



A Prospective Study on Prescription Pattern of Antihypertensive Drugs and Drug Interactions at a Tertiary Care Teaching Hospital

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Abstract

The main objective of this study was to study prescription pattern of antihypertensive drugs in Hanagal Shri Kumareshwar hospital and research centre, Bagalkot, Karnataka, India. The study was carried out from November 2013 to April 2014. Case sheets of patients diagnosed with hypertension were collected. The demographic details of the patients were collected, signs and symptoms were noted, therapeutic data was collected from the treatment chart and drug-drug interactions in the treatment were assessed by using Micromedex 2.0 software, rationality assessment was done using Joint National Committee 7 guidelines and Indian Hypertensive Guidelines-2 and statistical test was carried out using student's t test. During the hospital stay of 150 hypertensive cases 75 patients were male and 75 patients were female, diuretics were mostly prescribed 30.63% for hypertensive patients followed by calcium channel blockers 26.13%, combination therapy was used more when compared to mono drug therapy to maintain blood pressure. Out of 150 patients 136 prescriptions were rational and 14 were irrational. During this study a total of 252 drug-drug interactions were found. Results from the study showed that the choice of anti-hypertensive drugs reasonably comply with the JNC 7 and IGH guidelines on the management of hypertension and diuretics were the first choice of agents used to treat hypertension Which confirms a fairly good degree of compliance by clinicians with JNC 7 and IGH guidelines for the treatment of hypertension.

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Received Date: 12 Oct 2018

Accepted Date: 29 Oct 2018

Published Date: 31 Oct 2018

Citation:

Shalavadi MH, Chandrashekhara VM, Manohar K, Nihar K, Srikanth DRS. A Prospective Study on Prescription Pattern of Antihypertensive Drugs and Drug Interactions at a Tertiary Care Teaching Hospital. *Am J Pharmacol.* 2018; 1(2): 1010.

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Keywords: Blood pressure; Diuretics; Hypertension; Kidney; Calcium channel blocker; Drug interactions

Introduction

Hypertension is an elevated Blood Pressure and perfuse to tissues & organs. Elevated blood pressure means systolic BP greater or equal to 140 mmHg and diastolic blood pressure greater or equal to 90 mmHg (≥ 140 mmHg/90 mmHg). Hypertension has been recognized as a common cardiovascular disease & a major risk factor for congestive heart failure, ischemic heart disease, chronic renal failure and stroke [1].

Hypertension is a disease of complex aetiology, affecting 972 million people worldwide. Prevalence of HTN in India is reported to vary from 4% to 15% in urban and 2% to 8% in rural population. It is estimated that the worldwide prevalence of hypertension would increase from 26.4% in 2000 to 29.2% in 2025 [2]. Recent studies in India showed that hypertension is emerging as a major health problem. It is directly responsible for 57% of all deaths due to stroke and 24% of all deaths due to coronary heart disease [3]. The use of drugs in these patients must be rational; this implies that the appropriate drugs must be prescribed in the right dose, at correct time interval and for a sufficient duration of time [4]. Most patients with hypertension will require two or more drugs to control their hypertension and combination drug formulations may also be useful [5].

This study therefore envisages evaluation of the pattern, extent, rationality and frequency of use of the antihypertensive drugs in the treatment of essential hypertension for information to the esteemed medical fraternity [4,6].

In the view of above background the authors have fascinated to study the prescribing pattern of antihypertensive drugs which will help to check the rationality and drug-drug interactions of antihypertensive drugs prescriptions in S.N. Medical College and H.S.K Hospital and Research centre, Bagalkot with following objectives.

Table 1: Age group and gender wise categorization of hypertensive patients.

| Age | Sex | | Total No. of HTN patients | % of HTN patients |
|----------------------|--------------|----------------|---------------------------|-------------------|
| | No. of Males | No. of Females | | |
| 20 years to 29 years | 0 | 0 | 0 | 0% |
| 30 years to 39 yrs | 9 | 4 | 13 | 8.67% |
| 40 years to 49 years | 10 | 5 | 15 | 10% |
| 50 years to 59 years | 15 | 12 | 27 | 18% |
| 60 years 69 years | 16 | 24 | 40 | 26.67% |
| 70 years and above | 25 | 30 | 55 | 36.67% |
| Total | 75 | 75 | 150 | 100% |

Table 2: Pattern of drug regimen prescribed for hypertensive patients in a tertiary care hospital.

| Drug regimen | No. of prescriptions | % |
|---------------------------------|----------------------|-------------|
| Mono drug regimen | | |
| Furosemide | 14 | 9.66 |
| Torasemide | 2 | 1.38 |
| Hydrochlorothiazide | 1 | 0.69 |
| Ramipril | 7 | 4.83 |
| Telmisartan | 3 | 2.07 |
| Losartan | 3 | 2.07 |
| Olmesartan | 1 | 0.69 |
| Metosartan | 1 | 0.69 |
| Metoprolol | 8 | 5.52 |
| Propranolol | 5 | 3.45 |
| Atenolol | 2 | 1.38 |
| Nebivolol | 2 | 1.38 |
| Amlodipine | 19 | 13.1 |
| Total | 68 | 46.9 |
| Two drug regimen | | |
| Amlodipine+Atenolol | 13 | 8.97 |
| Amlodipine+Hydrochlorothiazide | 8 | 5.52 |
| Losartan+Hydrochlorothiazide | 1 | 0.69 |
| Amlodipine+Furosemide | 2 | 1.38 |
| Torasemide+Propranolol | 1 | 0.69 |
| Telmisartan+Hydrochlorothiazide | 2 | 1.38 |
| Labetolol+Amlodipine | 1 | 0.69 |
| Ramipril+Metoprolol | 4 | 2.76 |
| Torasemide+Hydrochlorothiazide | 3 | 2.07 |
| Torasemide+Spironolactone | 4 | 2.76 |
| Ramipril+Amlodipine | 2 | 1.38 |
| Amlodipine+Metoprolol | 1 | 0.69 |
| Furosemide+Metoprolol | 2 | 1.38 |
| Furosemide+Telmisartan | 1 | 0.69 |
| Telmisartan+Amlodipine | 1 | 0.69 |
| Losartan+Ramipril | 1 | 0.69 |
| Furosemide+Spironolactone | 2 | 1.38 |
| Furosemide+Ramipril | 4 | 2.76 |
| Furosemide+Losartan | 2 | 1.38 |

| | | |
|---|-----------|-------------|
| Ramipril+Torasemide | 1 | 0.69 |
| Amlodipine+Losartan | 1 | 0.69 |
| Total | 57 | 39.3 |
| Three drug regimen | | |
| Amlodipine+Atenolol+Furosemide | 3 | 2.07 |
| Furosemide+Losartan+Hydrochlorothiazide | 2 | 1.38 |
| Amlodipine+Metoprolol+Telmisartan | 1 | 0.69 |
| Amlodipine+Furosemide+Ramipril | 1 | 0.69 |
| Ramipril+Torasemide+Spironolactone | 1 | 0.69 |
| Losartan+Hydrochlorothiazide+Metosartan | 1 | 0.69 |
| Losartan+Hydrochlorothiazide+Metoprolol | 1 | 0.69 |
| Amlodipine+Furosemide+Spironolactone | 1 | 0.69 |
| Furosemide+Spironolactone+Ramipril | 1 | 0.69 |
| Amlodipine+Hydrochlorothiazide+Olmesartan | 1 | 0.69 |
| Amlodipine+Hydrochlorothiazide+Telmisartan | 1 | 0.69 |
| Amlodipine+Metoprolol+Hydrochlorothiazide | 1 | 0.69 |
| Total | 15 | 10.3 |
| ≥ 4 drug regimen | | |
| Furosemide+Amlodipine+Losartan+Hydrochlorothiazide | 1 | 0.69 |
| Bisoprolol+Amlodipine+Torasemide+Spironolactone | 1 | 0.69 |
| Furosemide+Clonidine+Amlodipine+Atenolol | 1 | 0.69 |
| Amlodipine+Atenolol+Furosemide+Prazosin | 1 | 0.69 |
| Amlodipine+Atenolol+Furosemide+Losartan+Hydrochlorothiazide | 1 | 0.69 |
| Total | 5 | 3.45 |

Materials and Methods

This was a prospective, longitudinal study conducted in Hanagal Shri Kumareshwar hospital, Bagalkot over six months on assessment of prescribing patterns of antihypertensive drugs. The patients included in the study were in-patients of either gender aged ≥ 18 years who have been diagnosed with primary and secondary hypertension in the Medicine Department of Hanagal Shri Kumareshwar hospital and research centre and Patients receiving anti-hypertensive drugs. The patients attending outpatient department and pregnant women were excluded.

The study was conducted by reviewing and collecting the case sheets of patients who were diagnosed with Hypertension. Patient demographic details such as name, age, sex were collected. Common and uncommon signs and symptoms observed in patients, past medical history of patients as well as family history were noted. Past

Table 3: Effect of antihypertensive drugs on hypertensive patients in a tertiary care hospital.

| Blood Pressure (Mean ± SEM) | On admission | On discharge | P-value | t-value |
|---------------------------------------|---------------|------------------|---------|---------|
| Amlodipine | | | | |
| SBP | 148.8 ± 6.417 | 130.1 ± 2.948 | 0.116 | 2.661 |
| DBP | 89.42 ± 3.649 | 79.16 ± 1.547* | 0.0138 | 2.589 |
| Furosemide | | | | |
| SBP | 147.6 ± 6.561 | 129.3 ± 3.847* | 0.0236 | 2.404 |
| DBP | 80.71 ± 3.225 | 77.57 ± 2.517 | 0.4493 | 0.7682 |
| Metoprolol | | | | |
| SBP | 150 ± 6.268 | 124 ± 3.910** | 0.0034 | 3.52 |
| DBP | 82.75 ± 5.126 | 76.25 ± 1.830 | 0.2522 | 1.194 |
| Ramipril | | | | |
| SBP | 137.1 ± 13.22 | 128.4 ± 1.601 | 0.5253 | 0.6543 |
| DBP | 84.29 ± 6.117 | 84.29 ± 6.117 | 0.9678 | 0.0412 |
| Amlodipine+Atenolol | | | | |
| SBP | 174.9 ± 8.690 | 132.3 ± 2.011*** | <0.0001 | 4.778 |
| DBP | 91.92 ± 2.747 | 80.46 ± 2.503** | 0.0051 | 3.084 |
| Amlodipine+Hydrochlorothiazide | | | | |
| SBP | 167.5 ± 11.46 | 135.4 ± 7.068* | 0.0317 | 2.386 |
| DBP | 88.75 ± 5.806 | 82.00 ± 2.952 | 0.3176 | 1.306 |
| Furosemide+Amlodipine | | | | |
| SBP | 170.0 ± 20.00 | 150.0 ± 10.00 | 0.4655 | 0.8944 |
| DBP | 80.00 ± 1.000 | 74.00 ± 4.000 | 0.2829 | 1.455 |
| Furosemide+Losartan | | | | |
| SBP | 175.0 ± 5.0 | 120.0 ± 20.0 | 0.1165 | 2.668 |
| DBP | 125.0 ± 25.0 | 82.5 ± 2.5 | 0.2328 | 1.692 |
| Metoprolol+Furosemide | | | | |
| SBP | 133.0 ± 13.00 | 125.0 ± 5.000 | 0.7935 | 0.5744 |
| DBP | 80.00 ± 1.000 | 80.00 ± 1.000 | 1 | 0 |
| Metoprolol+Ramipril | | | | |
| SBP | 150.0 ± 21.21 | 126.5 ± 3.948 | 0.3179 | 1.089 |
| DBP | 90.00 ± 12.25 | 81.00 ± 1.000 | 0.4915 | 0.7324 |
| Ramipril+Amlodipine | | | | |
| SBP | 160.0 ± 50.0 | 145.0 ± 5.00 | 0.7935 | 0.2985 |
| DBP | 90.00 ± 10.0 | 85.00 ± 5.00 | 0.6985 | 0.4472 |
| Ramipril+Metoprolol | | | | |
| SBP | 175.0 ± 32.27 | 130.0 ± 8.165 | 0.2252 | 1.352 |
| DBP | 106.5 ± 22.34 | 80.00 ± 7.071 | 0.4915 | 1.131 |

All the values are expressed as mean ± SEM, *P<0.05, **P<0.01 and ***P<0.001 [Unpaired Student *t* test] as compared to blood pressure on admission.

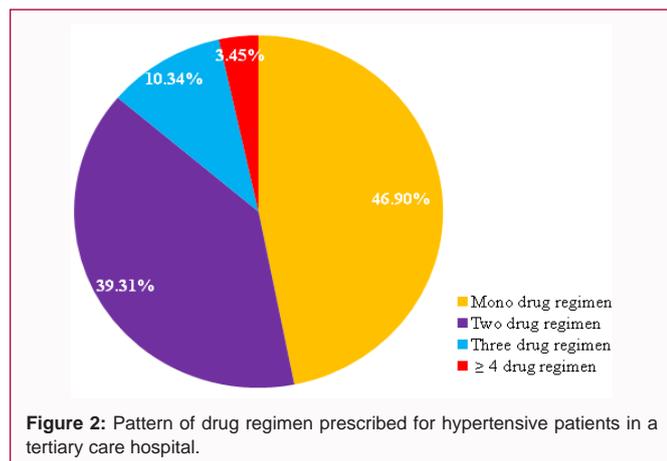
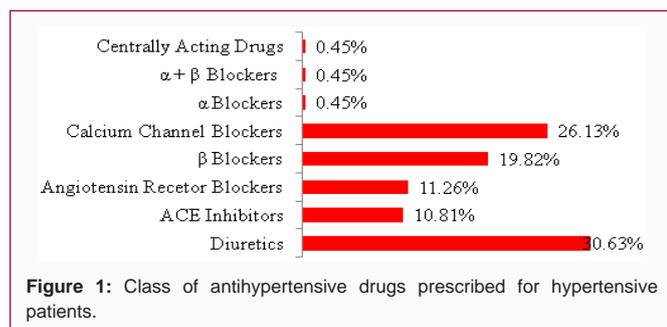
medication history of patients were also documented. Smoking, drinking and other social habits of the patients were noted in patient profile form. Therapeutic data such as name of drug, dose, frequency and duration of therapy were collected from treatment chart of patients. Drug interactions in treatment regimen of patients were assessed using drug data base Micromedex 2.0. Follow up of all patients were done until discharged from the hospital. Rationality assessment of the patient data were analysed as per the guidelines of JNC 7 and IHG-II. The data were collected and reported in forms like patient profile form, drug interaction and intervention reporting form.

Statistical data analysis was done using the statistical program Prism 0.5 software. Continuous data were presented as mean ± SEM, while categorical data was presented as percentages. Differences between means of two groups were compared using student's *t* test. A P-value less than 0.05 were considered as statistically significant.

Results

Age group and gender wise categorization of hypertensive patients

During the hospital stay of 150 cases out of 75 male patients 25 (33.3%) belong to 70 and above age groups followed by 16 (21.3%)



under 60 years to 69 years age group, 15 (20%) under 50-59 years age group, 10 (13.3%) under 40 years to 49 years age group and 9 (12%) under 30 years to 39 years age group. Out of 75 female patients 30 (40%) belong to 70 and above age groups followed by 24 (32%) under 60 years to 69 years age group, 12 (16%) under 50 years to 59 years age group, 5 (6.6%) under 40 years to 49 years age group & 4 (5.3%) under 30 years to 39 years age group [Table 1].

Class of anti hypertensive drugs prescribed for hypertensive patients

Eight different classes of antihypertensive drugs prescribed in 150 in-patients were assessed during study. During this period diuretics were mostly prescribed 68 (30.63%) for hypertensive patients followed by calcium channel blockers 58 (26.13%), β blockers 44 (19.82%), angiotensin receptor blockers 25 (11.26%), ACE inhibitors 24 (10.81%). α blockers, α + β blockers and centrally acting drugs prescribed were very less i.e., 1 prescription from each class (0.45%) [Figure 1].

Pattern of drug regimen prescribed for hypertensive patients

In this study Table 2 and Figure 2 reveals that the mono drug regimen were prescribed more 68 (46.9%) in hypertensive patients followed by two drug regimen 57 (39.31%) and three drug regimen were 15 (10.34%) prescriptions, but ≥ 4 drug combination were very less i.e., 5 (3.45%) prescriptions.

Assessment of rationality of antihypertensive drugs prescribed for patients

Rationality was assessed using JNC 7 and IGH guidelines out of 150 patients 136 (90.67%) patients were prescribed antihypertensive drugs rationally and remaining 14 (9.33%) patients were prescribed antihypertensive drugs irrationally in this 14 patient's 8 patients

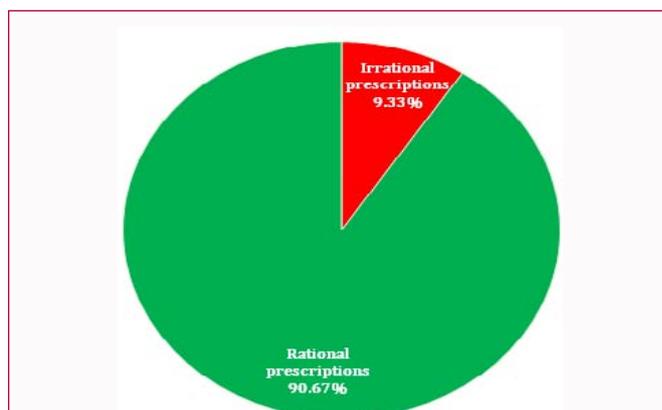


Figure 3: Assessment of rationality of antihypertensive drugs prescribed for patients in a tertiary care hospital.

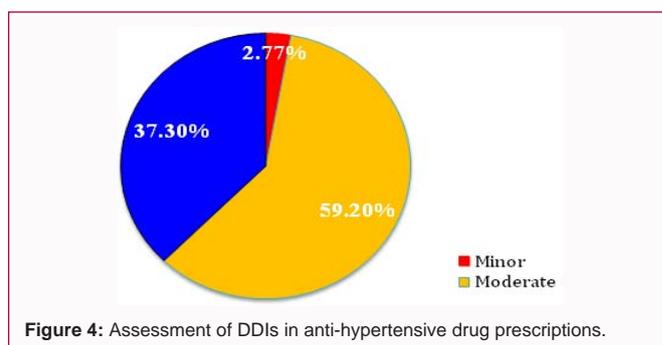


Figure 4: Assessment of DDIs in anti-hypertensive drug prescriptions.

were prescribed irrationally according to JNC 7, and 6 patients were prescribed irrationally according to both JNC 7 and IGH [Figure 3].

Study of efficacy of antihypertensive agents on hypertension patients

During the hospital stay various types of antihypertensive drugs were prescribed to patients to reduce SBP & DBP. Out of these Amlodipine significantly reduced DBP ($P=0.0138$), Furosemide reduced SBP significantly ($P=0.0236$) and a significant reduction was found in SBP ($P=0.0034$) on discharge when compared with respective BP on admission.

In combination therapy Amlodipine+Atenolol showed significant reduction in SBP ($P<0.0001$) and DBP ($P=0.0051$) on discharge when compared with BP on admission respectively and other combinations like Amlodipine+Hydrochlorothiazide show reduced SBP ($P=0.0317$) significantly on discharge as compared with SBP on admission [Table 3].

Comparison of efficacy between mono and combination therapy

Here 4 drugs and their 2 combinations were chosen to compare the efficacy of drugs. Table 3a reveals that mean reduction in SBP increased significantly ($P=0.018$) in the prescribed patients. Mean reduction in SBP with Amlodipine and Atenolol were found to be more efficient than in patients treated with Amlodipine alone. Likewise Table 3b reveals mean reduction in SBP increased significantly ($P=0.451$) in Furosemide and Losartan received patients as compared with Furosemide alone treated and there is significant increase in mean reduction in DBP in patients treated with combination of Furosemide and Losartan as compared with Furosemide alone. Other combinations do not show any significant differences [Table 4].

Table 4: Comparison of efficacy between mono and combination therapies of hypertension.

| Blood Pressure | Mono | Combination 1 | P-value | t-value | Combiantion 2 | P- value | t- value |
|-----------------------|-------------------|------------------------------|---------------------|---------|---------------------------------------|----------------------|----------|
| | Amlodipine | Amlodipine+Atenolol | | | Amlodipine+Hydrochlorothiazide | | |
| Mean reduction in SBP | 20.68 ± 5.013 | 42.62 ± 7.674 | 0.0180 [*] | 2.503 | 32.13 ± 10.08 | 0.267 | 1.135 |
| Mean Reduction in DBP | 10.26 ± 3.963 | 9.923 ± 2.802 | 0.9496 | 0.06372 | 6.750 ± 5.939 | 0.631 | 0.4862 |
| | Furosemide | Furosemide+amlodipine | | | Furosemide+losartan | | |
| Mean reduction in SBP | 18.29 ± 5.535 | 20.0 ± 3.0 | 0.9227 | 0.09881 | 55.0 ± 25.0 | 0.0451 [*] | 2.2 |
| Mean reduction in DBP | 3.143 ± 3.036 | 6.0 ± 4.0 | 0.7374 | 0.342 | 42.50 ± 27.50 | 0.0039 ^{**} | 3.449 |
| | Ramipril | Ramipril+Amlodipine | | | Furosemide+Ramipril | | |
| Mean Reduction in SBP | 7.286 ± 12.08 | 15.0 ± 55.0 | 0.8242 | 0.2306 | 45.0 ± 25.98 | 0.1646 | 1.513 |
| Mean reduction in DBP | 3.143 ± 3.036 | 6.0 ± 4.0 | 0.7374 | 0.342 | 42.50 ± 27.50 | 0.0039 ^{**} | 3.449 |
| | Metoprolol | Metoprolol+furosemide | | | Metoprolol+ramipril | | |
| Mean Reduction in SBP | 26.00 ± 8.255 | 8.0 ± 18.0 | 0.3633 | 0.9639 | 23.50 ± 17.95 | 0.8858 | 0.1473 |
| Mean Reduction in DBP | 6.50 ± 5.369 | 0.0 ± 1.0 | 0.5788 | 0.5785 | 9.0 ± 12.29 | 0.8299 | 0.2206 |

All the values are expressed as mean ± SEM, *P<0.05 [Student t test] as compared to blood pressure of patients treated with mono therapy. Reduction in SBP=SBP on admission - SBP on discharge and Reduction in DBP=DBP on admission-DBP on discharge.

Assessment of DDIs in anti hypertensive prescriptions

During the study a total of 252 DDI's were found.

Out of these 94 (34.30%) were major, 151 (59.92%) were moderate and 7 (2.77%) were minor drug interactions. Out of 94 major DDI's 36 were of Aspirin+Clopidogrel and 5 DDI's of Albuterol and Metoprolol. In 151 moderate interactions 23 DDI's were of Atorvastatin and Clopidogrel followed by 12 DDI's between Ampicillin+Atenolol [Figure 4].

Discussion

A prescription based study is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physicians and dispensing practice of pharmacists [7]. With increasing economic growth rate, India is not only facing the epidemic coronary artery diseases but also of obesity, diabetes mellitus and hypertension. Prevalence of hypertension is dramatically increasing in India [8]. Age probably represents an accumulation of environmental influences and body stresses. The prevalence of HTN in India is highest in age group 50 years to 59 years in males & 60 years to 64 years in females in urban areas where as in rural areas an age related increase is seen in both the sexes in the age group 60 years to 64 years [9]. This is in occurrence with our study where maximum numbers of patients were found in age group 50 years to 70 years. This represents that increasing in age is a risk factor to develop HTN in India.

In our study most prescribed class of antihypertensive drugs were diuretics followed by calcium channel blockers and β blockers. A similar study in Nigeria had reported comparable results [10]. Also diuretics constituted the most frequently prescribed drug class in other studies and according to JNC VII guidelines diuretics are the choices of drugs as first line for hypertension [11].

In our study it was observed that 53.1% of prescriptions containing combination therapy which was lower than recommendations and observations of several other studies demonstrated that the combination therapy was necessary in at least 70% of the study population prescriptions to attain optimal blood pressure control [12-14]. Mono drug therapy was recommended in 46.9% prescriptions in our hospital. Higher probability of 53.1% DDIs, due to combination drugs and Pharmacoeconomic considerations might be the reason which can be attributed to lesser inclination of physicians to go for combination therapy in our hospital. For comparison 73% of hypertensive patients were prescribed a combination of antihypertensive in a survey conducted in Nigeria [15]. In an Indian study 60% and 40% of patients received combination & mono therapy respectively [16]. On contrary, mono therapy was preferred for 51% of the patients in a Hong Kong study [17].

In our study rationality was assessed using Joint National Committee- VII and Indian Guidelines of Hypertension. These guidelines are intended to provide practitioners with a standard approach to the rational, safe, and effective use of antihypertensives for prevention of hypertension based on currently available clinical evidence and emerging issues. Rational recommendations of antihypertensives were very high in our study that is 136 (90.67%) rational prescriptions and 14 (9.33%) irrational prescriptions. Out of 14, 8 were irrational according to JNC-7 and 6 were irrational according to both JNC 7 and IGH guidelines. Finally this assessment indicates that in our hospital physicians were well adhered to both JNC 7 and IGH guidelines which was a good sign to control hypertension for patients visiting our hospital.

While studying efficacy of mono and combination therapy in our study it was observed that combination therapy showed significant raise in mean reduction in SBP and DBP. This once again proves

combination therapy has good control on hypertension which has been already proved worldwide. In contrast some of these combination therapies failed to show significant reduction in BP.

As we discussed above more than 50% of prescriptions were combination therapy, thus there was more possibility of DDIs and also various studies have shown that potential drug - drug interactions are frequent when patients receives multiple prescriptions [18]. In present study we found 252 DDIs in 150 prescriptions. A similar study was done in hospital of Jimma where they found 297 DDIs out of 332 prescriptions [19]. These potential DDIs can be reduced in presence of clinical pharmacists which was already proved in a study conducted in Thailand [20].

Finally we concluded that with time, there happened to be change in the treatment strategies and there by the prescription pattern. Our results showed that the choice of anti-hypertensive drugs reasonably comply with the JNC 7 and IGH guidelines on the management of hypertension, which confirms a fairly good degree of compliance by clinicians with JNC 7 and IGH guidelines. This study concludes the preferred use of diuretics, calcium channel blockers and β blockers as 1st, 2nd and 3rd choice of drugs for hypertension. However there is a need for improved patient education on medication adherence and greater attention by clinicians to issues of life style modifications, so as to improve BP control rate in this hospital.

Acknowledgements

We are thankful to Principal and Dean, S N Medical College and HSK Hospital and Research centre, Bagalkot, Karnataka, India, for providing necessary facilities and support during the course of this study.

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