exceeds the utilization of any other single agent. A similar pattern of CCB and amlodipine use has also been observed in some other studies.\(^\text{9,19,20}\) Advantages of amlodipine such as long half-life, sustained and consistent blood pressure control with once daily dosing, and improved compliance are factors that make it one of the novel antihypertensive agent and probably contribute to its predominant utilization.\(^\text{21}\)

In this study, ARB was prescribed in 76 (36.36%) cases while ACEI were prescribed in 26 (12.44%) cases. This result is likely due to the fact that many physicians in our setting are getting more conversant with current trends in hypertension management and may also be due to the fact that these medications are getting more accessible and affordable for our patients. As ACEI have been found to be very useful in preventing cardiovascular events and target organ damage in patients with hypertension. They have been shown to control blood pressure and reverse proteinuria in both hypertensive-diabetic patients and chronic kidney disease and also found to reduce mortality in patients with hypertensive heart failure.\(^\text{22}\)

The utilization of diuretics particularly that of the thiazides, was low 40 (19.14%) as compared to the other antihypertensive drug groups. Such underutilization of thiazides has been observed across many studies despite being recommended as the first choice antihypertensive consequent to their ability to prevent major cardiovascular events and low cost. The relatively less frequent use of thiazides could be a result of concerns regarding adverse effects and poor market availability.\(^\text{23}\)

The use of beta-blockers in 33 (15.79%) cases is mainly due to the combination of beta-blockers like atenolol or metoprolol to ameliorate reflex tachycardia which is sometimes associated with CCBs.

Consideration of comorbid conditions seems to take precedence over other factors while selecting an appropriate antihypertensive similar to other study.\(^\text{23}\)

A total of 22 fixed dose combinations were prescribed of which amlodipine and atenolol was most commonly prescribed (n=12). Fixed dose combinations are seen to improve adherence to treatment with advantages in blood pressure control and adverse effects.

Average anti-hypertensive drugs/prescription was 1.96±0.79 similar to other studies.\(^\text{24}\)
The average number of drugs per encounter was 3.22 in our study with median 2 and range of 1 to 9 which is in proximity to 3.8±1.1 drugs per prescription as reported earlier by Akici et al.25

90.9% prescriptions were in generic name. Increasing generic prescribing would rationalise the use and reduce the cost of drugs.26

LIMITATIONS

- Cross-sectional study design.
- Uni-centric and data was collected only from the outpatient department thus not representative of prescription patterns across the state.
- Small sample size.
- Special groups like pregnant women, mentally challenged patients, drug addicts, patients with CKD, CLD were not included in the study.

Larger studies involving different age groups and large number of patients are required to implement these findings to general population of India.

CONCLUSION

Hypertension is one of the most important non-communicable disease, throughout the globe with increasing prevalence, leading to morbidity and mortality like coronary artery disease, stroke, myocardial infarction. So strict control of blood pressure can reduce these cardiovascular events. There are plethora of guidelines and different class of drugs available to achieve the proper control of BP that is <140/80 without co-morbidities and <130/80 with co-morbidities like DM, CKD. As the treatment of hypertension is a lifelong measure, so judicious use of lifestyle modification and pharmacotherapy are very important to achieve the goal. The present study was undertaken to see the current drug utilisation of anti-hypertensive therapy within the acceptable guidelines. The result of the study showed that most commonly prescribed antihypertensive drugs are CCB (81.82%), ARB (36.36%), ACEI (12.44%), diuretics (19.14%), beta blockers (15.79%) per prescription survey in our hospital. This selection of drugs may be due to availability of drugs, choice of treating physician, presence and absence of co-morbidities. Most of the prescriptions (90.9%) were in generic name. There was no gender difference in selecting drugs in this study. Some prescriptions with fixed dose and multiple drugs were also found which included these current medications used. The survey of the prescriptions also showed rationality of the treatment as per guidelines. However, large study is required to substantiate this issue.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES
